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(54) Title: COMPOSITIONS AND METHODS FOR IN VIVO GENERATION OF CAR EXPRESSING CELLS

(57) Abstract: Aspects of this disclosure relate generally to the use of biomaterials for the in vivo generation of CAR expressing cells. In some embodiments, the biomaterials comprise one or more of a cell recruitment composition, a viral vector, and/or a cell activation agent.

WO 2022/040586 A3

COMPOSITIONS AND METHODS FOR IN VIVO GENERATION OF CAR EXPRESSING CELLS

RELATED APPLICATIONS

This application claims priority to U.S. Provisional Application 63/068,876 filed on August 21, 2020, and U.S. Provisional Application 63/154,609 filed on February 26, 2021, the entire contents of which are hereby incorporated by reference.

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on August 20, 2021, is named N2067-7176WO_SL.txt and is 987,095 bytes in size.

FIELD OF THE INVENTION

Aspects of this disclosure relate generally to the use of biomaterials for the in vivo generation of CAR expressing cells. In some embodiments, the biomaterials is comprised in a composition that further comprises one or more of a cell recruitment composition, a viral vector, and/or a cell activation agent.

BACKGROUND OF THE INVENTION

T cell adoptive transfer protocols show potential in a number of therapeutic applications, such as cancer, where CAR T cell therapies have recently been approved for the treatment of B cell malignancies. Current methodologies of CAR-T cell manufacture are performed ex vivo: extracting cells from a subject, engineering them to express a chimeric antigen receptor (CAR), and then reintroducing them into a subject for treatment of a disease, disorder, or condition, such as cancer. There remains a need in the art for efficient manufacturing of CAR expressing cells, including but not limited to, those which allow for site-specific delivery and/or in vivo production.

SUMMARY OF THE INVENTION

In some aspects, the disclosure features is a first composition comprising a biomaterial and a cell recruitment factor; and a second composition comprising a viral vector. In some

aspects, the disclosure features is a first composition comprising a biomaterial and a molecule (e.g., VEGF-C, IL-2, IL-7, IL-15 (e.g., hetIL-15 (IL15/sIL-15Ra)), GM-CSF, CXCL12, CXC3L1, CCL19, CCL21, CXCL10, or CXCL11); and a second composition comprising a viral vector.

In some aspects, the disclosure features a first composition comprising a biomaterial and a cell recruitment factor, wherein the biomaterial comprises a hydrogel, e.g., a cryogel, e.g., an alginate cryogel, and wherein the cell recruitment factor comprises an amino acid sequence according to SEQ ID NO: 741, or an amino acid sequence with at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto, provided that the amino acid at position 26 of SEQ ID NO: 741 is not Cysteine (C), optionally wherein the amino acid at position 26 of SEQ ID NO: 741 is Alanine (A).

In some aspects, the disclosure features a second composition comprising a mesoporous silica particle; a viral vector; and a cell activation agent.

In some aspects, the disclosure features a method of transducing cells of a subject in vivo or treating a disease, disorder, or condition in a subject. The method comprises: administering a biomaterial and a cell recruitment factor to a site (e.g., high subcutaneous space or subcutaneous space adjacent to dermis) in the subject, and administering a viral vector or a nucleic acid comprising a transgene to the subject; thereby transducing cells of the subject with the transgene. In some aspects, the disclosure features a method of transducing cells of a subject in vivo or treating a disease, disorder, or condition in a subject. The method comprises: administering a biomaterial and a molecule (e.g., VEGF-C, IL-2, IL-7, IL-15 (e.g., hetIL-15 (IL15/sIL-15Ra)), GM-CSF, CXCL12, CXC3L1, CCL19, CCL21, CXCL10, or CXCL11) to a site (e.g., high subcutaneous space or subcutaneous space adjacent to dermis) in the subject, and administering a viral vector or a nucleic acid comprising a transgene to the subject; thereby transducing cells of the subject with the transgene.

In some embodiments, the biomaterial and the cell recruitment factor are comprised in a first composition, and the viral vector or nucleic acid is comprised in a second composition. In some embodiments, the biomaterial and the molecule (e.g., VEGF-C, IL-2, IL-7, IL-15 (e.g.,

hetIL-15 (IL15/sIL-15Ra)), GM-CSF, CXCL12, CXC3L1, CCL19, CCL21, CXCL10, or CXCL11) are comprised in a first composition, and the viral vector or nucleic acid is comprised in a second composition.

In some aspects, the disclosure features a method of transducing cells of a subject in vivo or treating a disease, disorder, or condition in a subject, the method comprising: administering a viral vector or a nucleic acid comprising a transgene to a site in the subject, wherein the subject has previously been administered a biomaterial and a cell recruitment factor in an amount sufficient to induce lymphangiogenesis and/or recruitment of T cells to the site in the subject; thereby transducing the cells. In some aspects, the disclosure features a method of transducing cells of a subject in vivo or treating a disease, disorder, or condition in a subject, the method comprising: administering a viral vector or a nucleic acid comprising a transgene to a site in the subject, wherein the subject has previously been administered a biomaterial and a molecule (e.g., VEGF-C, IL-2, IL-7, IL-15 (e.g., hetIL-15 (IL15/sIL-15Ra)), GM-CSF, CXCL12, CXC3L1, CCL19, CCL21, CXCL10, or CXCL11) in an amount sufficient to induce lymphangiogenesis and/or recruitment of T cells to the site in the subject; thereby transducing the cells.

In any of the aspects herein, e.g., the compositions and methods above, any of the embodiments herein (e.g., below) may apply.

In some embodiments, the biomaterial comprises (i) comprises a hydrogel; (ii) comprises a cryogel; (iii) comprises a gelatin, hyaluronic acid, collagen, alginate, laminin, chitosan, silk fibroin, agarose, poly(ethylene glycol), poly-vinyl alcohol, and/or hydroxyethyl methylacrylate; (iv) comprises alginate hydrogel, optionally wherein the alginate hydrogel further comprises norbornene and/or tetrazine, optionally wherein the norbornene and/or tetrazine is covalently associated with, e.g., chemically linked to, or non-covalently associated with, e.g., adsorbed on, the alginate; and/or (v) comprises pores between about 10 μm to about 300 μm, e.g., between about 50 μm to about 300 μm, in diameter, or no pores; and/or (vi) is chemically crosslinked. In some embodiments, the first composition comprising the biomaterial further comprises laponite, optionally wherein the laponite is present at a concentration of about 0.15 mg/mL to about 0.35 mg/mL, e.g., about 0.25 mg/mL. In some embodiments, the biomaterial further comprises

laponite, optionally wherein the laponite is present at a concentration of about 0.15 mg/mL to about 0.35 mg/mL, e.g., about 0.25 mg/mL.

In some embodiments, the cell recruitment factor is: (i) noncovalently associated with, e.g., adsorbed on, the biomaterial; or (ii) covalently associated with, e.g., conjugated to, the biomaterial. In some embodiments, the cell recruitment factor: (i) induces lymphangiogenesis; (ii) induce growth of lymphatic endothelial cells; and/or (ii) recruits immune cells, optionally wherein the immune cells comprise T-cells and/or NK-cells.

In some embodiments, induction of lymphangiogenesis: (i) comprises an increase in the level of lymphatic endothelial cells (LECs) (e.g., CD45-CD31+PDPN+ cells), optionally wherein the level of LECs is increased by at least 10%, 20%, 30%, 40%, 50%, 60, 70%, 75%, 80%, 85%, 90%, 95%, 100%, or 2 00% as compared to a reference level (e.g., the level of LECs at a site in a subject prior to injection of the plurality of compositions or the first composition), when measured by an assay, e.g., a flow cytometry assay, e.g., as described in Example H or I; and/or (ii) results in at least 50 LECs (e.g., at least 75, 100, 125, 150, 200, 225, or 250 LECs) per milligram of tissue when measured by an assay, e.g., a flow cytometry assay, e.g., as described in Example H or I.

In some embodiments, the cell recruitment factor recruits T cells, optionally wherein the T cells comprise naïve T cells (e.g., CD45RA+CD62L+ T cells or CD45RA+CD62L+CCR7+CD27+CD95+ T cells). In some embodiments, recruitment of T cells comprises an increase in the level of T cells, optionally wherein the level of T cells is increased by at least 10%, 20%, 30%, 40%, 50%, 60, 70%, 75%, 80%, 85%, 90%, 95%, 100%, 200%, or 300% as compared to a reference level (e.g., the level of T cells at a site in a subject prior to injection of the plurality of compositions or the first composition), when measured by an assay, e.g., a flow cytometry assay, e.g., as described in Example H or I.

In some embodiments, the cell recruitment factor is chosen from VEGF-C, IL-2, IL-7, IL-15 (e.g., hetIL-15 (IL15/sIL-15Ra)), GM-CSF, CXCL12, CXC3L1, CCL19, CCL21, CXCL10, or CXCL11. In some embodiments, the cell recruitment factor comprises VEGF-C or a functional variant thereof; IL-15 (e.g., hetIL-15 (IL15/sIL-15Ra)) or a functional variant thereof; IL-7 or a functional variant thereof; or a combination thereof.

In some embodiments, the cell recruitment factor comprises VEGF-C, optionally wherein the VEGF-C: (i) comprises a mature VEGF-C peptide, optionally the minor or major mature

form or a mutated variant thereof; (ii) is a monomer or dimer; and/or (iii) is present in an effective amount, optionally, in an amount of less than or about 1 mg, less than or about 10 mg, greater than or about 10 µg, greater than or about 1 µg, between about 1 µg and 1 mg, between about 10 µg and 1 mg, between about 1 µg and 10 mg, or between about 10 µg and 10 mg.

In some embodiments, the VEGF-C comprises: (i) an amino acid sequence of any one of the sequences provided in Table 18 or a sequence with at least 95% sequence identity thereto, optionally wherein the sequence comprises or does not comprise a linker (e.g., a glycine-serine linker) and/or a his tag; and/or (ii) the amino acid substitution of C137A, numbered according to SEQ ID NO: 725.

In some embodiments, the cell recruitment factor comprises: (i) an amino acid sequence according to SEQ ID NO: 741, or an amino acid sequence with at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto, provided that the amino acid at position 26 of SEQ ID NO: 741 is not Cysteine (C), optionally wherein the amino acid at position 26 of SEQ ID NO: 741 is Alanine (A); (ii) the amino acid sequence according to SEQ ID NO: 743 or a sequence an amino acid sequence with at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto; (iii) the amino acid sequence according to SEQ ID NO: 740 or an amino acid sequence with at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto; (iv) the amino acid sequence according to SEQ ID NO: 736, or an amino acid sequence with at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto; (v) a linker, e.g., wherein the linker has a sequence of Gly-Ser, wherein optionally the linker is C-terminal of SEQ ID NO: 743 or a sequence having at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto; (vi) the amino acid sequence according to SEQ ID NO: 735, or an amino acid sequence with at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto; (vii) the amino acid sequence according to SEQ ID NO: 734, or an amino acid sequence with at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto; and/or (viii) the amino acid sequence according to SEQ ID NO: 733, or an amino acid sequence with at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

In some embodiments, any of the compositions, e.g., any of the first compositions, described herein further comprises IL-15 (e.g., hetIL-15 (IL15/sIL-15Ra)) or a functional variant thereof. In some embodiments, any of the compositions, e.g., any of the first compositions, described herein further comprises IL-7 or a functional variant thereof. In some embodiments, any of the compositions, e.g., any of the first compositions, described herein further comprises

IL-15 (e.g., hetIL-15 (IL15/sIL-15Ra)) or a functional variant thereof and IL-7 or a functional variant thereof.

In some embodiments, any of the methods described herein further comprises administration of IL-15 (e.g., hetIL-15 (IL15/sIL-15Ra)) or a functional variant thereof. In some embodiments, any of the methods described herein further comprises administration of IL-7 or a functional variant thereof. In some embodiments, any of the methods described herein further comprises administration IL-15 (e.g., hetIL-15 (IL15/sIL-15Ra)) and a functional variant thereof or IL-7 or a functional variant thereof.

In some embodiments, the second composition further comprises a particle. In some embodiments, the particle is a mesoporous particle, a silica particle and/or a mesoporous silica particle, optionally wherein the mesoporous silica particle is a mesoporous silica rod. In some embodiments, the mesoporous silica particle comprises a surface modification, optionally wherein the surface modification comprises: (a) a –OH (hydroxyl), amine, carboxylic acid, phosphonate, halide, azide, alkyne, epoxide, sulfhydryl, polyethyleneimine, a hydrophobic moiety, or salts thereof, optionally using a C1 to C20 alkyl or (O(CH2 CH2)1-25 linker; (b) a primary, secondary, tertiary, or quaternary amine; and/or (c) a polyethyleneimine having an average molecular weight of about 1000 to 20,000 Da, about 1,200 to 15,000 Da, about 1,500 to 12,000 Da, about 2,000 Da, about 3,000 Da, about 4,000 Da, about 5,000 Da, about 6,000 Da, about 7,000 Da, about 8,000 Da, about 9,000 Da, or about 10,000 Da, as measured by gel permeation chromatography (GPC). In some embodiments, the mesoporous silica particle (i) is a trimethylammonium functionalized mesoporous silica particle, e.g., a N,N,N-trimethylpropan-1-ammonium functionalized mesoporous silica particle; (iii) comprises a plurality of pores, optionally wherein the pores are between 2-50 nm in diameter; and/or (iv) comprises a surface area of at least about 100 m2/g.

In some embodiments, (i) the viral vector is noncovalently, e.g., electrostatically, or covalently associated with the mesoporous silica particle; and/or (ii) the cell activation agent is noncovalently or covalently associated with the mesoporous silica particle. In some embodiments, the viral vector comprises: (i) a lentivirus, retrovirus, adenovirus, adeno-associated virus, or herpes virus; and/or (ii) an expression vector comprising a recombinant polynucleotide comprising an expression control sequence operatively linked to a nucleotide sequence to be expressed. In some embodiments, the nucleotide sequence encodes: a chimeric

antigen receptor (CAR), an engineered TCR, a cytokine, a chemokine, an shRNA, or a polypeptide engineered to target a tumor antigen.

In some embodiments, the tumor antigen is selected from the group consisting of: TSHR, CD19, CD123, CD22, CD30, CD171, CS-1, CLL-1, CD33, EGFRvIII , GD2, GD3, BCMA, Tn Ag, PSMA, ROR1, FLT3, FAP, TAG72, CD38, CD44v6, CEA, EPCAM, B7H3, KIT, IL-13Ra2, Mesothelin, IL-11Ra, PSCA, PRSS21, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, CD20, Folate receptor alpha, ERBB2 (Her2/neu), MUC1, EGFR, NCAM, Prostase, PAP, ELF2M, Ephrin B2, IGF-I receptor, CAIX, LMP2, gp100, bcr-abl, tyrosinase, EphA2, Fucosyl GM1, sLe, GM3, TGS5, HMWMAA, o-acetyl-GD2, Folate receptor beta, TEM1/CD248, TEM7R, CLDN6, GPRC5D, CXORF61, CD97, CD179a, ALK, Polysialic acid, PLAC1, GloboH, NY-BR-1, UPK2, HAVCR1, ADRB3, PANX3, GPR20, LY6K, OR51E2, TARP, WT1, NY-ESO-1, LAGE-1a, MAGE-A1, legumain, HPV E6,E7, MAGE A1, ETV6-AML, sperm protein 17, XAGE1, Tie 2, MAD-CT-1, MAD-CT-2, Fos-related antigen 1, p53, p53 mutant, prostein, survivin and telomerase, PCTA-1/Galectin 8, MelanA/MART1, Ras mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, TRP-2, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP-4, SSX2, RAGE-1, human telomerase reverse transcriptase, RU1, RU2, intestinal carboxyl esterase, mut hsp70-2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3, FCRL5, IGLL1, and any combination thereof.

In some embodiments, the viral vector encodes a CAR that comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region, and a signaling domain, wherein: (i) the antigen binding domain binds an antigen selected from the group consisting of CD19, CD123, CD22, CD20, EGFRvIII , BCMA, Mesothelin, CD33, CLL-1, and any combination thereof; (ii) the transmembrane domain comprises a CD8 hinge; (iii) the costimulatory signaling region is selected from a 4-1BB or CD28 costimulatory signaling domain; and/or (iv) the signaling domain comprises a CD3 zeta signaling domain.

In some embodiments, the second composition further comprises a cell activation agent. In some embodiments, the cell activation agent comprises an agent that stimulates CD3/TCR complex and/or an agent that stimulates a costimulatory molecule and/or growth factor receptor. In some embodiments, the cell activation agent comprises a multispecific binding molecule

comprising: (A) an anti-CD3 binding domain, and (B) a costimulatory molecule binding domain (e.g., an anti-CD2 binding domain or an anti-CD28 binding domain).

In some embodiments, the anti-CD3 binding domain, e.g., an anti-CD3 scFv, is situated N-terminal of the costimulatory molecule binding domain, e.g., an anti-CD2 Fab or an anti-CD28 Fab; or the anti-CD3 binding domain, e.g., an anti-CD3 scFv, is situated C-terminal of the costimulatory molecule binding domain, e.g., an anti-CD2 Fab or an anti-CD28 Fab, optionally wherein: an Fc region is situated between the anti-CD3 binding domain and the costimulatory molecule binding domain; or the multispecific binding molecule comprises a CH2, and the anti-CD3 binding domain is situated N-terminal of the CH2.

In some embodiments of the second compositions and methods herein, the multispecific binding molecule comprises: (i) a first polypeptide comprising from N-terminal to C-terminal: VH of the anti-CD3 binding domain, VL of the anti-CD3 binding domain, VH of the costimulatory molecule binding domain, CH1, CH2, and CH3; and (ii) a second polypeptide comprising from N-terminal to C-terminal: VL of the costimulatory molecule binding domain and CL. In some embodiments, the multispecific binding molecule comprises: (i) a first polypeptide comprising from N-terminal to C-terminal: VH of the costimulatory molecule binding domain, CH1, CH2, CH3, VH of the anti-CD3 binding domain, and VL of the anti-CD3 binding domain; and (ii) a second polypeptide comprising from N-terminal to C-terminal: VL of the costimulatory molecule binding domain and CL. In some embodiments, the multispecific binding molecule comprises: (i) a first polypeptide comprising from N-terminal to C-terminal: VH of the costimulatory molecule binding domain, CH1, VH of the anti-CD3 binding domain, VL of the anti-CD3 binding domain, CH2, and CH3; and (ii) a second polypeptide comprising from N-terminal to C-terminal: VL of the costimulatory molecule binding domain and CL. In some embodiments, the anti-CD3 binding domain comprises an scFv and the costimulatory molecule binding domain is part of a Fab fragment.

In some embodiments, the cell activation agent comprises the amino acid sequence of any heavy chain provided in Table 20, or an amino acid sequence with at least 95% sequence identity thereto; and/or the amino acid sequence of any light chain provided in Table 20, or an amino acid sequence with at least 95% sequence identity thereto. In some embodiments, the cell activation agent is conjugated to or adsorbed on the particle, e.g., mesoporous silica particle.

In some embodiments, the multispecific binding molecule comprises an Fc region comprising: (i) a L234A, L235A, S267K, and P329A mutation (LALASKPA), numbered according to the Eu numbering system; (ii) a L234A, L235A, and P329G mutation (LALAPG), numbered according to the Eu numbering system; (iii) a G237A, D265A, P329A, and S267K mutation (GADAPASK), numbered according to the Eu numbering system; (iv) a L234A, L235A, and G237A mutation (LALAGA), numbered according to the Eu numbering system; (v) a D265A, P329A, and S267K mutation (DAPASK), numbered according to the Eu numbering system; (vi) a G237A, D265A, and P329A mutation (GADAPA), numbered according to the Eu numbering system; (vii) a L234A, L235A, and P329A mutation (LALAPA), numbered according to the Eu numbering system; or (viii) an amino acid sequence of any of the Fc regions in Table 20 or an amino acid sequence having at least 95% identity thereto.

In some embodiments, the multispecific binding molecule comprises: (i) a heavy chain comprising the amino acid sequence of any of SEQ ID NOs: 726, 1416, 893, 1417, or 895, or an amino acid sequence having at least 95% sequence identity thereto; and/or (ii) a light chain comprising the amino acid sequence of any of SEQ ID NOs: 728, 730, 892, or 894, or an amino acid sequence having at least 95% sequence identity thereto. In some embodiments, the multispecific binding molecule comprises: (i) a heavy chain comprising the amino acid sequence of SEQ ID NO: 726 or an amino acid sequence having at least 95% sequence identity thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 728, or an amino acid sequence having at least 95% sequence identity thereto; (ii) a heavy chain comprising the amino acid sequence of SEQ ID NO: 726 or an amino acid sequence having at least 95% sequence identity thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 730, or an amino acid sequence having at least 95% sequence identity thereto; (iii) a heavy chain comprising the amino acid sequence of SEQ ID NO: 1416 or an amino acid sequence having at least 95% sequence identity thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 728, or an amino acid sequence having at least 95% sequence identity thereto; (iv) a heavy chain comprising the amino acid sequence of SEQ ID NO: 1416 or an amino acid sequence having at least 95% sequence identity thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 730, or an amino acid sequence having at least 95% sequence identity thereto; (v) a heavy chain comprising the amino acid sequence of SEQ ID NO: 893 or an amino acid sequence having at least 95% sequence identity thereto, and a light chain comprising

the amino acid sequence of SEQ ID NO: 892, or an amino acid sequence having at least 95% sequence identity thereto; (vi) a heavy chain comprising the amino acid sequence of SEQ ID NO: 1417 or an amino acid sequence having at least 95% sequence identity thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 892, or an amino acid sequence having at least 95% sequence identity thereto; or (vii) a heavy chain comprising the amino acid sequence of SEQ ID NO: 895 or an amino acid sequence having at least 95% sequence identity thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 894, or an amino acid sequence having at least 95% sequence identity thereto.

In some embodiments, the second composition further comprises a first population of particles and a second population of particles, e.g., a first population of mesoporous silica particles and a second population of mesoporous silica particles, wherein the first population comprises the viral vector and the second population comprises a cell activation agent, e.g., wherein the viral vector is noncovalently associated with a particle of the first population and the cell activation agent is noncovalently associated with a particle of the second population.

In some embodiments, the composition, e.g., the first or second composition, is suitable for injectable use.

In some embodiments, the composition, e.g., the first or second composition, described herein further comprises a Tet2 inhibitor and/or a ZBTB32 inhibitor. In some embodiments, the Tet2 inhibitor comprises: (1) a gene editing system targeted to one or more sites within the gene encoding Tet2, or its corresponding regulatory elements; (2) a nucleic acid (e.g., an siRNA or shRNA) that inhibits expression of Tet2; (3) a protein (e.g., a dominant negative, e.g., catalytically inactive) Tet2, or a binding partner of Tet2 (e.g., a dominant negative binding partner of Tet2); (4) a small molecule that inhibits expression and/or function of Tet2; (5) a nucleic acid encoding any of (1)-(3); or (6) any combination of (1) –(5). In some embodiments, the ZBTB32 gene or one or more components thereof; (2) a nucleic acid encoding one or more components of the gene editing system; or (3) a combination of (1) and (2). In an embodiment, the ZBTB32 inhibitor comprises: (1) a gene editing system targeting the ZBTB32 gene or one or more components thereof. In an embodiment, the ZBTB32 inhibitor comprises (2) a nucleic acid encoding one or more components of the gene editing system. In an embodiment, the ZBTB32 inhibitor comprises a combination of (1) and (2).

In some embodiments, the methods described herein further comprise administering to the subject: (i) a Tet2 inhibitor, optionally wherein the Tet2 inhibitor comprises: (1) a gene editing system targeted to one or more sites within the gene encoding Tet2, or its corresponding regulatory elements; (2) a nucleic acid (e.g., an siRNA or shRNA) that inhibits expression of Tet2; (3) a protein (e.g., a dominant negative, e.g., catalytically inactive) Tet2, or a binding partner of Tet2 (e.g., a dominant negative binding partner of Tet2); (4) a small molecule that inhibits expression and/or function of Tet2; (5) a nucleic acid encoding any of (1)-(3); or (6) any combination of (1) –(5); and/or (ii) a ZBTB32 inhibitor, optionally wherein the ZBTB32 inhibitor comprises: (1) a gene editing system targeting the ZBTB32 gene or one or more components thereof; (2) a nucleic acid encoding one or more components of the gene editing system; or (3) a combination of (1) and (2). In an embodiment, the ZBTB32 inhibitor comprises: (1) a gene editing system targeting the ZBTB32 gene or one or more components thereof. In an embodiment, the ZBTB32 inhibitor comprises (2) a nucleic acid encoding one or more components of the gene editing system. In an embodiment, the ZBTB32 inhibitor comprises a combination of (1) and (2)

In some embodiments, the first composition is administered prior to the administration of the second composition, optionally wherein: (i) the first composition is administered about 1-4 weeks, e.g., about 2 weeks, prior to the administration of the second composition; or (ii) the first composition is administered at least two weeks prior to the administration of the second composition.

In some embodiments, any of the methods described herein further comprises evaluating, e.g., measuring, lymphangiogenesis in a sample from the subject (e.g., a sample from or close to the site of administration), wherein lymphangiogenesis is measured after the administration of the first composition and/or prior to the administration of the second composition, optionally wherein measuring lymphangiogenesis comprises acquiring a value for the level and/or activity of lymphatic endothelial cells (LECs) (e.g., CD45-CD31+PDPN+ cells) in the sample.

In some embodiments, any of the methods described herein further comprises evaluating, e.g., measuring, the recruitment of T cells in a sample from the subject (e.g., a sample from or close to the site of administration), wherein the recruitment of T cells is measured after the administration of the first composition and/or prior to the administration of the second composition, optionally wherein measuring the recruitment of T cells comprises acquiring a

value for the level and/or activity of T cells (e.g., naïve T cells, e.g., CD45RA+CD62L+ T cells and/or CD45RA+CD62L+CCR7+CD27+CD95+ T cells) in the sample.

In some embodiments, the subject has or has been diagnosed with having a disease, disorder, or condition; and/or the subject is a human.

In some embodiments, the disease, disorder, or condition comprises: (i) a cancer; (ii) a hematological cancer, optionally wherein the hematological cancer comprises a leukemia or lymphoma; (iii) a hematological cancer chosen from chronic lymphocytic leukemia (CLL), mantle cell lymphoma (MCL), multiple myeloma, acute lymphoid leukemia (ALL), Hodgkin lymphoma, B-cell acute lymphoid leukemia (BALL), T-cell acute lymphoid leukemia (TALL), small lymphocytic leukemia (SLL), B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt lymphoma, diffuse large B cell lymphoma (DLBCL), DLBCL associated with chronic inflammation, chronic myeloid leukemia, myeloproliferative neoplasms, follicular lymphoma, pediatric follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma (extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue), Marginal zone lymphoma, myelodysplasia, myelodysplastic syndrome, non-Hodgkin lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, splenic marginal zone lymphoma, splenic lymphoma/leukemia, splenic diffuse red pulp small B-cell lymphoma, hairy cell leukemia-variant, lymphoplasmacytic lymphoma, a heavy chain disease, plasma cell myeloma, solitary plasmocytoma of bone, extraosseous plasmocytoma, nodal marginal zone lymphoma, pediatric nodal marginal zone lymphoma, primary cutaneous follicle center lymphoma, lymphomatoid granulomatosis, primary mediastinal (thymic) large B-cell lymphoma, intravascular large B-cell lymphoma, ALK+ large B-cell lymphoma, large B-cell lymphoma arising in HHV8-associated multicentric Castleman disease, primary effusion lymphoma, B-cell lymphoma, acute myeloid leukemia (AML), or unclassifiable lymphoma; (iv) a solid cancer; (v) a solid cancer chosen from: one or more of mesothelioma, malignant pleural mesothelioma, non-small cell lung cancer, small cell lung cancer, squamous cell lung cancer, large cell lung cancer, pancreatic cancer, pancreatic ductal adenocarcinoma, esophageal adenocarcinoma , breast cancer, glioblastoma, ovarian cancer, colorectal cancer, prostate cancer, cervical cancer, skin cancer, melanoma, renal cancer, liver cancer, brain cancer, thymoma, sarcoma, carcinoma, uterine cancer, kidney cancer, gastrointestinal cancer, urothelial cancer,

pharynx cancer, head and neck cancer, rectal cancer, esophagus cancer, or bladder cancer, or a metastasis thereof; or (iv) an autoimmune disease, an inflammatory disease, or a transplant. In some embodiments, the disease, disorder, or condition is an autoimmune disease, an inflammatory disease, or a transplant and the CAR expressed binds to a B cell antigen, e.g., CD 19, CD20, CD22, CD123, FcRn5, FcRn2, BCMA, CS-1 and CD138.

In some embodiments, the disease, disorder, or condition comprises a solid tumor. In some embodiments, when treating a solid tumor with a CAR-expressing cell manufactured using the methods described herein, the cell expresses two CARs, the first CAR binds to a B cell antigen and the second CAR binds to a solid tumor antigen. In some embodiments, when treating a solid tumor with a CAR-expressing cell manufactured using the methods described herein, the cell expresses a multispecific CAR that comprises a first binding domain that binds to a B cell antigen and a second binding domain that binds to a solid tumor antigen. Without wishing to be bound by theory, expressing a CAR that binds to a B cell antigen in such cells may help improve the proliferation and/or survival of the CAR-expressing cells. B cell antigens (e.g., CD19 on normal B cells) may improve the proliferation and/or survival of such CAR-expressing cells even when the level of the tumor antigen is low (e.g., when the number of tumor cells is low, or before the CAR-expressing cells manufactured using the methods described herein encounter solid tumor cells).

In some embodiments, the disease, disorder, or condition comprises a myeloid tumor. In some embodiments, when treating a myeloid tumor with a CAR-expressing cell manufactured using the methods described herein, the cell expresses two CARs, the first CAR binds to a B cell antigen and the second CAR binds to a myeloid tumor antigen. In some embodiments, when treating a myeloid tumor with a CAR-expressing cell manufactured using the methods described herein, the cell expresses a multispecific CAR that comprises a first binding domain that binds to a B cell antigen and a second binding domain that binds to a myeloid tumor antigen. Without wishing to be bound by theory, expressing a CAR that binds to a B cell antigen in such cells may help improve the proliferation and/or survival of the CAR-expressing cells. B cell antigens (e.g., CD19 on normal B cells) may improve the proliferation and/or survival of such CAR-expressing cells even when the level of the tumor antigen is low (e.g., when the number of tumor cells is low, or before the CAR-expressing cells manufactured using the methods described herein encounter myeloid tumor cells).

In some embodiments of the methods or second compositions described herein, the viral vector or the nucleic acid encodes:

(i) a first CAR that binds to a B cell antigen (e.g., CD19) and a second CAR that binds to (a) a solid tumor antigen (e.g., EGFRvIII), (b) a myeloid tumor antigen, or (c) an antigen of a hematological tumor not of B-cell lineage; or

(2) a CAR that comprises a first binding domain that binds to a B cell antigen (e.g., CD19) and a second binding domain that binds to (a) a solid tumor antigen (e.g., EGFRvIII), (b) a myeloid tumor antigen, or (c) an antigen of a hematological tumor not of B-cell lineage.

In some embodiments, the B cell antigen is CD5, CD10, CD19, CD20, CD21, CD22, CD23, CD24, CD25, CD27, CD30, CD34, CD37, CD38, CD40, CD53, CD69, CD72, CD73, CD74, CD75, CD77, CD79a, CD79b, CD80, CD81, CD82, CD83, CD84, CD85, CD86, CD123, CD135, CD138, CD179, CD269, Flt3, ROR1, BCMA, FcRn5, FcRn2, CS-1, CXCR4, 5, 7, IL-7/3R, IL7/4/3R, or IL4R. In some embodiments, the B cell antigen is CD19, CD20, CD22, CD123, FcRn5, FcRn2, BCMA, CS-1 or CD138.

In some embodiments, the solid tumor antigen is EGFRvIII, mesothelin, GD2, Tn Ag, PSMA, TAG72, CD44v6, CEA, EPCAM, KIT, IL-13Ra2, leguman , GD3, CD171, IL-11Ra, PSCA, MAD-CT-1, MAD-CT-2, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, folate receptor alpha, ERBBs (e.g., ERBB2), Her2/neu, MUC1, EGFR, NCAM, Ephrin B2, CAIX, LMP2, sLe, HMWMAA, o-acetyl-GD2, folate receptor beta, TEM1/CD248, TEM7R, FAP, Legumain, HPV E6 or E7, ML-IAP, CLDN6, TSHR, GPRC5D, ALK, Polysialic acid, Fos-related antigen, neutrophil elastase, TRP-2, CYP1B1, sperm protein 17, beta human chorionic gonadotropin, AFP, thyroglobulin, PLAC1, globoH, RAGE1, MN-CA IX, human telomerase reverse transcriptase, intestinal carboxyl esterase, mut hsp 70-2, NA-17, NY-BR-1, UPK2, HAVCR1, ADRB3, PANX3, GPR20, Ly6k, OR51E2, TARP, GFRα4, or a peptide of any of these antigens presented on MHC.

In some embodiments, also contemplated herein is a kit comprising a first composition described herein and a second composition described herein.

In some aspects, the disclosure features a method of treating a disease, disorder, or condition in a subject, the method comprising: administering a viral vector or a nucleic acid

comprising a transgene to a site in the subject that has been induced to undergo lymphangiogenesis at the site, thereby transducing the cells.

In some aspects, the disclosure features a method of preparing a subject to receive a viral vector encoding a chimeric antigen receptor (CAR), comprising administering to the subject a biomaterial and a cell recruitment factor, thereby preparing the subject to receive the viral vector encoding the CAR. In some aspects, the disclosure features a method of preparing a subject to receive a viral vector encoding a chimeric antigen receptor (CAR), comprising administering to the subject a biomaterial and a molecule (e.g., VEGF-C, IL-2, IL-7, IL-15 (e.g., hetIL-15 (IL15/sIL-15Ra)), GM-CSF, CXCL12, CXC3L1, CCL19, CCL21, CXCL10, or CXCL11), thereby preparing the subject to receive the viral vector encoding the CAR.

In some embodiments, preparing comprises induction of lymphangiogenesis and/or recruitment of T cells (e.g., e.g., CD45RA+CD62L+ T cells and/or CD45RA+CD62L+CCR7+CD27+CD95+ T cells). In some embodiments, the method further comprises administering the viral vector encoding the CAR, optionally wherein the viral vector is conjugated to a particle (e.g., a mesoporous silica particle that comprises or does not comprise a cell activation agent).

Also contemplated herein is a composition, comprising a biomaterial comprising a cell recruitment factor; a first population of mesoporous silica particles; a viral vector; and, optionally, a cell activation agent. Also contemplated herein is a composition, comprising a biomaterial and a cell recruitment factor; a first population of mesoporous silica particles; a viral vector; and, optionally, a cell activation agent.

In some embodiments, the biomaterial comprises a hydrogel, optionally a cryogel. In some embodiments, the cryogel comprises gelatin, hyaluronic acid, collagen, alginate, laminin, chitosan, silk fibroin, agarose, poly(ethylene glycol), poly-vinyl alcohol, and/or hydroxyethyl methylacrylate. In some embodiments, the composition comprising the cryogel further comprises laponite. In some embodiments, the cryogel comprises pores between about 10 to 300 μm in diameter, optionally between about 50 to 300 μm. In some embodiments, the cryogel is chemically cross-linked.

In some embodiments, the cell recruitment factor selectively recruits immune cells, optionally T-cells and/or NK-cells. In some embodiments, the cell recruitment factor is selected from the group consisting of CCL19, CXCL9, CXCL10, XCL1, IL-2, IL-7, CCL21, GM-CSF, CCL17, CCL22, CCL20, CCL27, IL-15, lymphotoxin alpha, lymphotoxin beta, VEGF-C, FLT3L, G-CSF, PDGF, S100A8/A9, CSF-1, CXCL8, CCL20, CCL17, CCR5, CCR6, CCL2, VEGF, Angiopoietin-2, PGE2, LTB4, CXC3L1, CCL19, CCL21, CXCL10, CXCL11, and/or CXCL12. In some embodiments, the VEGF-C is selected from the group consisting of immature VEGF-C peptide or mature VEGF-C peptide. In some embodiments, the mature VEGF-C peptide is the minor mature form or major mature form. In some embodiments, the mature VEGF-C peptide is a wild type minor mature form or a wild type major mature form. In some embodiments, the mature VEGF-C peptide is a modified minor mature form or a modified major mature form. In some embodiments, the mature VEGF-C peptide is a modified minor mature form comprising a mutation at Cysteine 137 (e.g., C137A) or a modified major mature form comprising a mutation at Cysteine 137 (e.g., C137A). In some embodiments, the mature VEGF-C peptide is a modified minor mature form comprising a C137A mutation or a modified major mature form comprising a C137A mutation. In some embodiments, the mature VEGF-C peptide is present as a dimer or monomer. In some embodiments, the VEGF-C is a dimer of the major mature form further comprising a C137A mutation in each monomer. In some embodiments, the VEGF-C is a dimer of the minor mature form further comprising a C137A mutation in each monomer. In some embodiments, the VEGF-C is selected from a sequence provided in **Table 18**, optionally, wherein the his tag is not included in the sequence. In some embodiments, the VEGF-C is present in an effective amount, optionally in an amount of less than or about 1 mg, less than or about 10 mg, greater than or about 10 μg, greater than or about 1 μg, between about 1 μg and 1 mg, between about 10 μg and 1 mg, between about 1 μg and 10 mg, or between about 10 μg and 10 mg.

In some embodiments, the first population of mesoporous silica particles are surface modified. In some embodiments, the surface modification on the first population of mesoporous silica particles is –OH (hydroxyl), amine, carboxylic acid, phosphonate, halide, azide, alkyne, epoxide, sulfhydryl, polyethyleneimine, a hydrophobic moiety, or salts thereof, optionally using a C_1 to C_{20} alkyl or $(-O(CH2-CH_2-)_{1-25}$ linker. In some embodiments, the surface modification on the first population of mesoporous silica particles is a primary, secondary, tertiary, or

quaternary amine. In some embodiments, the surface modification on the first population of mesoporous silica particles is a polyethyleneimine having an average molecular weight of about 1000 to 20,000 Da, about 1,200 to 15,000 Da, about 1,500 to 12,000 Da, about 2,000 Da, about 3,000 Da, about 4,000 Da, about 5,000 Da, about 6,000 Da, about 7,000 Da, about 8,000 Da, about 9,000 Da, or about 10,000 Da, as measured by gel permeation chromatography (GPC). In some embodiments, mesoporous silica particles comprise pores of between 2-50 nm in diameter. In some embodiments, the mesoporous silica particles have a surface area of at least about 100 m^2/g. In some embodiments, the composition is suitable for injectable use. In some embodiments, the mesoporous silica particles are in the form of mesoporous silica rods.

In some embodiments, the viral vector is conjugated to first population of the mesoporous silica particles. In some embodiments, the viral vector is electrostatically or covalently conjugated to the first population of mesoporous silica particles. In some embodiments, the viral vector is a retrovirus, adenovirus, adeno-associated virus, herpes virus, or lentivirus. In some embodiments, the viral vector comprises an expression vector comprising a recombinant polynucleotide comprising an expression control sequence operatively linked to a nucleotide sequence to be expressed. In some embodiments, the nucleotide sequence encodes a chimeric antigen receptor (CAR), an engineered TCR, one or more cytokines, one or more chemokines, an shRNA to block an inhibitory molecule, or wherein the nucleotide sequence comprises an mRNA to induce expression of a protein. In some embodiments, the nucleotide sequence encodes a polypeptide engineered to target a tumor antigen. In some embodiments, the polypeptide targets a tumor antigen selected from the group consisting of: TSHR, CD19, CD123, CD22, CD30, CD171, CS-1, CLL-1, CD33, EGFRvIII , GD2, GD3, BCMA, Tn Ag, PSMA, ROR1, FLT3, FAP, TAG72, CD38, CD44v6, CEA, EPCAM, B7H3, KIT, IL-13Ra2, Mesothelin, IL-11Ra, PSCA, PRSS21, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, CD20, Folate receptor alpha, ERBB2 (Her2/neu), MUC1, EGFR, NCAM, Prostase, PAP, ELF2M, Ephrin B2, IGF-I receptor, CAIX, LMP2, gp100, bcr-abl, tyrosinase, EphA2, Fucosyl GM1, sLe, GM3, TGS5, HMWMAA, o-acetyl-GD2, Folate receptor beta, TEM1/CD248, TEM7R, CLDN6, GPRC5D, CXORF61, CD97, CD179a, ALK, Polysialic acid, PLAC1, GloboH, NY-BR-1, UPK2, HAVCR1, ADRB3, PANX3, GPR20, LY6K, OR51E2, TARP, WT1, NY-ESO-1, LAGE-1a, MAGE-A1, legumain, HPV E6,E7, MAGE A1, ETV6-AML, sperm protein 17, XAGE1, Tie 2, MAD-CT-1, MAD-CT-2, Fos-related antigen 1, p53, p53 mutant, prostein,

survivin and telomerase, PCTA-1/Galectin 8, MelanA/MART1, Ras mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, TRP-2, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP-4, SSX2, RAGE-1, human telomerase reverse transcriptase, RU1, RU2, intestinal carboxyl esterase, mut hsp70-2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3, FCRL5, IGLL1, and any combination thereof. In some embodiments, the protein is a CAR that comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region, and a signaling domain. In some embodiments, the signaling domain is a CD3 zeta signaling domain. In some embodiments, the costimulatory signaling region is selected from 41BB (i.e., CD137), CD27, ICOS, and/or CD28.

In some embodiments, the cell activation agent is conjugated to or absorbed on the first population of mesoporous silica particles or a second population of mesoporous silica particles. In some embodiments, the cell activation agent is a T cell stimulating compound, an anti-idiotype antibody to a CAR antigen binding domain, and/or a tumor antigen. In some embodiments, the T-cell stimulating compound is IL-2, IL-15, anti-CD2 mAb, anti-CD3 mAb, anti-CD28 mAb, neo-antigen peptides, peptides from shared antigens such as TRP2, gp100, tumor cell lysate, CD19, CD20, CD22, ROR1, mesothelin, CD33/IL3Ra, c-Met, PSMA, Glycolipid F77, EGFRvIII, GD-2, NY-ESO-1 TCR, and/or MAGE A3 TCR. In some embodiments, the cell activation agent comprises a CD3/TCR complex and/or an agent that stimulates a costimulatory molecule and/or growth factor receptor, optionally, wherein the cell activation agent is a multispecific binding molecule comprising an agent that stimulates a CD3/TCR complex and an agent that stimulates a costimulatory molecule and/or growth factor receptor. In some embodiments, the cell activation is selected from a sequence provided in **Table 20**. In some embodiments, the cell activation agent is conjugated to the second population of mesoporous silica particles or to a lipid envelope on the surface of the second population of mesoporous silica particles. In some embodiments, the composition further comprises a cytokine. In some embodiments, the cytokine is conjugated to or adsorbed on the first or second population of mesoporous silica particles. In some embodiments, the cytokine is IL-1, IL-2, IL-4, IL-5, IL-7, IL-10, IL-12, IL-15, IL-17, IL-21, or transforming growth factor beta (TGF-β), or an agonist thereof, a mimetic thereof, a variant thereof, a functional fragment thereof, or a combination thereof.

Also contemplated herein is a method of transducing cells in vivo comprising administering a biomaterial comprising a cell recruitment factor; a first population of mesoporous silica particles; a viral vector; and, optionally, a cell activation agent to a subject. In some embodiments, the components are administered simultaneously or sequentially. In some embodiments, the biomaterial comprising the cell recruitment factor is administered first. In some embodiments, the first population of mesoporous silica rods, the viral vector, and, optionally, the cell activation agent is administered simultaneously and, optionally, after the biomaterial.

Also contemplated herein is a method of transducing cells in vivo comprising administering a biomaterial and a cell recruitment factor; a first population of mesoporous silica particles; a viral vector; and, optionally, a cell activation agent to a subject. In some embodiments, the components are administered simultaneously or sequentially. In some embodiments, the biomaterial and the cell recruitment factor are administered first. In some embodiments, the first population of mesoporous silica rods, the viral vector, and, optionally, the cell activation agent is administered simultaneously and, optionally, after the biomaterial and the cell recruitment factor.

Also contemplated herein is a method of transducing cells in vivo comprising administering a biomaterial and a molecule (e.g., VEGF-C, IL-2, IL-7, IL-15 (e.g., hetIL-15 (IL15/sIL-15Ra)), GM-CSF, CXCL12, CXC3L1, CCL19, CCL21, CXCL10, or CXCL11); a first population of mesoporous silica particles; a viral vector; and, optionally, a cell activation agent to a subject. In some embodiments, the components are administered simultaneously or sequentially. In some embodiments, the biomaterial and the molecule are administered first. In some embodiments, the first population of mesoporous silica rods, the viral vector, and, optionally, the cell activation agent is administered simultaneously and, optionally, after the biomaterial and the molecule.

In some embodiments, the biomaterial comprises a hydrogel, optionally a cryogel. In some embodiments, the cryogel comprises gelatin, hyaluronic acid, collagen, alginate, laminin, chitosan, silk fibroin, agarose, poly(ethylene glycol), poly-vinyl alcohol, and/or hydroxyethyl methylacrylate. In some embodiments, the composition comprising the cryogel further comprises laponite. In some embodiments, the cryogel comprises pores between about 10 to 300

μm in diameter, optionally between about 50 to 300 μm. In some embodiments, the cryogel is chemically cross-linked.

In some embodiments, the cell recruitment factor selectively recruits immune cells, optionally T-cells and/or NK-cells. In some embodiments, the cell recruitment factor is selected from the group consisting of CCL19, CXCL9, CXCL10, XCL1, IL-2, IL-7, CCL21, GM-CSF, CCL17, CCL22, CCL20, CCL27, IL-15, lymphotoxin alpha, lymphotoxin beta, VEGF-C, FLT3L, G-CSF, PDGF, S100A8/A9, CSF-1, CXCL8, CCL20, CCL17, CCR5, CCR6, CCL2, VEGF, Angiopoietin-2, PGE2, LTB4, CXC3L1, CCL19, CCL21, CXCL10, CXCL11, and/or CXCL12. In some embodiments, the VEGF-C is selected from the group consisting of immature VEGF-C peptide or mature VEGF-C peptide. In some embodiments, the mature VEGF-C peptide is the minor mature form or major mature form. In some embodiments, the mature VEGF-C peptide is a wild type minor mature form or a wild type major mature form. In some embodiments, the mature VEGF-C peptide is a modified minor mature form or a modified major mature form. In some embodiments, the mature VEGF-C peptide is a modified minor mature form comprising a mutation at Cysteine 137 (e.g., C137A) or a modified major mature form comprising a mutation at Cysteine 137 (e.g., C137A). In some embodiments, the mature VEGF-C peptide is a modified minor mature form comprising a C137A mutation or a modified major mature form comprising a C137A mutation. In some embodiments, the mature VEGF-C peptide is present as a dimer or monomer. In some embodiments, the VEGF-C is a dimer of the major mature form further comprising a C137A mutation in each monomer. In some embodiments, the VEGF-C is a dimer of the minor mature form further comprising a C137A mutation in each monomer. In some embodiments, the VEGF-C is selected from **Table 18**, optionally, wherein the his tag is not included in the sequence. In some embodiments, the VEGF-C is present in an effective amount, optionally in an amount of less than or about 1 mg, less than or about 10 mg, greater than or about 10 μg, greater than or about 1 μg, between about 1 μg and 1 mg, between about 10 μg and 1 mg, between about 1 μg and 10 mg, or between about 10 μg and 10 mg.

In some embodiments, the first population of mesoporous silica particles are surface modified. In some embodiments, the surface modification on the first population of mesoporous silica particles is –OH (hydroxyl), amine, carboxylic acid, phosphonate, halide, azide, alkyne, epoxide, sulfhydryl, polyethyleneimine, a hydrophobic moiety, or salts thereof, optionally using a C_1 to C_{20} alkyl or $(-O(CH2-CH_2-)_{1-25}$ linker. In some embodiments, the surface modification

on the first population of mesoporous silica particles is a primary, secondary, tertiary, or quaternary amine. In some embodiments, the surface modification on the first population of mesoporous silica particles is a polyethyleneimine having an average molecular weight of about 1000 to 20,000 Da, about 1,200 to 15,000 Da, about 1,500 to 12,000 Da, about 2,000 Da, about 3,000 Da, about 4,000 Da, about 5,000 Da, about 6,000 Da, about 7,000 Da, about 8,000 Da, about 9,000 Da, or about 10,000 Da, as measured by gel permeation chromatography (GPC). In some embodiments, mesoporous silica particles comprise pores of between 2-50 nm in diameter. In some embodiments, the mesoporous silica particles have a surface area of at least about 100 m^2/g. In some embodiments, the composition is suitable for injectable use. In some embodiments, the mesoporous silica particles are in the form of mesoporous silica rods.

In some embodiments, the viral vector is conjugated to first population of the mesoporous silica particles. In some embodiments, the viral vector is electrostatically or covalently conjugated to the first population of mesoporous silica particles. In some embodiments, the viral vector is a retrovirus, adenovirus, adeno-associated virus, herpes virus, or lentivirus. In some embodiments, the viral vector comprises an expression vector comprising a recombinant polynucleotide comprising an expression control sequence operatively linked to a nucleotide sequence to be expressed. In some embodiments, the nucleotide sequence encodes a chimeric antigen receptor (CAR), an engineered TCR, one or more cytokines, one or more chemokines, an shRNA to block an inhibitory molecule, or wherein the nucleotide sequence comprises an mRNA to induce expression of a protein. In some embodiments, the nucleotide sequence encodes a polypeptide engineered to target a tumor antigen. In some embodiments, the polypeptide targets a tumor antigen selected from the group consisting of: TSHR, CD19, CD123, CD22, CD30, CD171, CS-1, CLL-1, CD33, EGFRvIII , GD2, GD3, BCMA, Tn Ag, PSMA, ROR1, FLT3, FAP, TAG72, CD38, CD44v6, CEA, EPCAM, B7H3, KIT, IL-13Ra2, Mesothelin, IL-11Ra, PSCA, PRSS21, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, CD20, Folate receptor alpha, ERBB2 (Her2/neu), MUC1, EGFR, NCAM, Prostase, PAP, ELF2M, Ephrin B2, IGF-I receptor, CAIX, LMP2, gp100, bcr-abl, tyrosinase, EphA2, Fucosyl GM1, sLe, GM3, TGS5, HMWMAA, o-acetyl-GD2, Folate receptor beta, TEM1/CD248, TEM7R, CLDN6, GPRC5D, CXORF61, CD97, CD179a, ALK, Polysialic acid, PLAC1, GloboH, NY-BR-1, UPK2, HAVCR1, ADRB3, PANX3, GPR20, LY6K, OR51E2, TARP, WT1, NY-ESO-1, LAGE-1a, MAGE-A1, legumain, HPV E6,E7, MAGE A1, ETV6-AML, sperm protein 17,

XAGE1, Tie 2, MAD-CT-1, MAD-CT-2, Fos-related antigen 1, p53, p53 mutant, prostein, survivin and telomerase, PCTA-1/Galectin 8, MelanA/MART1, Ras mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, TRP-2, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP-4, SSX2, RAGE-1, human telomerase reverse transcriptase, RU1, RU2, intestinal carboxyl esterase, mut hsp70-2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3, FCRL5, IGLL1, and any combination thereof. In some embodiments, the protein is a CAR that comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region, and a signaling domain. In some embodiments, the signaling domain is a CD3 zeta signaling domain. In some embodiments, the costimulatory signaling region is selected from 41BB (i.e., CD137), CD27, ICOS, and/or CD28.

In some embodiments, the cell activation agent is conjugated to or absorbed on the first population of mesoporous silica particles or a second population of mesoporous silica particles. In some embodiments, the cell activation agent is a T cell stimulating compound, an anti-idiotype antibody to a CAR antigen binding domain, and/or a tumor antigen. In some embodiments, the T-cell stimulating compound is IL-2, IL-15, anti-CD2 mAb, anti-CD3 mAb, anti-CD28 mAb, neo-antigen peptides, peptides from shared antigens such as TRP2, gp100, tumor cell lysate, CD19, CD20, CD22, ROR1, mesothelin, CD33/IL3Ra, c-Met, PSMA, Glycolipid F77, EGFRvIII, GD-2, NY-ESO-1 TCR, and/or MAGE A3 TCR. In some embodiments, the cell activation agent comprises a CD3/TCR complex and/or an agent that stimulates a costimulatory molecule and/or growth factor receptor, optionally, wherein the cell activation agent is a multispecific binding molecule comprising an agent that stimulates a CD3/TCR complex and an agent that stimulates a costimulatory molecule and/or growth factor receptor. In some embodiments, the cell activation is selected from a sequence provided in **Table 20**. In some embodiments, the cell activation agent is conjugated to the second population of mesoporous silica particles or to a lipid envelope on the surface of the second population of mesoporous silica particles. In some embodiments, the composition further comprises a cytokine. In some embodiments, the cytokine is conjugated to or adsorbed on the first or second population of mesoporous silica particles. In some embodiments, the cytokine is IL-1, IL-2, IL-4, IL-5, IL-7, IL-10, IL-12, IL-15, IL-17, IL-21, or transforming growth factor beta (TGF-β), or

an agonist thereof, a mimetic thereof, a variant thereof, a functional fragment thereof, or a combination thereof.

Also contemplated herein is a method of treating a subject having a disease, disorder, or condition comprising administering a biomaterial comprising a cell recruitment factor; a first population of mesoporous silica particles; a viral vector; and, optionally, a cell activation agent to a subject. In some embodiments, the components are administered simultaneously or sequentially. In some embodiments, the biomaterial comprising the cell recruitment factor is administered first. In some embodiments, the first population of mesoporous silica rods, the viral vector, and, optionally, the cell activation agent is administered simultaneously and, optionally, after the biomaterial.

Also contemplated herein is a method of treating a subject having a disease, disorder, or condition comprising administering a biomaterial and a cell recruitment factor; a first population of mesoporous silica particles; a viral vector; and, optionally, a cell activation agent to a subject. In some embodiments, the components are administered simultaneously or sequentially. In some embodiments, the biomaterial and the cell recruitment factor are administered first. In some embodiments, the first population of mesoporous silica rods, the viral vector, and, optionally, the cell activation agent is administered simultaneously and, optionally, after the biomaterial and the cell recruitment factor.

Also contemplated herein is a method of treating a subject having a disease, disorder, or condition comprising administering a biomaterial and a molecule (e.g., VEGF-C, IL-2, IL-7, IL-15 (e.g., hetIL-15 (IL15/sIL-15Ra)), GM-CSF, CXCL12, CXC3L1, CCL19, CCL21, CXCL10, or CXCL11); a first population of mesoporous silica particles; a viral vector; and, optionally, a cell activation agent to a subject. In some embodiments, the components are administered simultaneously or sequentially. In some embodiments, the biomaterial and the molecule are administered first. In some embodiments, the first population of mesoporous silica rods, the viral vector, and, optionally, the cell activation agent is administered simultaneously and, optionally, after the biomaterial and the molecule.

In some embodiments, the subject has cancer. In some embodiments, the subject has cancer expressing one or more tumor antigen selected from the group consisting of: TSHR, CD19, CD123, CD22, CD30, CD171, CS-1, CLL-1, CD33, EGFRvIII , GD2, GD3, BCMA, Tn Ag, PSMA, ROR1, FLT3, FAP, TAG72, CD38, CD44v6, CEA, EPCAM, B7H3, KIT, IL-

13Ra2, Mesothelin, IL-11Ra, PSCA, PRSS21, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, CD20, Folate receptor alpha, ERBB2 (Her2/neu), MUC1, EGFR, NCAM, Prostase, PAP, ELF2M, Ephrin B2, IGF-I receptor, CAIX, LMP2, gp100, bcr-abl, tyrosinase, EphA2, Fucosyl GM1, sLe, GM3, TGS5, HMWMAA, o-acetyl-GD2, Folate receptor beta, TEM1/CD248, TEM7R, CLDN6, GPRC5D, CXORF61, CD97, CD179a, ALK, Polysialic acid, PLAC1, GloboH, NY-BR-1, UPK2, HAVCR1, ADRB3, PANX3, GPR20, LY6K, OR51E2, TARP, WT1, NY-ESO-1, LAGE-1a, MAGE-A1, legumain, HPV E6,E7, MAGE A1, ETV6-AML, sperm protein 17, XAGE1, Tie 2, MAD-CT-1, MAD-CT-2, Fos-related antigen 1, p53, p53 mutant, prostein, survivin and telomerase, PCTA-1/Galectin 8, MelanA/MART1, Ras mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, TRP-2, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP-4, SSX2, RAGE-1, human telomerase reverse transcriptase, RU1, RU2, intestinal carboxyl esterase, mut hsp70-2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3, FCRL5, IGLL1, and any combination thereof.

In some embodiments, the biomaterial comprises a hydrogel, optionally a cryogel. In some embodiments, the cryogel comprises gelatin, hyaluronic acid, collagen, alginate, laminin, chitosan, silk fibroin, agarose, poly(ethylene glycol), poly-vinyl alcohol, and/or hydroxyethyl methylacrylate. In some embodiments, the composition comprising the cryogel further comprises laponite. In some embodiments, the cryogel comprises pores between about 10 to 300 μm in diameter, optionally between about 50 to 300 μm. In some embodiments, the cryogel is chemically cross-linked.

In some embodiments, the cell recruitment factor selectively recruits immune cells, optionally T-cells and/or NK-cells. In some embodiments, the cell recruitment factor is selected from the group consisting of CCL19, CXCL9, CXCL10, XCL1, IL-2, IL-7, CCL21, GM-CSF, CCL17, CCL22, CCL20, CCL27, IL-15, lymphotoxin alpha, lymphotoxin beta, VEGF-C, FLT3L, G-CSF, PDGF, S100A8/A9, CSF-1, CXCL8, CCL20, CCL17, CCR5, CCR6, CCL2, VEGF, Angiopoietin-2, PGE2, LTB4, CXC3L1, CCL19, CCL21, CXCL10, CXCL11, and/or CXCL12. In some embodiments, the VEGF-C is selected from the group consisting of immature VEGF-C propeptide or mature VEGF-C peptide. In some embodiments, the mature VEGF-C peptide is the minor mature form or major mature form. In some embodiments, the mature

VEGF-C peptide is a wild type minor mature form or a wild type major mature form. In some embodiments, the mature VEGF-C peptide is a modified minor mature form or a modified major mature form. In some embodiments, the mature VEGF-C peptide is a modified minor mature form comprising a mutation at Cysteine 137 (e.g., C137A) or a modified major mature form comprising a mutation at Cysteine 137 (e.g., C137A). In some embodiments, the mature VEGF-C peptide is a modified minor mature form comprising a C137A mutation or a modified major mature form comprising a C137A mutation. In some embodiments, the mature VEGF-C peptide is present as a dimer or monomer. In some embodiments, the VEGF-C is a dimer of the major mature form further comprising a C137A mutation in each monomer. In some embodiments, the VEGF-C is a dimer of the minor mature form further comprising a C137A mutation in each monomer. In some embodiments, the VEGF-C is selected from **Table 18**, optionally, wherein the his tag is not included in the sequence. In some embodiments, the VEGF-C is present in an effective amount, optionally in an amount of less than or about 1 mg, less than or about 10 mg, greater than or about 10 µg, greater than or about 1 µg, between about 1 µg and 1 mg, between about 10 µg and 1 mg, between about 1 µg and 10 mg, or between about 10 µg and 10 mg.

In some embodiments, the first population of mesoporous silica particles are surface modified. In some embodiments, the surface modification on the first population of mesoporous silica particles is –OH (hydroxyl), amine, carboxylic acid, phosphonate, halide, azide, alkyne, epoxide, sulfhydryl, polyethyleneimine, a hydrophobic moiety, or salts thereof, optionally using a C_1 to C_{20} alkyl or $(-O(CH2-CH_2-)_{1-25}$ linker. In some embodiments, the surface modification on the first population of mesoporous silica particles is a primary, secondary, tertiary, or quaternary amine. In some embodiments, the surface modification on the first population of mesoporous silica particles is a polyethyleneimine having an average molecular weight of about 1000 to 20,000 Da, about 1,200 to 15,000 Da, about 1,500 to 12,000 Da, about 2,000 Da, about 3,000 Da, about 4,000 Da, about 5,000 Da, about 6,000 Da, about 7,000 Da, about 8,000 Da, about 9,000 Da, or about 10,000 Da, as measured by gel permeation chromatography (GPC). In some embodiments, mesoporous silica particles comprise pores of between 2-50 nm in diameter. In some embodiments, the mesoporous silica particles have a surface area of at least about 100 m^2/g. In some embodiments, the composition is suitable for injectable use. In some embodiments, the mesoporous silica particles are in the form of mesoporous silica rods.

In some embodiments, the viral vector is conjugated to first population of the mesoporous silica particles. In some embodiments, the viral vector is electrostatically or covalently conjugated to the first population of mesoporous silica particles. In some embodiments, the viral vector is a retrovirus, adenovirus, adeno-associated virus, herpes virus, or lentivirus. In some embodiments, the viral vector comprises an expression vector comprising a recombinant polynucleotide comprising an expression control sequence operatively linked to a nucleotide sequence to be expressed. In some embodiments, the nucleotide sequence encodes a chimeric antigen receptor (CAR), an engineered TCR, one or more cytokines, one or more chemokines, an shRNA to block an inhibitory molecule, or wherein the nucleotide sequence comprises an mRNA to induce expression of a protein. In some embodiments, the nucleotide sequence encodes a polypeptide engineered to target a tumor antigen. In some embodiments, the polypeptide targets a tumor antigen selected from the group consisting of: TSHR, CD19, CD123, CD22, CD30, CD171, CS-1, CLL-1, CD33, EGFRvIII , GD2, GD3, BCMA, Tn Ag, PSMA, ROR1, FLT3, FAP, TAG72, CD38, CD44v6, CEA, EPCAM, B7H3, KIT, IL-13Ra2, Mesothelin, IL-11Ra, PSCA, PRSS21, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, CD20, Folate receptor alpha, ERBB2 (Her2/neu), MUC1, EGFR, NCAM, Prostase, PAP, ELF2M, Ephrin B2, IGF-I receptor, CAIX, LMP2, gp100, bcr-abl, tyrosinase, EphA2, Fucosyl GM1, sLe, GM3, TGS5, HMWMAA, o-acetyl-GD2, Folate receptor beta, TEM1/CD248, TEM7R, CLDN6, GPRC5D, CXORF61, CD97, CD179a, ALK, Polysialic acid, PLAC1, GloboH, NY-BR-1, UPK2, HAVCR1, ADRB3, PANX3, GPR20, LY6K, OR51E2, TARP, WT1, NY-ESO-1, LAGE-1a, MAGE-A1, legumain, HPV E6,E7, MAGE A1, ETV6-AML, sperm protein 17, XAGE1, Tie 2, MAD-CT-1, MAD-CT-2, Fos-related antigen 1, p53, p53 mutant, prostein, survivin and telomerase, PCTA-1/Galectin 8, MelanA/MART1, Ras mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, TRP-2, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP-4, SSX2, RAGE-1, human telomerase reverse transcriptase, RU1, RU2, intestinal carboxyl esterase, mut hsp70-2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3, FCRL5, IGLL1, and any combination thereof. In some embodiments, the protein is a CAR that comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region, and a signaling domain. In some

embodiments, the signaling domain is a CD3 zeta signaling domain. In some embodiments, the costimulatory signaling region is selected from 41BB (i.e., CD137), CD27, ICOS, and/or CD28.

In some embodiments, the cell activation agent is conjugated to or absorbed on the first population of mesoporous silica particles or a second population of mesoporous silica particles. In some embodiments, the cell activation agent is a T cell stimulating compound, an anti-idiotype antibody to a CAR antigen binding domain, and/or a tumor antigen. In some embodiments, the T-cell stimulating compound is IL-2, IL-15, anti-CD2 mAb, anti-CD3 mAb, anti-CD28 mAb, neo-antigen peptides, peptides from shared antigens such as TRP2, gp100, tumor cell lysate, CD19, CD20, CD22, ROR1, mesothelin, CD33/IL3Ra, c-Met, PSMA, Glycolipid F77, EGFRvIII, GD-2, NY-ESO-1 TCR, and/or MAGE A3 TCR. In some embodiments, the cell activation agent comprises a CD3/TCR complex and/or an agent that stimulates a costimulatory molecule and/or growth factor receptor, optionally, wherein the cell activation agent is a multispecific binding molecule comprising an agent that stimulates a CD3/TCR complex and an agent that stimulates a costimulatory molecule and/or growth factor receptor. In some embodiments, the cell activation is selected from a sequence provided in **Table 20**. In some embodiments, the cell activation agent is conjugated to the second population of mesoporous silica particles or to a lipid envelope on the surface of the second population of mesoporous silica particles. In some embodiments, the composition further comprises a cytokine. In some embodiments, the cytokine is conjugated to or adsorbed on the first or second population of mesoporous silica particles. In some embodiments, the cytokine is IL-1, IL-2, IL-4, IL-5, IL-7, IL-10, IL-12, IL-15, IL-17, IL-21, or transforming growth factor beta (TGF-β), or an agonist thereof, a mimetic thereof, a variant thereof, a functional fragment thereof, or a combination thereof.

Those skilled in the art will recognize or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following enumerated embodiments.

Enumerated Embodiments

1. A composition, comprising:
   (a) biomaterial comprising a cell recruitment factor;

(b) a first population of mesoporous silica particles;

(c) a viral vector; and

(d) optionally, a cell activation agent.

2. The composition of embodiment 1, wherein the biomaterial comprises a hydrogel, optionally a cryogel.

3. The composition of embodiment 2, wherein the cryogel:

(a) comprises gelatin, hyaluronic acid, collagen, alginate, laminin, chitosan, silk fibroin, agarose, poly(ethylene glycol), poly-vinyl alcohol, and/or hydroxyethyl methylacrylate, optionally, wherein the cryogel further comprises laponite;

(b) comprises pores between about 10 to 300 μm in diameter, optionally between about 50 to 300 μm; and/or

(c) is chemically cross-linked.

4. The composition of any one of the preceding embodiments, wherein the cell recruitment factor is selected from the group consisting of CCL19, CXCL9, CXCL10, XCL1, IL-2, IL-7, CCL21, GM-CSF, CCL17, CCL22, CCL20, CCL27, IL-15, lymphotoxin alpha, lymphotoxin beta, VEGF-C, FLT3L, G-CSF, PDGF, S100A8/A9, CSF-1, CXCL8, CCL20, CCL17, CCR5, CCR6, CCL2, VEGF, Angiopoietin-2, PGE2, LTB4, CXC3L1, CCL19, CCL21, CXCL10, CXCL11, and/or CXCL12.

5. The composition of any one of the preceding embodiments, wherein the cell recruitment factor selectively recruits immune cells, optionally T-cells and/or NK-cells.

6. The composition of embodiment 5, wherein the cell recruitment factor is selected from the group consisting of:

(a) IL-2, IL-7, CCL21, IL-15, GM-CSF, and/or VEGF-C for the recruitment of T-cells; and/or

(b) CXCL12, CXC3L1, CCL19, CCL21, CXCL10, and/or CXCL11 for the recruitment of NK-cells.

7. The composition of any one of the preceding embodiments, wherein the cell recruitment factor is VEGF-C, optionally as a monomer or a dimer.

8. The composition of embodiment 7, wherein the VEGF-C is a mature VEGF-C peptide, optionally the minor or major mature form or a mutated variant each thereof.

9. The composition of embodiment 8, wherein the mature VEGF-C peptide comprises a C137A mutation.

10. The composition of any one of embodiments 7 to 9, wherein the VEGF-C comprises a sequence provided in **Table 18**, optionally, wherein the his tag is not included in the sequence.

11. The composition of embodiment 10, wherein the VEGF-C comprises a dimer of one or more of a sequence provided in **Table 18**, optionally, wherein the his tag is not included in the sequence.

12. The composition of any one of embodiments 7 to 10, wherein the VEGF-C is present in an effective amount, optionally, in an amount of less than or about 1 mg, less than or about 10 mg, greater than or about 10 μg, greater than or about 1 μg, between about 1 μg and 1 mg, between about 10 μg and 1 mg, between about 1 μg and 10 mg, or between about 10 μg and 10 mg.

13. The composition of any one of the preceding embodiments, wherein the viral vector is conjugated to the first population of mesoporous silica particles.

14. The composition of embodiment 13, wherein the viral vector is electrostatically or covalently conjugated to the first population of mesoporous silica particles.

15. The composition of any one of the preceding embodiments, wherein the first population of mesoporous silica particles are surface modified.

16. The composition of embodiment 15, wherein the surface modification on the first population of mesoporous silica particles is –OH (hydroxyl), amine, carboxylic acid, phosphonate, halide, azide, alkyne, epoxide, sulfhydryl, polyethyleneimine, a hydrophobic moiety, or salts thereof, optionally using a C_1 to C_{20} alkyl or $(-O(CH2-CH_2-)_{1-25}$ linker.

17. The composition of embodiment 15, wherein the surface modification on the first population of mesoporous silica particles is a primary, secondary, tertiary, or quaternary amine.

18. The composition of embodiment 15, wherein the surface modification on the first population of mesoporous silica particles is a polyethyleneimine having an average molecular weight of about 1000 to 20,000 Da, about 1,200 to 15,000 Da, about 1,500 to 12,000 Da, about 2,000 Da, about 3,000 Da, about 4,000 Da, about 5,000 Da, about 6,000 Da, about 7,000 Da, about 8,000 Da, about 9,000 Da, or about 10,000 Da, as measured by gel permeation chromatography (GPC).

19. The composition of any one of the preceding embodiments, wherein the viral vector is a retrovirus, adenovirus, adeno-associated virus, herpes virus, or lentivirus.

20. The composition of any one of the preceding embodiments, wherein the viral vector comprises an expression vector comprising a recombinant polynucleotide comprising an expression control sequence operatively linked to a nucleotide sequence to be expressed.

21. The composition of embodiment 20, wherein the nucleotide sequence encodes a chimeric antigen receptor (CAR), an engineered TCR, one or more cytokines, one or more chemokines, an shRNA to block an inhibitory molecule, or wherein the nucleotide sequence comprises an mRNA to induce expression of a protein.

22. The composition of embodiment 21, wherein the nucleotide sequence encodes a polypeptide engineered to target a tumor antigen.

23. The composition of embodiment 22, wherein the tumor antigen selected from the group consisting of: TSHR, CD19, CD123, CD22, CD30, CD171, CS-1, CLL-1, CD33, EGFRvIII , GD2, GD3, BCMA, Tn Ag, PSMA, ROR1, FLT3, FAP, TAG72, CD38, CD44v6, CEA, EPCAM, B7H3, KIT, IL-13Ra2, Mesothelin, IL-11Ra, PSCA, PRSS21, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, CD20, Folate receptor alpha, ERBB2 (Her2/neu), MUC1, EGFR, NCAM, Prostase, PAP, ELF2M, Ephrin B2, IGF-I receptor, CAIX, LMP2, gp100, bcr-abl, tyrosinase, EphA2, Fucosyl GM1, sLe, GM3, TGS5, HMWMAA, o-acetyl-GD2, Folate receptor beta, TEM1/CD248, TEM7R, CLDN6, GPRC5D, CXORF61, CD97, CD179a, ALK, Polysialic acid, PLAC1, GloboH, NY-BR-1, UPK2, HAVCR1, ADRB3, PANX3, GPR20, LY6K, OR51E2, TARP, WT1, NY-ESO-1, LAGE-1a, MAGE-A1, legumain, HPV E6,E7, MAGE A1, ETV6-AML, sperm protein 17, XAGE1, Tie 2, MAD-CT-1, MAD-CT-2, Fos-related antigen 1, p53, p53 mutant, prostein, survivin and telomerase, PCTA-1/Galectin 8, MelanA/MART1, Ras mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, TRP-2, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP-4, SSX2, RAGE-1, human telomerase reverse transcriptase, RU1, RU2, intestinal carboxyl esterase, mut hsp70-2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3, FCRL5, IGLL1, and any combination thereof.

24. The composition of any one of the preceding embodiments, wherein the vector encodes a CAR that comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region, and a signaling domain.

25. The composition of embodiment 24, wherein:

(a) the antigen binding domain binds an antigen selected from CD19, CD123, CD22, CD20, EGFRvIII , BCMA, Mesothelin, CD33, CLL-1, and any combination thereof;

(b) the transmembrane domain comprises a CD8 hinge;

(c) the costimulatory signaling region is selected from a 4-1BB or CD28 costimulatory signaling domain; and/or

(d) the signaling region comprises a CD3 zeta signaling domain.

26. The composition of any one of the preceding embodiments, wherein the cell activation agent is a T cell stimulating compound, an anti-idiotype antibody to a CAR antigen binding domain, or the tumor antigen.

27. The composition of any one of the preceding embodiments, wherein the cell activation agent:

(a) comprises a CD3/TCR complex and/or an agent that stimulates a costimulatory molecule and/or growth factor receptor;

(b) is a multispecific binding molecule comprising n agent that stimulates a CD3/TCR complex and an agent that stimulates a costimulatory molecule and/or growth factor receptor; and/or

(c) comprises a sequence provided in **Table 20** and/or provided in one or more format according to **Figure 37**.

28. The composition of any one of the preceding embodiments, wherein the cell activation agent is conjugated to or adsorbed on the first population of mesoporous silica particles, a second population of mesoporous silica particles, or to a lipid envelope on the surface of the second population of mesoporous silica particles.

29. The composition of any one of the preceding embodiments, wherein the mesoporous silica particles are mesoporous silica rods.

30. The composition of any of the preceding embodiments, wherein the mesoporous silica particles comprise pores of between 2-50 nm in diameter.

31. The composition of any of the preceding embodiments, wherein the mesoporous silica particles have a surface area of at least about 100 m^2/g.

32. The composition of any of the preceding embodiments, wherein the composition is suitable for injectable use.

33. A method of transducing cells in vivo comprising administering the composition of any one of embodiments 1 to 32, each component being administered simultaneously or sequentially.

34. A method of treating a disease, disorder, or condition comprising administering the composition of any one of embodiments 1 to 32, each component being administered simultaneously or sequentially.

35. The method of embodiment 34, wherein the disease, disorder, or condition is cancer.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 presents a series of surface modifications on mesoporous silica particles.

FIG. 2 presents results from staining for viral envelope protein (VSV-G) on MSR surface after adsorption of VSV-G pseudotyped lentivirus onto MSRs. The control MSRs are presented on the top panel and virus-incubated rods are on the bottom panel.

FIG. 3 is a schematic of virus adsorption on MSRs and transduction of T cells.

FIG. 4 provides results from GFP expression by T cells incubated with free lentivirus or MSR-bound lentivirus. Dilution of virus-coated MSRs from 40 μg/ml starting concentration is as indicated. The "1x lenti" condition is equivalent to the amount of virus incubated with the MSR conditions. The "2x lenti" condition is equivalent to twice the amount used to coat the MSR conditions.

FIG. 5 provides a schematic of overall strategy for ligand presentation on MSR surface. Liposomes are incubated with MSRs to form a supported lipid bilayer. Ligands can be coupled to the MSR-lipid bilayer using streptavidin-biotin interactions.

FIG. 6 shows a picture of MSRs coated with POPC liposomes containing 1 mol% PE-carboxyfluorescein. Bright field (left), fluorescence (middle), and overlay (right) images are shown.

FIG. 7 depicts the peptide sequence of EGFRvIII CAR-binding peptide (LEEKKGNYVVTDH (SEQ ID NO: 756)).

FIG. 8 illustrates cytokine production of EGFRvIII CARTs by peptide immobilization on MSRs. Results provide interferon-gamma and interleukin-2 production of EGFRvIII CARTs stimulated by lipid-coated MSRs (1% PE-biotin in the lipid coating) presenting EGFRvIII-CAR binding peptide compared to control conditions control conditions.

FIG. 9 illustrates the proliferation of EGFRvIII CARTs by peptide immobilization on MSRs. A lipid-coated MSR composition of 0.01% PE-biotin was used for peptide immobilization, and the MSR concentration was 30 μg/ml in the well. Cell counts were performed at day 7 of culture under the indicated conditions.

FIGs. 10A and 10B illustrate the proliferation of EGFRvIII CARTs and final cellular composition by peptide immobilization on MSRs. The starting MSR concentration was 50 μg/ml with and the dilutions of MSRs from this starting concentration are as indicated in the axis. **FIG. 10A** shows the percentage of CD4 and CD8 T cells at the end of culture period with the indicated materials. **FIG. 10B** depicts the FACS analysis of CD8+ and CD4+ CAR T cells diluting CFSE during a 3-day culture period using MSRs with varying amount of EGFRvIII CAR-binding peptide with or without anti-CD28 on the MSR surface.

FIGs. 11A and 11B illustrate the proliferation of BCMA CARTs and final cellular composition by BCMA protein immobilization on MSRs. The starting MSR concentration was 50 μg/ml with and the dilutions of MSRs from this starting concentration are as indicated in the axis. **FIG. 11A** shows percentage of CD4 and CD8 T cells at the end of culture period with the indicated materials. **FIG. 11B** demonstrates FACS analysis of CD8+ and CD4+ CAR T cells diluting CFSE during a 3-day culture period using MSRs with varying amount of EGFRvIII CAR-binding peptide with or without anti-CD28 on the MSR surface.

FIG. 12 presents a schematic of simultaneous stimulation and transduction of unstimulated human T cells using MSRs, according to some embodiments. Two populations of MSRs are created – 1) MSRs presenting agonistic CD3/CD28 antibodies to stimulate T cells, 2) Positively charged PEI-MSRs that have been bound with lentivirus to facilitate viral delivery to the T cells. The two types of MSRs can be mixed together in different ratios to adjust the amount of stimulation and virus that the T cells are exposed to.

FIG. 13 illustrates the transduction efficiency of T cells exposed to stimulatory (anti-CD3/CD28 antibody-immobilized MSRs) and PEI-MSRs incubated with virus. T cells were incubated with different amounts of stimulating rods (Stim 1.00 represents 70 μg/ml MSRs) and exposed to GFP-lentivirus at different multiplicities of infection (MOI) either bound to PEI-MSRs or in free virus form. The top concentration of MSRs in the virus conditions was 22 μg/ml.

FIG. 14 illustrates transduction efficiency of T cells exposed to stimulatory (anti-CD3/CD28 antibody-immobilized) MSRs and PEI-MSRs incubated with virus. Plots show transduction efficiency as a function of the concentration of stimulatory MSRs at various total amounts of virus. The MSR concentration of stimulating MSR condition 1.0 is 70 μg/ml. The concentration of MSRs in the PEI MSR condition 1 is 22 μg/ml. Transduction was assessed at 3 days after initiation of the culture.

FIG. 15 provides results from comparison of virus delivery strategies for transduction efficiency. In the "PEI" and "free" conditions T cells were stimulated with a "high" level of CD3/CD28 antibodies bound to MSRs (MSR concentration 70 μg/ml), and given virus either associated with PEI-MSRs or freely delivered in the media, respectively (virus concentration 1.0 contains 22 μg/ml MSRs, MOI ~6.7). In the "PEI+CD3/CD28" the virus and CD3/CD28 agonistic antibodies were bound to PEI-MSRs (concentration 1.0 is 22 μg/ml MSRs). Transduction was assessed at 3 days after initiation of the culture.

FIG. 16 provides results from comparison of various delivery strategies for transduction in PBMC population. Conditions as in FIG. 15 were added to PBMCs. The proportion of transduced cells in each cell type was quantified. Transduction was assessed at 3 days after initiation of the culture.

FIG. 17 provides the different transduction fractions in PBMCs with various virus delivery strategies. Top panel provides the total cell composition present in PBMC populations under the conditions of FIG. 15. Bottom panel provides the composition of the transduced cell fraction present after virus delivery using the conditions of FIG. 15. Transduction was assessed at 3 days after initiation of the culture.

FIG. 18 provides a non-limiting exemplary schematic of the composition disclosed herein for use as a cancer therapeutic wherein (A) depicts delivering the growth factor VEGF-C that induces lymphangiogenesis of pre-existing skin lymphatic capillaries; (B) depicts the

generated lymphatic endothelial cells secrete chemokines (such as CCL21) that attract immune cells (primarily naive T cells) from the blood circulation into the dermis on top of the gel; (C) depicts lymphatic endothelial cells educating T cells – not to be bound by theory, Applicants believe that such education could yield a high proportion of stem cell memory phenotype, which in turn may be more potent cells once transduced; after T cells are recruited to this priming site, (D) depicts lentivirus encoding for one or more chimeric antigen receptors (CARs) being delivered in combination with mesoporous silica rods to prevent systemic spread – not to be bound by theory, Applicants believe that local positioning of the virus could favor transduction of locally recruited T cells and that activation could further improve transduction, prevent leakage, and transduction of unwanted cells; (E) and (F) depict transduced and educated cells returning into systemic circulation via the skin lymphatics, lymph nodes and thoracic duct – not to be bound by theory, Applicants believe that such cells will further expand in response to tumor antigen.

FIGs. 19A-19C lay out the characteristics of various VEGF-C protein variants. **FIG. 19A** provides a schematic of both natural and modified VEGF-C. Immature VEGF-C (#1) is normally found intracellularly with N-terminal and C-terminal propeptide sequences. Once released, VEGF-C protein undergoes proteolytic cleavage and is present in the extracellular space as minor or major mature form (#2, #7) in dimer or monomer form. Stabilized dimers of major (#9) and minor mature (#8) form were engineered by inserting the C137A mutation into the sequences. The main difference between minor mature and major mature forms is the presence of an additional short propeptide sequence on the minor mature form N-terminus. Not to be bound by theory, Applicants believe the additional short propeptide appears to boost dimer formation as well as protein expression in both HEK293T and CHO MaKo cells. **FIG. 19B** depicts an SDS-polyacrylamide gel subjected to electrophoresis under non-reducing (NR) and reducing conditions (R) loaded with purified VEGF-C variants. Details of the wells with the corresponding VEGF-C variant are shown in **FIG. 19C** and presence of dimer (**) and monomer (*) have been indicated with asterix. The immature VEGF-C with the full length propepitde (#1) is produced as a dimer, among some impurities (wells 2 and 3); the removal of the propeptide leads to the production of two major mature VEGF-C forms (#2), one non-covalent dimer form (wells 5, 6) and a monomeric form (wells 8, 9); adding the mutation C137A in #2 leads to the production of a covalent dimer (well 21, 22) and a monomer form (well 24,

25). A short N-terminal propeptide is left attached to the protein to generate a minor mature VEGF-C form (#7) in non-covalent dimer (wells 11,12) or in monomeric form (wells 15,16). Not to be bound by theory, Applicants have determined that the C137A mutation to #7 VEGF-C leads to the generation of VEGF-C dimer only (wells 18,19) which may be suitable for large scale production. Rows 1, 4, 7, 10, 13, 14, 17, 20, 23 and 26 show the molecular weight marker in kDa.

FIGs. 20A-20C show the results of HDLECs sprouting assay with various VEGF-C variants. Dimeric VEGF-C forms appeared to demonstrate good in vitro activity. **FIG. 20A** depicts the experimental setup of in vitro sprouting assay on human dermal lymphatic endothelial cells (HDLECs) to test biological activity of VEGF-C variants. After incubation cells were **FIG. 20B** assessed for proliferation by WT-8 assay and **FIG. 20C** imaged for tube formation after phalloidin staining. Tube formation images show that the major and minor mature forms (#2, 7, 8, 9) stimulate better sprouting of HDLECs than immature form (#1). Not to be bound by theory, it is believed that the dimeric forms (#2D,7D,8D,9D) superior sprouting activity renders them preferable to monomeric forms (#2M,7M,9M).

FIGs. 21A-21D show the release rate of VEGF-C from alginate cryogel formulations, as well as proof of concept that it can be injected subcutaneously in a mouse. **FIG. 21A** provides a non-limiting, exemplary schematic of alginate cryogels manufacturing. Alginate liquid prepolymer is mixed with laponite and protein of interest, then frozen and thawed again before injection to generate porous matrix. **FIG. 21B** shows the modulation of VEGF-C release in vitro by different types of alginate gels: alginate nanoporous (gelification occurs before cryogelation so no pores are formed), alginate cryogel (after freeze and cryogelation, porous), and alginate cryogel with 0.25% laponite. 0.25% laponite alginate cryogel is showing a controlled and long-lasting release of VEGF-C protein in vitro. **FIG. 21C** shows the modulation of VEGF-C release profile in vitro from 0.25% or 0.5% laponite alginate cryogels loaded with 10μg or 50μg VEGF-C. 30% of the total VEGF-C is released from the gels and given the controlled release profile, 0.25% laponite alginate cryogel was chosen for in vivo work. **FIG. 21D** is an image depicting cryogel injected subcutaneously in mice with a 16G needle.

FIGs. 22A-22C depict induction of in vivo lymphoangiogensis by VEGF-C in naive mouse skin. Not to be bound by theory, the minor mature covalent dimeric VEGF-C appears to have superior efficacy. **FIG. 22A** depicts the in vivo experimental setup and **FIG. 22B** shows

representative dot plots showing in vivo lymphangiogenesis assessed by staining of lymphatic endothelial cells (CD45-, CD31+, PDPN+) by flow cytometry after skin digestion performed 14 days after cryogel implantation. In **FIG. 22C**, lymphangiogenesis in mouse skin quantified after staining as lymphatic endothelial cells counts/mg. Covalent dimers (#8, #9) show high in vivo lymphangiogenesis. Accordingly, #8 was used in further experiments. PDPN: podoplanin.

FIGs. 23A-23E show that skin lymphatics respond to 10μg VEGF-C (#7 variant, SEQ ID NO: 734) delivered by alginate cryogels and lymphangiogenesis peaks 14 days after cryogel implant, which corresponds to peak immune-infiltration in naïve skin of C57/BL6 mice. **FIG. 23A** depicts the in vivo dose response of VEGF-C loaded into alginate cryogels (1, 10, 20, 50 μg) and lymphangiogenesis induction (represented as total lymphatic endothelial cells (LECs) counts/mg tissue, upper graph) and time course of lymphangiogenesis after delivery of 10μg VEGF-C (lower graph). These results indicated that 10μg of VEGF-C induced high in vivo lympahangiogenesis and that peak lymphangiogenesis was observed 14 days after subcutaneous cryogel delivery. **FIG. 23B** Representative plots of LECs (CD45-CD31+PDPN+) and blood endothelial cells (BECs, CD45-CD31+PDPN-) staining isolated after skin digestion of C57/BL6 mice 14 days after gel implant. **FIG. 23C** Quantification of endothelial cells as total cell counts/mg tissue. **FIG. 23D** Quantification represented as total cell counts/mg tissue of CD4+ T cells and CD8+ T cells. LECs counts correlate with T cells infiltrates, especially of a naïve phenotype (CD62L+, CD44-). Bar graphs include 5 independent experiment pooled for VEGF-C and control conditions, VEGF-C n=30, control n=18, naïve n=3 and are represented as mean+SEM, Mann-Whitney non-parametric t-test, ****, $p<0.0001$; **, $p<0.01$. **FIG. 23E** shows quantification of indicated cell types (LECs, CD4 T cells, or CD8 T cells) per mg of tissue over the days following VEGF-C alginate cryogel injection.

FIGs. 24A-24C confirm that VEGF-C #8 produced in CHO MaKo cells is functional. In **FIG. 24A**, HDLECs in vitro sprouting assay shows comparable activity of VEGF-C protein #8 produced in CHO cells (8CHO) compared to #8 produced in HEK293T cells. In **FIG. 24B**, comparable bioactivity was confirmed also in vivo by staining LECs after skin digestion 14 days after cryogel delivery. **FIG. 24C** shows quantification of lymphangiogenesis as total LECs counts/mg tissue in mice injected with blank cryogel or cryogel loaded with #8HEK or #8CHO VEGF-C. BECs (CD45-CD31+PDPN-) are not affected by the VEGF-C #8 delivery, while peak lymphangiogenesis corresponded to peak immune infiltration of CD4 and CD8 T cells (CD45+)

in the skin on top of the cryogels on day 14 after cryogel delivery. n>9. Bar graphs represented as mean+SEM, Mann-Whitney non-parametric t-test between CHO vs control, HEK vs control or CHO vs HEK, ****, p<0.0001; **, p<0.01

FIGs. 25A-25C demonstrate that VEGF-C also induces lymphangiogensis in immunocompromised NSG mice and mouse LECs efficiently recruit human peripheral blood monoculear cells (PBMCs). **FIG. 25A** provides representative flow cytometry plots of skin LECs and BECs statining in NSG, C57/BL6 mice 14 days after VEGF-C (variant #8, minor mature form with C137A mutation, SEQ ID NO: 736) or blank cryogel delivery. **FIG. 25B** lays out the experimental setup of gel delivery in NSG mice and subsequent intravenous injection of human PBMCs (on day 10). Mice were euthanized and analyzed for lymphangiogenesis and immune infiltration in the skin on day 17 post gel implant. **FIG. 25C** shows quantification represented as total counts/mg of LECs, total T cells (CD45+ CD3+) CD8 (CD3+ CD8+) and CD4 (CD3+ CD4+) T cells subsets, as well as B cells (CD45+CD19+). These data demonstrate that T cells are the main cell types of PBMCs recruited in NSG mice.

FIGs. 26A-26B provide a schematic of VEGF-C delivery in mouse skin generating a secondary priming site for T cells to be educated and transduced after injection of viral particles bound to mesoporous silica particles (MSPs), e.g., homogenized mesoporous silica rods (MSRs), in combination with MSP-bound STARTERS (e.g., homogenized MSR-bound STARTERS) (**FIG. 26A**) or free virus in combination with MSP-bound STARTERS (e.g., homogenized MSR-bound STARTERS) (**FIG. 26B**).

FIGs. 27A-27B provide characterization of loading capacity of MSPs, in particular homogenized MSRs, with CD 19 CAR encoding lentivirus. Trimethylammonium MSRs were co-incubated with GFP-expressing lentivirus at various amounts according to functional titer as determined by cell-based transduction assays. The amount of virus in three fractions was characterized – viral loading solution (initial input added to the MSRs), MSR-bound virus (amount remaining bound to the MSRs after incubation and washing), and unbound virus (the amount in the solution remaining after co-incubation of MSRs and virus). MSR and virus were co-incubated for 30 minutes on ice, the supernatant was removed (Unbound Virus) and the MSRs were washed twice prior to assessing MSR-bound virus. The untouched Viral Loading Solutions from each condition were also analyzed. In **FIG. 27A**, results show the majority of the virus in the input Virus Loading Solution is retained in the MSR-bound virus fraction after

adsorption and washing. The amount of virus adsorbed to the MSRs increases with the amount of virus in the Virus Loading Solution. **FIG. 27A** shows the calculated fraction of MSR-bound virus relative to the Virus Loading Solution has a strong efficiency of loading and retention on the MSRs following adsorption and washing.

FIG. 28 provides characterization of retention of virus on MSPs, in particular homogenized MSRs. Lentivirus and MSRs were co-incubated for 30 minutes on ice, and the MSRs were washed twice. MSRs were then cultured in R10 medium containing 10% FCS or OpTmizer serum-free medium, and the input virus stock was incubated in media as well. The supernatant was removed at the indicated times after the start of incubation and analyzed for total virus content. Results indicate that the MSRs release only a fraction of the input virus over the first 18 hours.

FIGs. 29A-29C show functional generation of CAR-T cells using MSP, in particular homogenized MSR, bound to a CD19 CAR encoding (CAR19) virus. CARTs were generated either with free lentivirus (CAR-free) or with lentivirus bound to trimethylammonium MSRs (CAR-MSR). The MOI used for CAR-free transduction and the MOI of total virus used for adsorption to MSRs in the CAR-MSR condition is indicated. These MOIs were chosen to produce CARTs with similar transduction efficiency between the two conditions. MSRs were washed after the adsorption step, thus the total amount of virus in the transduction of the T cells in the MSR condition may occur at a lower MOI than indicated. 4.3e6 TU/virus per 1 mg of MSRs was used in the co-incubation of MSR and virus prior to washing and plating with T cells. T cells were treated with Construct 4 (**Table 20, FIG. 38A-38B**) and the indicated virus preparation for 1 day, followed by washing and culture for an additional 3 days. **FIG. 29A** shows CAR+% measured at day 4 after transduction. Cells were used in killing assays with Nalm6-Luc cells at day 4 post-transduction and co-incubated at the indicated Effector:Target (E:T ratio; T cells) after normalizing for total cells and CAR+ cells. Results indicate that **FIG. 29B** specific killing activity and **FIG. 29C** interferon-gamma release during the co-incubation for 24 hours were comparable between CAR-MSR and CAR-free, showing that transduction by formulation with MSRs produces equivalently functional CARTs in vitro compared to conventional free virus transduction.

FIGs. 30A-30B demonstrate that MSR injectability was improved through size reduction by homogenization. MSRs were homogenized using a bead mixer to reduce their size and

improve injectability. In **FIG. 30A**, size reduction was seen in terms of MSR length, and this allowed injection through a smaller diameter needle into the intradermal space. In **FIG. 30A**, standard trimethylammonium MSRs or homogenized MSRs were adsorbed with lentivirus and a dilution series of this complex was created and used to transduce T cells with a GFP-encoding lentivirus. Homogenization of MSRs did not substantially alter transduction performance *in vitro*.

FIGs. 31A-31B depict an hematoxylin and eosin (H&E) stained section of skin containing adjacent cryogel and MSPs, in particular homogenized MSRs. Blank alginate cryogels were injected subcutaneously and 7 days later viral particles (4e6 TU) free or bound to MSRs were injected in the intradermal space on top of the gel with insulin syringe (for MSR-virus group) or Hamilton syringe (for free virus). 72h after viral delivery, mice were euthanized, and tissues (skin and draining lymph node) were harvested for immunohistochemistry analysis. To facilitate the delivery of VEGF-C to the lymphatic capillaries, the cryogel was implanted into the high subcutaneous space on top of the panniculus muscle. **FIG. 31A**, which depicts H&E stained sections, demonstrated the location of the subcutaneous cryogel superficial to the panniculus muscle in the hypodermis. The MSPs, in particular homogenized MSRs, appeared as lightly eosinophilic granular material admixed with mononuclear cells positioned at the dermal-hypodermal junction adjacent to the implanted cryogel (**FIG. 31A** and **FIG. 31B** for close up).

FIGs. 32A-32B show in situ hybridization for CAR mRNA on sections of skin. In situ hybridization to detect CAR mRNA transcript demonstrated robust signal within regions corresponding to the injected MSP, in particular homogenized MSR, in mice injected with MSR-bound virus (**FIG. 32A**), while it detected diffuse signal in cells infiltrating the gel, as well as cells adjacent to it in the free virus condition (**FIG. 32B**). Not to be bound by theory, Applicants believe these data support the notion that MSPs, in particular homogenized MSRs, may maintain the virus localized in the dermis where the T cells are infiltrating the skin.

FIGs. 33A-33B show a mouse injected with MSP-virus, in particular homogenized MSR-virus, had less CAR mRNA transcript positive cells in draining lymph node compared to free virus group. In situ hybridization for CAR mRNA on sections of draining lymph node (dLN). In situ hybridization detected only one CAR mRNA transcript positive cells within the dLN of mice injected with MSR-bound virus (**FIG. 33**A), while mice injected with free-virus

showed few CAR mRNA transcript positive cells in the subcapsular sinus consistent with local drainage of the virus or the cells from the site of cryogel implantation (**FIG. 33**B).

FIGs. 34A-34C show the generation of CD19+ CART cells in vivo and B cells depletion in the spleen. **FIG. 34A** provides a timeline for experimental setup of in vivo CART manufacturing. On day 0 VEGF-C loaded alginate cryogels were injected subcutaneously in NSG mice. On day 10 (3 days before we know peak lymphangiogeneiss is achieved), PBMCs are intravenously injected into mice and 7 days later (on day 17) MSP-virus (in particular homogenized MSR-virus), free-virus or PBS as control were injected in the respective groups together with MSP-STARTERS, in particular homogenized MSR-STARTERS, to possibly promote T cells activation and favor T cells transduction. On day 35 mice were euthanized and spleen, blood and can were collected to determine if in vivo CD19 CAR encoding viral delivery elicited transduction of T Cells recruited by VEGF-C induced lymphangiogenesis. **FIG. 34B** provides representative flow cytometry (FACS) plots of immune populations showing B cells depletion and T cells transduction (CD19 CAR+ cells) in the spleen of mice treated with free virus or MSP-virus, in particular homogenized MSR-virus. **FIG. 34C** is a quantification of B cells depletion and CAR-T cells in the spleen of the mice in all groups.

FIG. 35 demonstrates that minimal transduction of non-T cells by the composition. Provided are representative flow cytometry (FACS) plots of human CD11b+ monocytes, mouse monocytes (non-functional in NSG mouse), as well as stromal cells in the spleen of mice treated with free virus or MSP-virus, in particular homogenized MSR-virus, or PBS control. Few human monocytic cells showed a positive staining for CD 19 CAR.

FIGs. 36A-36B show B cell depletion correlates with CAR-T cell expansion in spleen and blood. In **FIG. 36A**, CART cells (total counts/mg tissue) are plotted versus B cells (total counts/mg tissue) in spleen, and, in **FIG. 36B**, CART cells (blood, represented as total cell counts/μl) are plotted versus B cell depletion (spleen, represented as total cell counts/mg tissue).

FIG. 37A-37C provide exemplary schema for bispecific antibodies, including single bispecific antibody schema (**FIG. 37A**), multimeric bispecific antibody schema (**FIG. 37B**), and a figure legend (**FIG. 37C**).

FIG. 38. T cells are recruited at the site of implant. FIG. 38 shows experimental setup (above) and representative image (below) of IHC analysis of CD3 on mouse skin receiving the cryogel-VEGF-C implant plus MSP-virus and MSP-STARTERS 18 days after viral delivery.

FIG. 39. CAR ISH signal in mononuclear cells surrounding the gel. FIG. 39 shows representative images of CAR ISH analysis (CD19 CAR RNA) of cells in mouse skin receiving the cryogel-VEGF-C implant plus MSP-virus and MSP-STARTERS 18 days after viral delivery.

FIG. 40. Locally in vivo generated CAR-T cells migrate to the spleen and correlate with B cell depletion. FIG. 40 is representative image of CAR ISH analysis of cells in mouse spleen receiving the cryogel-VEGF-C implant plus MSP-virus and MSP-STARTERS 18 days after viral delivery.

FIGs. 41A-41B. Generation of in vivo CAR- T cells correlates with B cells killing at the implant site and in the spleen. Representative image of fluorescently labelled CD19+ B cells and CD3+ T cells at the implant site (**FIG. 41A**, fluorescent image upper panel and brightfield image lower panel), as well as in the spleen (**FIG. 41B**) of mice receiving the cryogel-VEGF-C implant plus MSP-virus and MSP-STARTERS 18 days after viral delivery.

FIGs. 42A-42B. Analysis of circulating human T cells in NSG mice over time. FIG. 42A shows experimental design and groups. FIG. 42B is a set of graphs showing flow cytometry analysis over time of implanted mice. Flow cytometry data represented as Mean ± SEM.

FIGs. 43A-43B. B cell depletion in circulation correlates with CART cells expansion. Flow cytometry analysis over time of CART cells (**FIG. 43A**) and B cells (**FIG. 43B**) in the circulation of implanted mice. Flow cytometry data represented as Mean ± SEM (in **FIGs. 43A** and **43B**) or as individual curves for each mouse (**FIG. 43B**).

FIGs. 44A-44B. Strong correlation of CART cell expansion with B cell depletion in the circulation and in the spleen. Correlation of B cell number and T cell number in the blood (**FIG. 44A**) and in the spleen (**FIG. 44B**) of mice treated with the different conditions. Cell number represents cell counts/mg tissue or counts/µl for blood determined during flow cytometry analysis.

FIGs. 45A-45B. Quantification of CART cell expansion and corresponding B cell depletion in the spleen 18 days after viral delivery. Quantification of CART (**FIG. 45A**) and B cells (**FIG. 45B**) counts/mg tissue in the spleen of treated mice. Flow cytometry data represented as Mean ± SEM.

FIGs. 46A-46D. CART cell expansion correlates to lymphangiogenesis as well as local B cell depletion in the skin 18 days after viral delivery. Quantification of CART (**FIG. 46A**) and B cells (FIG. 46B) counts/mg tissue in the spleen of treated mice. Flow cytometry data represented

as Mean ± SEM. Correlation plot of B cell number and CART cell number (**FIG. 46C**) as well as CART cell number and lymphatic endothelial cell (LEC) number (**FIG. 46D**) in the skin. In correlation plots, cell numbers are represented as counts/mg tissue.

FIG. 47. GFP transgene expression as a function of MSP dose.

FIG. 48A-48B depicts schema of the 17 different multispecific constructs comprising a CD3 antigen binding domain comprising a heavy and light chain derived from an anti-CD3 antibody and, in all but control Constructs 11, 14, and 17, an a CD28 or CD2 antigen binding domain, as noted, comprising a heavy and light chain derived from an anti-CD28 or CD2 antibody, respectively. Not to be bound by theory, it is appreciated that any one or more of these constructs may be used as a cell activation agent as disclosed herein.

Construct 1 comprises an anti-CD3 scFv fused to an anti-CD2 Fab, which is further fused to an Fc region. Construct 1 comprises a first chain and a second chain. The first chain comprises, from the N-terminus to the C-terminus, anti-CD2 VL and CL. The second chain comprises, from the N-terminus to the C-terminus, anti-CD3 VH, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VL, (G4S)4 linker (SEQ ID NO: 29), anti-CD2 VH, CH1, CH2, and CH3. Construct 2 comprises an anti-CD3 scFv fused to an anti-CD28 Fab, which is further fused to an Fc region. Construct 2 comprises a first chain and a second chain. The first chain comprises, from the N-terminus to the C-terminus, anti-CD28 VL and CL. The second chain comprises, from the N-terminus to the C-terminus, anti-CD3 VH, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VL, (G4S)4 linker (SEQ ID NO: 29), anti-CD28 VH, CH1, CH2, and CH3.

Construct 3 comprises an anti-CD2 Fab fused to an Fc region, which is further fused to an anti-CD3 scFv. Construct 3 comprises a first chain and a second chain. The first chain comprises, from the N-terminus to the C-terminus, anti-CD2 VL and CL. The second chain comprises, from the N-terminus to the C-terminus, anti-CD2 VH, CH1, CH2, CH3, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VH, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VL. Construct 4 comprises an anti-CD28 Fab fused to an Fc region, which is further fused to an anti-CD3 scFv. Construct 4 comprises a first chain and a second chain. The first chain comprises, from the N-terminus to the C-terminus, anti-CD28 VL and CL. The second chain comprises, from the N-terminus to the C-terminus, anti-CD28 VH, CH1, CH2, CH3, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VH, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VL.

Construct 5 comprises an anti-CD2 Fab fused to an anti-CD3 scFv, which is further fused to an Fc region. Construct 5 comprises a first chain and a second chain. The first chain comprises, from the N-terminus to the C-terminus, anti-CD2 VL and CL. The second chain comprises, from the N-terminus to the C-terminus, anti-CD2 VH, CH1, (G4S)2 linker (SEQ ID NO: 767), anti-CD3 VH, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VL, (G4S)4 linker (SEQ ID NO: 29), CH2, and CH3. Construct 6 comprises an anti-CD28 Fab fused to an anti-CD3 scFv, which is further fused to an Fc region. Construct 6 comprises a first chain and a second chain. The first chain comprises, from the N-terminus to the C-terminus, anti-CD28 VL and CL. The second chain comprises, from the N-terminus to the C-terminus, anti-CD28 VH, CH1, (G4S)2 linker (SEQ ID NO: 767), anti-CD3 VH, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VL, (G4S)4 linker (SEQ ID NO: 29), CH2, and CH3.

Construct 7 comprises an anti-CD3 scFv fused to an Fc region, which is further fused to an anti-CD2 Fab. Construct 7 comprises a first chain and a second chain. The first chain comprises, from the N-terminus to the C-terminus, anti-CD2 VL and CL. The second chain comprises, from the N-terminus to the C-terminus, anti-CD3 VH, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VL, (G4S) linker (SEQ ID NO: 768), CH2, CH3, (G4S)4 linker (SEQ ID NO: 29), anti-CD2 VH, and CH1. Construct 8 comprises an anti-CD3 scFv fused to an Fc region, which is further fused to an anti-CD28 Fab. Construct 8 comprises a first chain and a second chain. The first chain comprises, from the N-terminus to the C-terminus, anti-CD28 VL and CL. The second chain comprises, from the N-terminus to the C-terminus, anti-CD3 VH, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VL, (G4S) linker (SEQ ID NO: 768), CH2, CH3, (G4S)4 linker (SEQ ID NO: 29), anti-CD28 VH, and CH1.

Construct 9 comprises an anti-CD2 Fab fused to a first Fc region and an anti-CD3 scFv fused to a second Fc region. Construct 9 comprises a first chain, a second chain, and a third chain. The first chain comprises, from the N-terminus to the C-terminus, anti-CD2 VL and CL. The second chain comprises, from the N-terminus to the C-terminus, anti-CD2 VH, CH1, CH2, and CH3. The third chain comprises, from the N-terminus to the C-terminus, anti-CD3 VH, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VL, (G4S) linker (SEQ ID NO: 768), CH2, and CH3. Construct 10 comprises an anti-CD28 Fab fused to a first Fc region and an anti-CD3 scFv fused to a second Fc region. Construct 10 comprises a first chain, a second chain, and a third chain. The first chain comprises, from the N-terminus to the C-terminus, anti-CD28 VL and CL. The

second chain comprises, from the N-terminus to the C-terminus, anti-CD28 VH, CH1, CH2, and CH3. The third chain comprises, from the N-terminus to the C-terminus, anti-CD3 VH, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VL, (G4S) linker (SEQ ID NO: 768), CH2, and CH3.

Construct 11 comprises an anti-CD3 scFv fused to an Fc region. Construct 11 comprises a first chain and a second chain. The first chain comprises, from the N-terminus to the C-terminus, CH2 and CH3. The second chain comprises, from the N-terminus to the C-terminus, anti-CD3 VH, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VL, (G4S) linker (SEQ ID NO: 768), CH2, and CH3.

Construct 12 comprises an anti-CD2 Fab fused to a first Fc region and an anti-CD3 scFv fused to a second Fc region. Construct 12 comprises a first chain, a second chain, and a third chain. The first chain comprises, from the N-terminus to the C-terminus, anti-CD2 VL and CL. The second chain comprises, from the N-terminus to the C-terminus, anti-CD2 VH, CH1, CH2, and CH3. The third chain comprises, from the N-terminus to the C-terminus, anti-CD3 VH, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VL, (G4S) linker (SEQ ID NO: 768), CH2, CH3, (G4S)3 linker (SEQ ID NO: 30), and Matrilin1. Construct 13 comprises an anti-CD28 Fab fused to a first Fc region and an anti-CD3 scFv fused to a second Fc region. Construct 13 comprises a first chain, a second chain, and a third chain. The first chain comprises, from the N-terminus to the C-terminus, anti-CD28 VL and CL. The second chain comprises, from the N-terminus to the C-terminus, anti-CD28 VH, CH1, CH2, and CH3. The third chain comprises, from the N-terminus to the C-terminus, anti-CD3 VH, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VL, (G4S) linker (SEQ ID NO: 768), CH2, CH3, (G4S)3 linker (SEQ ID NO: 30), and Matrilin1.

Construct 14 comprises an anti-CD3 scFv fused to an Fc region. Construct 14 comprises a first chain and a second chain. The first chain comprises, from the N-terminus to the C-terminus, CH2 and CH3. The second chain comprises, from the N-terminus to the C-terminus, anti-CD3 VH, (G4S)4, linker (SEQ ID NO: 29), anti-CD3 VL, (G4S) linker (SEQ ID NO: 768), CH2, CH3, (G4S)3 linker (SEQ ID NO: 30), and Matrilin1.

Construct 15 comprises an anti-CD2 Fab fused to a first Fc region and an anti-CD3 scFv fused to a second Fc region. Construct 15 comprises a first chain, a second chain, and a third chain. The first chain comprises, from the N-terminus to the C-terminus, anti-CD2 VL and CL. The second chain comprises, from the N-terminus to the C-terminus, anti-CD2 VH, CH1, CH2, and CH3. The third chain comprises, from the N-terminus to the C-terminus, anti-CD3 VH,

(G4S)4 linker (SEQ ID NO: 29), anti-CD3 VL, (G4S) linker (SEQ ID NO: 768), CH2, CH3, (G4S) linker (SEQ ID NO: 768), and the coiled-coil domain of cartilage oligomeric matrix protein (COMPcc). Construct 16 comprises an anti-CD28 Fab fused to a first Fc region and an anti-CD3 scFv fused to a second Fc region. Construct 16 comprises a first chain, a second chain, and a third chain. The first chain comprises, from the N-terminus to the C-terminus, anti-CD28 VL and CL. The second chain comprises, from the N-terminus to the C-terminus, anti-CD28 VH, CH1, CH2, and CH3. The third chain comprises, from the N-terminus to the C-terminus, anti-CD3 VH, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VL, (G4S) linker (SEQ ID NO: 768), CH2, CH3, (G4S) linker (SEQ ID NO: 768), and COMPcc.

Construct 17 comprises an anti-CD3 scFv fused to an Fc region. Construct 17 comprises a first chain and a second chain. The first chain comprises, from the N-terminus to the C-terminus, CH2 and CH3. The second chain comprises, from the N-terminus to the C-terminus, anti-CD3 VH, (G4S)4 linker (SEQ ID NO: 29), anti-CD3 VL, (G4S) linker (SEQ ID NO: 768), CH2, CH3, (G4S) linker (SEQ ID NO: 768), and COMPcc.

Exemplary sequences of Construct 1 to Construct 17 are provided in Table 20. Additional sequences (e.g., the anti-CD3 binders disclosed herein, the anti-CD28 binders disclosed herein, the anti-CD2 binders disclosed herein, or the Fc regions disclosed herein) can be used to generate Construct 1 to Construct 17.

FIGs. 49A-49B shows the binding information (**FIG. 49A**) and configuration (**FIG. 49B**) of second generation STARTERS molecules. "F5 ANTI-CD3 (2)" refers to an F5 construct with an anti-CD3 binder based on ANTI-CD3 (2).

FIGs. 50A-50B show the binder information (**FIG. 50A**) and configuration (**FIG. 50B**) of third generation STARTERS molecules.

FIG. 51A shows the configuration of the STARTERS molecule tested in Example J. **FIGs. 51B and 51C** show T cell activation and transduction mediated by MSP-lentivirus-STARTERS mixtures. The concentration of the STARTERS molecule in each dilution of the MSP-lentivirus-STARTERS mixture is shown on the x-axis. The formulations generated from both MSP batches yielded similar T cell activation (FIG. 51B) and transduction (FIG. 51C) efficiencies in vitro. Delivering the STARTERS molecule bound to MSPs ("Batch 1" and "Batch 2" in FIGs. 51B-C) enhanced activation and transduction as compared to soluble delivery of the STARTERS molecule ("No MSP" in FIGs. 51B-C). Day 1 in FIG. 51B and Day 4 in FIG. 51C

refer to the time after the start of the T cell culture (i.e., when the cells and MSP-STARTERS-virus were initially mixed together).

FIGs. 52A and 52B show T cell activation and transduction mediated by MSP-lentivirus-STARTERS mixtures. GFP-encoding lentivirus and the STARTERS molecule were loaded onto full-size ("MSP") or size-reduced MSPs, where size reduction was achieved using bead homogenization ("Bead homogenized") or sonication ("Sonicated") of MSPs. The ratio of lentivirus to T cells (MOI) in each dilution of the MSP-lentivirus-STARTERS mixture is shown on the x-axis. Size reduction of MSPs did not negatively impact in vitro potency with respect to T cell activation (FIG. 52A) and transduction (FIG. 52B). Both bead homogenization and sonication yielded comparable results to the full-sized MSPs.

FIGs. 53A and 53B show the design of the in vivo study. **FIG. 53C** is a correlation plot between CD19 CAR-T expansion and B cell depletion in the blood of mice at day 18 post-injectable 2 injection. **FIG. 53D** shows bioluminescence measurements of luciferase-expressing NALM6 tumors engrafted into NSG mice for 4 days, and then treated with a dose of 3e5 adoptively transferred CAR+ T cells from an initial cohort of mice undergoing the in vivo CART generation process. Images are from 13 days post-adoptive transfer. Mice were treated with a dose of 3e5 CAR-Ts manufactured using free virus ("Free virus") or MSP-delivered virus ("MSP virus"). Also shown are control groups where tumors were treated with transferred PBMCs from donor mice with no CARTs ("PBMC control") or where tumors were not untreated ("NALM6"). The mouse labeled "a" received 1.5e5 CAR+ cells from the free virus group. The mouse labeled "b" received 2.3e5 CAR+ cells from the free virus group. **FIGs. 53E, 53F, and 53G** are plots showing CART% of total T cells in circulation (FIG. 53E), the amount of CARTs in circulation (FIG. 53F), and the amount of circulating CD3+ T cells (FIG. 53G) 13 days after intradermal injection of injectable 2 at the cryogel site. **FIGs. 53H, 53I, and 53J** are plots of mice selected for circulating lymphocyte adoptive transfer into NALM6 challenged mice, showing the amount of circulating T cells (FIG. 53H), the amount of circulating CART cells (FIG. 53I), and CART% of total T cells in circulation (FIG. 53J) 18 days after intradermal injection of injectable 2. **FIGs. 53K and 53L** show results from combined flow cytometry analysis of blood from mice used for adoptive transfer and remaining mice enrolled in the study, showing the amount of circulating T cells (FIG. 53K) and the amount of CART cells in circulation (FIG. 53L) 18 or 19 days after intradermal injection of injectable 2.

FIGs. 54A, 54B, 54C, and 54D are graphs showing in vitro release data. FIG. 54A shows data for H2a hydogel (200 kDa [HA-N_3]-24%; 9% crosslinked) and H4a hydrogel (700kDa [HA-N_3]-16%; 18% crosslinked). FIG. 54B shows data for H4a hydrogel (700kDa [HA-N_3]-16%; 18% crosslinked; no laponite), H5a hydrogel (700kDa [HA-N_3]-16%; 18% crosslinked; 0.25 mg/ml laponite), and H6a hydrogel (700kDa [HA-N_3]-16%; 18% crosslinked; 1 mg/ml laponite). FIG. 54C shows data for H5a hydrogel (in situ; 0.25 mg/ml laponite) and H5b hydrogel (particles; 0.25 mg/ml laponite). FIG. 54D shows data for H6a hydrogel (in situ; 1 mg/ml laponite) and H6b hydrogel (particles; 1 mg/ml laponite).

FIGs. 55A and 55B are graphs showing in vivo PD response at day 7.

DETAILED DESCRIPTION

Definitions

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 the invention pertains.

The term "a" and "an" refers to one or to more than one (i.e., to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

The term "about" when referring to a measurable value such as an amount, a temporal duration, and the like, is meant to encompass variations of ±20% or in some instances ±10%, or in some instances ±5%, or in some instances ±1%, or in some instances ±0.1% from the specified value, as such variations are appropriate to perform the disclosed methods.

As used herein, the term "cell recruitment factor" refers to an agent capable of recruiting cells, for example immune cells. Non-limiting examples of such recruitment factors include IL-2, IL-7, CCL21, IL 5, GM-CSF, CCL19, CXCL9, CXCL10, XCL1, lymphotoxin alpha, lymphotoxin beta, and VEGF-C. Such factors are known to recruit immune cells, such as T-cells. Further non-limiting examples of cell recruitment factors that recruit specific cell types include skin homing chemokines such as but not limited to CCL17, CCL22, CCL20, and CCL27; myeloid cell chemoattractants such as but not limited to FLT3L, G-CSF, PDGF, S100A8/A9, CSF-1, CXCL8, CCL20, CCL17, CCR5, CCR6, CCL2, VEGF, Angiopoietin-2, CXCL12, PGE2, and

LTB4; and NK-specific recruitment factors such as but not limited to CXC3L1, CCL19, CCL21, CXCL10, CXCL11, and CXCL12

As used herein, the term "cell activation agent" refers to an agent capable of activating a cell to perform a given function – for example, with T-cells, engagement of endogenous or engineered receptors (e.g., a CAR) or cell-surface markers activate T-cells to proliferate and, in certain cases, secrete appropriate cytokines.

The term "Chimeric Antigen Receptor" or alternatively a "CAR" refers to a recombinant polypeptide construct comprising at least an extracellular antigen binding domain, a transmembrane domain and a cytoplasmic signaling domain (also referred to herein as "an intracellular signaling domain") comprising a functional signaling domain derived from a stimulatory molecule as defined below. In some embodiments, the domains in the CAR polypeptide construct are in the same polypeptide chain, e.g., comprise a chimeric fusion protein. In some embodiments, the domains in the CAR polypeptide construct are not contiguous with each other, e.g., are in different polypeptide chains, e.g., as provided in an RCAR as described herein.

In some aspects, the cytoplasmic signaling domain comprises a primary signaling domain (e.g., a primary signaling domain of CD3-zeta). In some aspects, the cytoplasmic signaling domain further comprises one or more functional signaling domains derived from at least one costimulatory molecule as defined below. In some aspects, the costimulatory molecule is chosen from 41BB (i.e., CD137), CD27, ICOS, and/or CD28. In some aspects, the CAR comprises a chimeric fusion protein comprising an extracellular antigen recognition domain, a transmembrane domain and an intracellular signaling domain comprising a functional signaling domain derived from a stimulatory molecule. In some aspects, the CAR comprises a chimeric fusion protein comprising an extracellular antigen recognition domain, a transmembrane domain and an intracellular signaling domain comprising a functional signaling domain derived from a co-stimulatory molecule and a functional signaling domain derived from a stimulatory molecule. In some aspects, the CAR comprises a chimeric fusion protein comprising an extracellular antigen recognition domain, a transmembrane domain and an intracellular signaling domain comprising two functional signaling domains derived from one or more co-stimulatory molecule(s) and a functional signaling domain derived from a stimulatory molecule. In some aspects, the CAR comprises a chimeric fusion protein comprising an extracellular antigen

recognition domain, a transmembrane domain and an intracellular signaling domain comprising at least two functional signaling domains derived from one or more co-stimulatory molecule(s) and a functional signaling domain derived from a stimulatory molecule. In some aspects the CAR comprises an optional leader sequence at the amino-terminus (N-ter) of the CAR fusion protein. In some aspects, the CAR further comprises a leader sequence at the N-terminus of the extracellular antigen recognition domain, wherein the leader sequence is optionally cleaved from the antigen recognition domain (e.g., an scFv) during cellular processing and localization of the CAR to the cellular membrane.

A CAR that comprises an antigen binding domain (e.g., an scFv, a single domain antibody, or TCR (e.g., a TCR alpha binding domain or TCR beta binding domain)) that targets a specific tumor marker X, wherein X can be a tumor marker as described herein, is also referred to as XCAR. For example, a CAR that comprises an antigen binding domain that targets BCMA is referred to as BCMA CAR. The CAR can be expressed in any cell, e.g., an immune effector cell as described herein (e.g., a T cell or an NK cell).

The term "signaling domain" refers to the functional portion of a protein which acts by transmitting information within the cell to regulate cellular activity via defined signaling pathways by generating second messengers or functioning as effectors by responding to such messengers.

The term "antibody," as used herein, refers to a protein, or polypeptide sequence derived from an immunoglobulin molecule which specifically binds with an antigen. Antibodies can be polyclonal or monoclonal, multiple or single chain, or intact immunoglobulins, and may be derived from natural sources or from recombinant sources. Antibodies can be tetramers of immunoglobulin molecules.

The term "antibody fragment" refers to at least one portion of an antibody, that retains the ability to specifically interact with (e.g., by binding, steric hindrance, stabilizing/destabilizing, spatial distribution) an epitope of an antigen. Examples of antibody fragments include, but are not limited to, Fab, Fab', F(ab')2, Fv fragments, scFv antibody fragments, disulfide-linked Fvs (sdFv), a Fd fragment consisting of the VH and CH1 domains, linear antibodies, single domain antibodies such as sdAb (either VL or VH), camelid VHH domains, multi-specific antibodies formed from antibody fragments such as a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region, and an isolated CDR or other epitope binding

fragments of an antibody. An antigen binding fragment can also be incorporated into single domain antibodies, maxibodies, minibodies, nanobodies, intrabodies, diabodies, triabodies, tetrabodies, v-NAR and bis-scFv (see, e.g., Hollinger and Hudson, *Nature Biotechnology* 23:1126-1136, 2005). Antigen binding fragments can also be grafted into scaffolds based on polypeptides such as a fibronectin type III (Fn3) (see U.S. Patent No.: 6,703,199, which describes fibronectin polypeptide minibodies).

The portion of the CAR of the invention comprising an antibody or antibody fragment thereof may exist in a variety of forms where the antigen binding domain is expressed as part of a contiguous polypeptide chain including, for example, a single domain antibody fragment (sdAb), a single chain antibody (scFv), a humanized antibody or bispecific antibody (Harlow et al., 1999, In: Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, NY; Harlow et al., 1989, In: Antibodies: A Laboratory Manual, Cold Spring Harbor, New York; Houston et al., 1988, Proc. Natl. Acad. Sci. USA 85:5879-5883; Bird et al., 1988, Science 242:423-426). In some aspects, the antigen binding domain of a CAR composition of the invention comprises an antibody fragment. In a further aspect, the CAR comprises an antibody fragment that comprises a scFv. The precise amino acid sequence boundaries of a given CDR can be determined using any of a number of well-known schemes, including those described by Kabat et al. (1991), "Sequences of Proteins of Immunological Interest," 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD ("Kabat" numbering scheme), Al-Lazikani et al., (1997) JMB 273,927-948 ("Chothia" numbering scheme), or a combination thereof.

As used herein, the term "binding domain" or "antibody molecule" refers to a protein, e.g., an immunoglobulin chain or fragment thereof, comprising at least one immunoglobulin variable domain sequence. The term "binding domain" or "antibody molecule" encompasses antibodies and antibody fragments. In some embodiments, an antibody molecule is a multispecific antibody molecule, e.g., it comprises a plurality of immunoglobulin variable domain sequences, wherein a first immunoglobulin variable domain sequence of the plurality has binding specificity for a first epitope and a second immunoglobulin variable domain sequence of the plurality has binding specificity for a second epitope. In some embodiments, a multispecific antibody molecule is a bispecific antibody molecule. A bispecific antibody has specificity for no more than two antigens. A bispecific antibody molecule is characterized by a first immunoglobulin variable domain sequence which has binding specificity for a first epitope and a

second immunoglobulin variable domain sequence that has binding specificity for a second epitope.

The terms "bispecific antibody" and "bispecific antibodies" refer to molecules that combine the antigen binding sites of two antibodies within a single molecule. Thus, a bispecific antibody is able to bind two different antigens simultaneously or sequentially. Methods for making bispecific antibodies are well known in the art. Various formats for combining two antibodies are also known in the art. Forms of bispecific antibodies of the invention include, but are not limited to, a diabody, a single-chain diabody, Fab dimerization (Fab-Fab), Fab-scFv, and a tandem antibody, as known to those of skill in the art.

The term "antibody heavy chain," refers to the larger of the two types of polypeptide chains present in antibody molecules in their naturally occurring conformations, and which normally determines the class to which the antibody belongs.

The term "antibody light chain," refers to the smaller of the two types of polypeptide chains present in antibody molecules in their naturally occurring conformations. Kappa (κ) and lambda (λ) light chains refer to the two major antibody light chain isotypes.

The term "recombinant antibody" refers to an antibody which is generated using recombinant DNA technology, such as, for example, an antibody expressed by a bacteriophage or yeast expression system. The term should also be construed to mean an antibody which has been generated by the synthesis of a DNA molecule encoding the antibody and which DNA molecule expresses an antibody protein, or an amino acid sequence specifying the antibody, wherein the DNA or amino acid sequence has been obtained using recombinant DNA or amino acid sequence technology which is available and well known in the art.

The term "antigen" or "Ag" refers to a molecule that provokes an immune response. This immune response may involve either antibody production, or the activation of specific immunologically competent cells, or both. The skilled artisan will understand that any macromolecule, including virtually all proteins or peptides, can serve as an antigen. Furthermore, antigens can be derived from recombinant or genomic DNA. A skilled artisan will understand that any DNA, which comprises a nucleotide sequences or a partial nucleotide sequence encoding a protein that elicits an immune response, therefore encodes an "antigen" as that term is used herein. Furthermore, one skilled in the art will understand that an antigen need not be encoded solely by a full-length nucleotide sequence of a gene. It is readily apparent that the

present invention includes, but is not limited to, the use of partial nucleotide sequences of more than one gene and that these nucleotide sequences are arranged in various combinations to encode polypeptides that elicit the desired immune response. Moreover, a skilled artisan will understand that an antigen need not be encoded by a "gene" at all. It is readily apparent that an antigen can be synthesized or can be derived from a biological sample or might be a macromolecule besides a polypeptide. Such a biological sample can include, but is not limited to a tissue sample, a tumor sample, a cell or a fluid with other biological components.

The term "multispecific binding molecule" refers to a molecule that specifically binds to at least two antigens and comprise two or more antigen-binding domains. The antigen-binding domains can each independently be an antibody fragment (*e.g.*, scFv, Fab, nanobody), a ligand, or a non-antibody derived binder (*e.g.*, fibronectin, Fynomer, DARPin).

The term "monovalent" as used herein in the context of a multispecific binding molecule, antibody (e.g., bispecific antibody), or antibody fragment refers to a multispecific binding molecule, antibody (e.g., bispecific antibody), or antibody fragment in which there is a single antigen binding domain for each antigen to which the multispecific binding molecule, antibody (e.g., bispecific antibody), or antibody fragment binds.

The term "bivalent" as used herein in the context of a multispecific binding molecule, antibody (e.g., bispecific antibody), or antibody fragment refers to a multispecific binding molecule, antibody (e.g., bispecific antibody), or antibody fragment in which there is are two antigen binding domains for each antigen to which the multispecific binding molecule, antibody (e.g., bispecific antibody), or antibody fragment binds.

The term "multimer" refers to an aggregate of a plurality of molecules (such as but not limited to antibodies (e.g. bispecific antibodies), optionally conjugated to one another.

The term "anti-cancer effect" refers to a biological effect which can be manifested by various means, including but not limited to, e.g., a decrease in tumor volume, a decrease in the number of cancer cells, a decrease in the number of metastases, an increase in life expectancy, decrease in cancer cell proliferation, decrease in cancer cell survival, or amelioration of various physiological symptoms associated with the cancerous condition. An "anti-cancer effect" can also be manifested by the ability of the peptides, polynucleotides, cells and antibodies in prevention of the occurrence of cancer in the first place. The term "anti-tumor effect" refers to a biological effect which can be manifested by various means, including but not limited to, e.g., a

decrease in tumor volume, a decrease in the number of tumor cells, a decrease in tumor cell proliferation, or a decrease in tumor cell survival.

The term "autologous" refers to any material derived from the same individual to whom it is later to be re-introduced into the individual.

The term "allogeneic" refers to any material derived from a different animal of the same species as the individual to whom the material is introduced. Two or more individuals are said to be allogeneic to one another when the genes at one or more loci are not identical. In some aspects, allogeneic material from individuals of the same species may be sufficiently unlike genetically to interact antigenically.

The term "xenogeneic" refers to a graft derived from an animal of a different species.

The term "cancer" refers to a disease characterized by the uncontrolled growth of aberrant cells. Cancer cells can spread locally or through the bloodstream and lymphatic system to other parts of the body. Examples of various cancers are described herein and include but are not limited to, breast cancer, prostate cancer, ovarian cancer, cervical cancer, skin cancer, pancreatic cancer, colorectal cancer, renal cancer, liver cancer, brain cancer, lymphoma, leukemia, lung cancer and the like. The terms "tumor" and "cancer" are used interchangeably herein, e.g., both terms encompass solid and liquid, e.g., diffuse or circulating, tumors. As used herein, the term "cancer" or "tumor" includes premalignant, as well as malignant cancers and tumors.

As described herein, "conjugated to" means associated with or attached to by any means as described herein, optionally covalently or non-covalently and/or directly or via linker.

"Derived from" as that term is used herein, indicates a relationship between a first and a second molecule. It generally refers to structural similarity between the first molecule and a second molecule and does not connotate or include a process or source limitation on a first molecule that is derived from a second molecule. For example, in the case of an intracellular signaling domain that is derived from a CD3zeta molecule, the intracellular signaling domain retains sufficient CD3zeta structure such that it has the required function, namely, the ability to generate a signal under the appropriate conditions. It does not connotate or include a limitation to a particular process of producing the intracellular signaling domain, e.g., it does not mean that, to provide the intracellular signaling domain, one must start with a CD3zeta sequence and delete unwanted sequence, or impose mutations, to arrive at the intracellular signaling domain.

The phrase "disease associated with expression of a tumor antigen as described herein" includes, but is not limited to, a disease associated with expression of a tumor antigen as described herein or condition associated with cells which express a tumor antigen as described herein including, e.g., proliferative diseases such as a cancer or malignancy or a precancerous condition such as a myelodysplasia, a myelodysplastic syndrome or a preleukemia; or a noncancer related indication associated with cells which express a tumor antigen as described herein. In some aspects, a cancer associated with expression of a tumor antigen as described herein is a hematological cancer. In some aspects, a cancer associated with expression of a tumor antigen as described herein is a solid cancer. Further diseases associated with expression of a tumor antigen described herein include, but not limited to, e.g., atypical and/or non-classical cancers, malignancies, precancerous conditions or proliferative diseases associated with expression of a tumor antigen as described herein. Non-cancer related indications associated with expression of a tumor antigen as described herein include, but are not limited to, e.g., autoimmune disease, (e.g., lupus), inflammatory disorders (allergy and asthma) and transplantation. In some embodiments, the tumor antigen-expressing cells express, or at any time expressed, mRNA encoding the tumor antigen. In some embodiments, the tumor antigen -expressing cells produce the tumor antigen protein (e.g., wild-type or mutant), and the tumor antigen protein may be present at normal levels or reduced levels. In some embodiments, the tumor antigen -expressing cells produced detectable levels of a tumor antigen protein at one point, and subsequently produced substantially no detectable tumor antigen protein.

The term "stimulation," refers to a primary response induced by binding of a stimulatory molecule (e.g., a TCR/CD3 complex or CAR) with its cognate ligand (or tumor antigen in the case of a CAR) thereby mediating a signal transduction event, such as, but not limited to, signal transduction via the TCR/CD3 complex or signal transduction via the appropriate NK receptor or signaling domains of the CAR. Stimulation can mediate altered expression of certain molecules.

The term "stimulatory molecule," refers to a molecule expressed by an immune cell (e.g., T cell, NK cell, B cell) that provides the cytoplasmic signaling sequence(s) that regulate activation of the immune cell in a stimulatory way for at least some aspect of the immune cell signaling pathway. In some aspects, the signal is a primary signal that is initiated by, for instance, binding of a TCR/CD3 complex with an MHC molecule loaded with peptide, and which leads to mediation of a T cell response, including, but not limited to, proliferation,

activation, differentiation, and the like. A primary cytoplasmic signaling sequence (also referred to as a "primary signaling domain") that acts in a stimulatory manner may contain a signaling motif which is known as immunoreceptor tyrosine-based activation motif or ITAM. Examples of an ITAM containing-cytoplasmic signaling sequence that is of particular use in the invention include, but are not limited to, those derived from CD3 zeta, common FcR gamma (FCER1G), Fc gamma RIIa, FcR beta (Fc Epsilon R1b), CD3 gamma, CD3 delta, CD3 epsilon, CD79a, CD79b, DAP10, and DAP12. In a specific CAR of the invention, the intracellular signaling domain in any one or more CARS of the invention comprises an intracellular signaling sequence, e.g., a primary signaling sequence of CD3-zeta. In a specific CAR of the invention, the primary signaling sequence of CD3-zeta is a sequence provided as SEQ ID NO: 18, or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like. In a specific CAR of the invention, the primary signaling sequence of CD3-zeta is the sequence as provided in SEQ ID NO:20, or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape, and the like.

The term "Fc silent" refers to an Fc domain that has been modified to have minimal interaction with effector cells. Silenced effector functions may be obtained by mutation in the Fc region of the antibodies and have been described in the art, such as, but not limited to, LALA and N297A (Strohl, W., 2009, Curr. Opin. Biotechnol. vol. 20(6):685-691); and D265A (Baudino et al., 2008, J. Immunol. 181: 6664- 69) see also Heusser et al., WO2012065950. Examples of Fc silencing mutations include the LALA mutant comprising L234A and L235A mutation in the IgG1 Fc amino acid sequence, DAPA (D265A, P329A) (see, *e.g.*, US 6,737,056), N297A, DANAPA (D265A, N297A, and P329A), and/or LALADANAPS (L234A, L235A, D265A, N297A and P331S), numbered according to the Eu numbering system. Further, non-limiting exemplary embodiments of silencing mutations include LALAGA (L234A, L235A, and G237A), LALASKPA (L234A, L235A, S267K, and P329A), DAPASK (D265A, P329A, and S267K), GADAPA (G237A, D265A, and P329A), GADAPASK (G237A, D265A, P329A, and S267K), LALAPG (L234A, L235A, and P329G), and LALAPA (L234A, L235A, and P329A), numbered according to the Eu numbering system. Unless otherwise specified herein, numbering of amino acid residues in the Fc region or constant region is according to the Eu numbering system, also called the Eu index, as described in Kabat,

et al., Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991).

The term "CD3/TCR complex" refers to a complex on the T-cell surface comprising a TCR with including a TCR alpha and TCR beta chain; CD3 including one CD3 gamma chain, one CD3 delta chain, and two CD3 epsilon chains; and a zeta domain. UniProt accession numbers P01848 (TCR alpha, constant domain), P01850 (TCR beta, constant domain 1), A0A5B9 (TCR beta, constant domain 2), P09693 (CD3 gamma), P04234 (CD3 delta), P07766 (CD3 epsilon) provide exemplary human sequences for these chains, with the exception of the zeta chain, responsible for intracellular signaling, which is discussed in further detail below. Further relevant accession numbers include A0A075B662 (murine TCR alpha, constant domain), A0A0A6YWV4 and/or A0A075B5J3 (murine TCR beta, constant domain 1), A0A075B5J4 (murine TCR beta, constant domain 2), P11942 (murine CD3 gamma), P04235 (murine CD3 delta), P22646 (murine CD3 epsilon).

The term "CD28" refers to a T-cell specific glycoprotein CD28, also referred to as Tp44, as well as all alternate names thereof, which functions as a costimulatory molecule. UniProt accession number P10747 provides exemplary human CD28 amino acid sequences (see also HGNC: 1653, Entrez Gene: 940, Ensembl: ENSG00000178562, and OMIM: 186760). Further relevant CD28 sequences include UniProt accession number P21041 (murine CD28).

The term "ICOS" refers to inducible T-cell costimulator, also referred to as AILIM, CVID1, CD278, as well as all alternate names thereof, which functions as a costimulatory molecule. UniProt accession number Q9Y6W8 provides exemplary human ICOS amino acid sequences (see also HGNC: 5351, Entrez Gene: 29851, Ensembl: ENSG00000163600, and OMIM: 604558). Further relevant ICOS sequences include UniProt accession number Q9WVS0 (murine ICOS).

The term "CD27" refers to T-cell activation antigen CD27, Tumor necrosis factor receptor superfamily member 7, T14, T-cell activation antigen S152, Tp55, as well as alternate names thereof, which functions as a costimulatory molecule. UniProt accession number P26842 provides exemplary human CD27 amino acid sequences (see also HGNC: 11922, Entrez Gene: 939, Ensembl: ENSG00000139193, and OMIM: 186711). Further relevant CD27 sequences include UniProt accession number P41272 (murine CD27).

The term "CD25" refers to IL-2 subunit alpha, TAC antigen, p55, insulin dependent diabetes mellitus 10, IMD21, P55, TCGFR, as well as alternate names thereof, which functions as a growth factor receptor. UniProt accession number P01589 provides exemplary human CD25 amino acid sequences (see also HGNC: 6008, Entrez Gene: 3559, Ensembl: ENSG00000134460, and OMIM: 147730). Further relevant CD25 sequences include UniProt accession number P01590 (murine CD25).

The term "4-1BB" refers to CD137 or Tumor necrosis factor receptor superfamily member 9, as well as alternate names thereof, which functions as a costimulatory molecule. UniProt accession number Q07011 provides exemplary human 4-1BB amino acid sequences (see also HGNC: 11924, Entrez Gene: 3604, Ensembl: ENSG00000049249, and OMIM: 602250). Further relevant 4-1BB sequences include UniProt accession number P20334 (murine 4-1BB).

The term "IL6RA" refers to IL-6 receptor subunit alpha or CD126, as well as alternate names thereof, which functions as a growth factor receptor. UniProt accession number P08887 provides exemplary human IL6RA amino acid sequences (see also HGNC: 6019, Entrez Gene: 3570, Ensembl: ENSG00000160712, and OMIM: 147880 Further relevant IL6RA sequences include UniProt accession number P22272 (murine IL6RA).

The term "IL6RB" refers to IL-6 receptor subunit beta or CD130, as well as alternate names thereof, which functions as a growth factor receptor. UniProt accession number P40189 provides exemplary human IL6RB amino acid sequences. Further relevant IL6RB sequences include UniProt accession number Q00560 (murine IL6RB).
The term "CD2" refers to T-cell surface antigen T11/Leu-5/CD2, lymphocyte function antigen 2, T11, or erythrocyte/rosette/LFA-3 receptor, as well as alternate names thereof, , which functions as a growth factor receptor. UniProt accession number P06729 provides exemplary human CD2 amino acid sequences (see also HGNC: 1639, Entrez Gene: 914, Ensembl: ENSG00000116824, and OMIM: 186990). Further relevant CD2 sequences include UniProt accession number P08920 (murine CD2).

The term "antigen presenting cell" or "APC" refers to an immune system cell such as an accessory cell (e.g., a B-cell, a dendritic cell, and the like) that displays a foreign antigen complexed with major histocompatibility complexes (MHC□s) on its surface. T-cells may

recognize these complexes using their T-cell receptors (TCRs). APCs process antigens and present them to T-cells.

An "intracellular signaling domain," as the term is used herein, refers to an intracellular portion of a molecule. The intracellular signaling domain generates a signal that promotes an immune effector function of the CAR containing cell, e.g., a CART cell. Examples of immune effector function, e.g., in a CART cell, include cytolytic activity and helper activity, including the secretion of cytokines.

In some embodiments, the intracellular signaling domain can comprise a primary intracellular signaling domain. Exemplary primary intracellular signaling domains include those derived from the molecules responsible for primary stimulation, or antigen dependent simulation. In some embodiments, the intracellular signaling domain can comprise a costimulatory intracellular domain. Exemplary costimulatory intracellular signaling domains include those derived from molecules responsible for costimulatory signals, or antigen independent stimulation. For example, in the case of a CART, a primary intracellular signaling domain can comprise a cytoplasmic sequence of a T cell receptor, and a costimulatory intracellular signaling domain can comprise cytoplasmic sequence from co-receptor or costimulatory molecule.

A primary intracellular signaling domain can comprise a signaling motif which is known as an immunoreceptor tyrosine-based activation motif or ITAM. Examples of ITAM containing primary cytoplasmic signaling sequences include, but are not limited to, those derived from CD3 zeta, common FcR gamma (FCER1G), Fc gamma RIIa, FcR beta (Fc Epsilon R1b), CD3 gamma, CD3 delta, CD3 epsilon, CD79a, CD79b, DAP10, and DAP12.

The term "zeta" or alternatively "zeta chain", "CD3-zeta" or "TCR-zeta" refers to CD247. Swiss-Prot accession number P20963 provides exemplary human CD3 zeta amino acid sequences. A "zeta stimulatory domain" or alternatively a "CD3-zeta stimulatory domain" or a "TCR-zeta stimulatory domain" refers to a stimulatory domain of CD3-zeta or a variant thereof (e.g., a molecule having mutations, e.g., point mutations, fragments, insertions, or deletions). In some embodiments, the cytoplasmic domain of zeta comprises residues 52 through 164 of GenBank Acc. No. BAG36664.1 or a variant thereof (e.g., a molecule having mutations, e.g., point mutations, fragments, insertions, or deletions). In some embodiments, the "zeta stimulatory domain" or a "CD3-zeta stimulatory domain" is a sequence provided as SEQ ID NO: 9 or 10, or a variant thereof (e.g., a molecule having mutations, e.g., point mutations, fragments,

insertions, or deletions). Alternatively or in addition, the term "zeta" or alternatively "zeta chain", "CD3-zeta" (or "CD3zeta , CD3 zeta or CD3z) or "TCR-zeta" is defined as the protein provided as GenBan Acc. No. BAG36664.1, or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like, and a "zeta stimulatory domain" or alternatively a "CD3-zeta stimulatory domain" or a "TCR-zeta stimulatory domain" is defined as the amino acid residues from the cytoplasmic domain of the zeta chain, or functional derivatives thereof, that are sufficient to functionally transmit an initial signal necessary for T cell activation. In some aspects the cytoplasmic domain of zeta comprises residues 52 through 164 of GenBank Acc. No. BAG36664.1 or the equivalent residues from a non-human species, e.g., mouse, rodent, monkey, ape and the like, that are functional orthologs thereof. In some aspects, the "zeta stimulatory domain" or a "CD3-zeta stimulatory domain" is a sequence provided as SEQ ID NO:18. In some aspects, the "zeta stimulatory domain" or a "CD3-zeta stimulatory domain" is a sequence provided as SEQ ID NO:20.

The term a "costimulatory molecule" refers to a cognate binding partner on a T cell that specifically binds with a costimulatory ligand, thereby mediating a costimulatory response by the T cell, such as, but not limited to, proliferation. Costimulatory molecules are cell surface molecules other than antigen receptors or their ligands that are contribute to an efficient immune response. Costimulatory molecules include, but are not limited to, an MHC class I molecule, BTLA and a Toll ligand receptor, as well as OX40, CD27, CD28, CDS, ICAM-1, LFA-1 (CD11a/CD18), ICOS (CD278), and 4-1BB (CD137). Further examples of such costimulatory molecules include CDS, ICAM-1, GITR, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD160, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, NKG2C, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, and a ligand that specifically binds with CD83.

A costimulatory intracellular signaling domain can be the intracellular portion of a costimulatory molecule. A costimulatory molecule can be represented in the following protein

families: TNF receptor proteins, Immunoglobulin-like proteins, cytokine receptors, integrins, signaling lymphocytic activation molecules (SLAM proteins), and activating NK cell receptors. Examples of such molecules include CD27, CD28, 4-1BB (CD137), OX40, GITR, CD30, CD40, ICOS, BAFFR, HVEM, ICAM-1, lymphocyte function-associated antigen-1 (LFA-1), CD2, CDS, CD7, CD287, LIGHT, NKG2C, NKG2D, SLAMF7, NKp80, NKp30, NKp44, NKp46, CD160, B7-H3, and a ligand that specifically binds with CD83, and the like.
The intracellular signaling domain can comprise the entire intracellular portion, or the entire native intracellular signaling domain, of the molecule from which it is derived, or a functional fragment or derivative thereof.

"Immune effector cell," as that term is used herein, refers to a cell that is involved in an immune response, e.g., in the promotion of an immune effector response. Examples of immune effector cells include T cells, e.g., alpha/beta T cells and gamma/delta T cells, B cells, natural killer (NK) cells, natural killer T (NKT) cells, mast cells, and myeloid-derived phagocytes.
"Immune effector function or immune effector response," as that term is used herein, refers to function or response, e.g., of an immune effector cell, that enhances or promotes an immune attack of a target cell. E.g., an immune effector function or response refers a property of a T or NK cell that promotes killing or inhibition of growth or proliferation, of a target cell. In the case of a T cell, primary stimulation and co-stimulation are examples of immune effector function or response.

The term "encoding" or "encode" refers to the inherent property of specific sequences of nucleotides in a polynucleotide, such as a gene, a cDNA, or an mRNA, to serve as templates for synthesis of other polymers and macromolecules in biological processes having either a defined sequence of nucleotides (e.g., rRNA, tRNA and mRNA) or a defined sequence of amino acids and the biological properties resulting therefrom. Thus, a gene, cDNA, or RNA, encodes a protein if transcription and translation of mRNA corresponding to that gene produces the protein in a cell or other biological system. Both the coding strand, the nucleotide sequence of which is identical to the mRNA sequence and is usually provided in sequence listings, and the non-coding strand, used as the template for transcription of a gene or cDNA, can be referred to as encoding the protein or other product of that gene or cDNA.

Unless otherwise specified, a "nucleotide sequence encoding an amino acid sequence" includes all nucleotide sequences that are degenerate versions of each other and that encode the

same amino acid sequence. The phrase nucleotide sequence that encodes a protein or a RNA may also include introns to the extent that the nucleotide sequence encoding the protein may in some version contain an intron(s).

The term "effective amount" or "therapeutically effective amount" are used interchangeably herein, and refer to an amount of a compound, formulation, material, or composition, as described herein effective to achieve a particular biological result.
The term "endogenous" refers to any material from or produced inside an organism, cell, tissue or system.

The term "exogenous" refers to any material introduced from or produced outside an organism, cell, tissue or system.

The term "expression" refers to the transcription and/or translation of a particular nucleotide sequence driven by a promoter.

As used herein the term "extended release agent" refers to an agent that releases a given composition, e.g., a viral vector (e.g., a lentiviral vector) and/or a cell activation agent, over a longer period of time than a comparable immediate release formulation. In some embodiments, the extended release agent is formulated for administration by injection.

The term "transfer vector" refers to a composition of matter which comprises an isolated nucleic acid and which can be used to deliver the isolated nucleic acid to the interior of a cell. Numerous vectors are known in the art including, but not limited to, linear polynucleotides, polynucleotides associated with ionic or amphiphilic compounds, plasmids, and viruses. Thus, the term "transfer vector" includes an autonomously replicating plasmid or a virus. The term should also be construed to further include non-plasmid and non-viral compounds which facilitate transfer of nucleic acid into cells, such as, for example, a polylysine compound, liposome, and the like. Examples of viral transfer vectors include, but are not limited to, adenoviral vectors, adeno-associated virus vectors, retroviral vectors, lentiviral vectors, and the like.

The term "expression vector" refers to a vector comprising a recombinant polynucleotide comprising an expression control sequence operatively linked to a nucleotide sequence to be expressed. An expression vector comprises sufficient cis-acting elements for expression; other elements for expression can be supplied by the host cell or in an in vitro expression system. Expression vectors include all those known in the art, including cosmids, plasmids (e.g., naked

or contained in liposomes) and viruses (e.g., lentiviruses, retroviruses, adenoviruses, and adeno-associated viruses, "viral vectors") that incorporate the recombinant polynucleotide.

The term "lentivirus" refers to a genus of the Retroviridae family. Lentiviruses are unique among the retroviruses in being able to infect non-dividing cells; they can deliver a significant amount of genetic information into the DNA of the host cell, so they are one of the most efficient methods of a gene delivery vector. HIV, SIV, and FIV are all examples of lentiviruses.

The term "lentiviral vector" refers to a vector derived from at least a portion of a lentivirus genome, including especially a self-inactivating lentiviral vector as provided in Milone et al., Mol. Ther. 17(8): 1453–1464 (2009). Other examples of lentivirus vectors that may be used in the clinic, include but are not limited to, e.g., the LENTIVECTOR® gene delivery technology from Oxford BioMedica, the LENTIMAX™ vector system from Lentigen and the like. Nonclinical types of lentiviral vectors are also available and would be known to one skilled in the art.

The term "homologous" or "identity" refers to the subunit sequence identity between two polymeric molecules, e.g., between two nucleic acid molecules, such as, two DNA molecules or two RNA molecules, or between two polypeptide molecules. When a subunit position in both of the two molecules is occupied by the same monomeric subunit; e.g., if a position in each of two DNA molecules is occupied by adenine, then they are homologous or identical at that position. The homology between two sequences is a direct function of the number of matching or homologous positions; e.g., if half (e.g., five positions in a polymer ten subunits in length) of the positions in two sequences are homologous, the two sequences are 50% homologous; if 90% of the positions (e.g., 9 of 10), are matched or homologous, the two sequences are 90% homologous.

"Humanized" forms of non-human (e.g., murine) antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab□, F(ab□)2, or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. For the most part, humanized antibodies and antibody fragments thereof are human immunoglobulins (recipient antibody or antibody fragment) in which residues from a complementary-determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit

having the desired specificity, affinity, and capacity. In some instances, Fv framework region (FR) residues of the human immunoglobulin are replaced by corresponding non-human residues. Furthermore, a humanized antibody/antibody fragment can comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. These modifications can further refine and optimize antibody or antibody fragment performance. In general, the humanized antibody or antibody fragment thereof will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or a significant portion of the FR regions are those of a human immunoglobulin sequence. The humanized antibody or antibody fragment can also comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin. For further details, see Jones et al., Nature, 321: 522-525, 1986; Reichmann et al., *Nature*, 332: 323-329, 1988; Presta, *Curr. Op. Struct. Biol.*, 2: 593-596, 1992.

"Fully human" refers to an immunoglobulin, such as an antibody or antibody fragment, where the whole molecule is of human origin or consists of an amino acid sequence identical to a human form of the antibody or immunoglobulin.

The term "isolated" means altered or removed from the natural state. For example, a nucleic acid or a peptide naturally present in a living animal is not "isolated," but the same nucleic acid or peptide partially or completely separated from the coexisting materials of its natural state is "isolated." An isolated nucleic acid or protein can exist in substantially purified form, or can exist in a non-native environment such as, for example, a host cell.

The term "operably linked" or "transcriptional control" refers to functional linkage between a regulatory sequence and a heterologous nucleic acid sequence resulting in expression of the latter. For example, a first nucleic acid sequence is operably linked with a second nucleic acid sequence when the first nucleic acid sequence is placed in a functional relationship with the second nucleic acid sequence. For instance, a promoter is operably linked to a coding sequence if the promoter affects the transcription or expression of the coding sequence. Operably linked DNA sequences can be contiguous with each other and, e.g., where necessary to join two protein coding regions, are in the same reading frame.

The term "nucleic acid" or "polynucleotide" refers to deoxyribonucleic acids (DNA) or ribonucleic acids (RNA) and polymers thereof in either single- or double-stranded form. Unless

specifically limited, the term encompasses nucleic acids containing known analogues of natural nucleotides that have similar binding properties as the reference nucleic acid and are metabolized in a manner similar to naturally occurring nucleotides. Unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conservatively modified variants thereof (e.g., degenerate codon substitutions), alleles, orthologs, SNPs, and complementary sequences as well as the sequence explicitly indicated. Specifically, degenerate codon substitutions may be achieved by generating sequences in which the third position of one or more selected (or all) codons is substituted with mixed-base and/or deoxyinosine residues (Batzer et al., Nucleic Acid Res. 19:5081 (1991); Ohtsuka et al., J. Biol. Chem. 260:2605-2608 (1985); and Rossolini et al., Mol. Cell. Probes 8:91-98 (1994)).

The terms "peptide," "polypeptide," and "protein" are used interchangeably, and refer to a compound comprised of amino acid residues covalently linked by peptide bonds. A protein or peptide must contain at least two amino acids, and no limitation is placed on the maximum number of amino acids that can comprise a protein's or peptide's sequence. Polypeptides include any peptide or protein comprising two or more amino acids joined to each other by peptide bonds. As used herein, the term refers to both short chains, which also commonly are referred to in the art as peptides, oligopeptides and oligomers, for example, and to longer chains, which generally are referred to in the art as proteins, of which there are many types. "Polypeptides" include, for example, biologically active fragments, substantially homologous polypeptides, oligopeptides, homodimers, heterodimers, variants of polypeptides, modified polypeptides, derivatives, analogs, fusion proteins, among others. A polypeptide includes a natural peptide, a recombinant peptide, or a combination thereof.

The term "promoter" refers to a DNA sequence recognized by the synthetic machinery of the cell, or introduced synthetic machinery, required to initiate the specific transcription of a polynucleotide sequence.

The term "promoter/regulatory sequence" refers to a nucleic acid sequence which is required for expression of a gene product operably linked to the promoter/regulatory sequence. In some instances, this sequence may be the core promoter sequence and in other instances, this sequence may also include an enhancer sequence and other regulatory elements which are required for expression of the gene product. The promoter/regulatory sequence may, for example, be one which expresses the gene product in a tissue specific manner.

The term "constitutive promoter" refers to a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a cell under most or all physiological conditions of the cell.

The term "inducible promoter" refers to a nucleotide sequence which, when operably linked with a polynucleotide which encodes or specifies a gene product, causes the gene product to be produced in a cell substantially only when an inducer which corresponds to the promoter is present in the cell.

The term "tissue-specific promoter" refers to a nucleotide sequence which, when operably linked with a polynucleotide encodes or specified by a gene, causes the gene product to be produced in a cell substantially only if the cell is a cell of the tissue type corresponding to the promoter.

The terms "cancer associated antigen" or "tumor antigen" interchangeably refers to a molecule (typically a protein, carbohydrate or lipid) that is expressed on the surface of a cancer cell, either entirely or as a fragment (e.g., MHC/peptide), and which is useful for the preferential targeting of a pharmacological agent to the cancer cell. In some embodiments, a tumor antigen is a marker expressed by both normal cells and cancer cells, e.g., a lineage marker, e.g., CD19 on B cells. In some embodiments, a tumor antigen is a cell surface molecule that is overexpressed in a cancer cell in comparison to a normal cell, for instance, 1-fold over expression, 2-fold overexpression, 3-fold overexpression or more in comparison to a normal cell. In some embodiments, a tumor antigen is a cell surface molecule that is inappropriately synthesized in the cancer cell, for instance, a molecule that contains deletions, additions or mutations in comparison to the molecule expressed on a normal cell. In some embodiments, a tumor antigen will be expressed exclusively on the cell surface of a cancer cell, entirely or as a fragment (e.g., MHC/peptide), and not synthesized or expressed on the surface of a normal cell. In some embodiments, the CARs of the present invention include CARs comprising an antigen binding domain (e.g., antibody or antibody fragment) that binds to a MHC presented peptide. Normally, peptides derived from endogenous proteins fill the pockets of Major histocompatibility complex (MHC) class I molecules and are recognized by T cell receptors (TCRs) on CD8 + T lymphocytes. The MHC class I complexes are constitutively expressed by all nucleated cells. In cancer, virus-specific and/or tumor-specific peptide/MHC complexes represent a unique class of cell surface targets for immunotherapy. TCR-like antibodies targeting peptides derived from

viral or tumor antigens in the context of human leukocyte antigen (HLA)-A1 or HLA-A2 have been described (see, e.g., Sastry et al., J Virol. 2011 85(5):1935-1942; Sergeeva et al., Blood, 2011 117(16):4262-4272; Verma et al., J Immunol 2010 184(4):2156-2165; Willemsen et al., Gene Ther 2001 8(21) :1601-1608; Dao et al., Sci Transl Med 2013 5(176) :176ra33; Tassev et al., Cancer Gene Ther 2012 19(2):84-100). For example, TCR-like antibody can be identified from screening a library, such as a human scFv phage displayed library.

The term "tumor-supporting antigen" or "cancer-supporting antigen" interchangeably refer to a molecule (typically a protein, carbohydrate or lipid) that is expressed on the surface of a cell that is, itself, not cancerous, but supports the cancer cells, e.g., by promoting their growth or survival e.g., resistance to immune cells. Exemplary cells of this type include stromal cells and myeloid-derived suppressor cells (MDSCs). The tumor-supporting antigen itself need not play a role in supporting the tumor cells so long as the antigen is present on a cell that supports cancer cells.

As used herein, "in vitro transcribed RNA" refers to RNA, preferably mRNA, that has been synthesized in vitro. Generally, the in vitro transcribed RNA is generated from an in vitro transcription vector. The in vitro transcription vector comprises a template that is used to generate the in vitro transcribed RNA.

As used herein, a "poly(A)" is a series of adenosines attached by polyadenylation to the mRNA. In a preferred embodiment of a construct for transient expression, the polyA is between 50 and 5000 (SEQ ID NO: 34), preferably greater than 64, more preferably greater than 100, most preferably greater than 300 or 400. poly(A) sequences can be modified chemically or enzymatically to modulate mRNA functionality such as localization, stability or efficiency of translation.

As used herein in connection with expression, e.g., expression of a CAR molecule, "transient" refers to expression of a non-integrated transgene for a period of hours, days or weeks, wherein the period of time of expression is less than the period of time for expression of the gene if integrated into the genome or contained within a stable plasmid replicon in the host cell.

As used herein, the terms "treat", "treatment" and "treating" refer to the reduction or amelioration of the progression, severity and/or duration of a proliferative disorder, or the amelioration of one or more symptoms (preferably, one or more discernible symptoms) of a

proliferative disorder resulting from the administration of one or more therapies (e.g., one or more therapeutic agents such as a CAR of the invention). In specific embodiments, the terms "treat", "treatment" and "treating" refer to the amelioration of at least one measurable physical parameter of a proliferative disorder, such as growth of a tumor, not necessarily discernible by the patient. In other embodiments the terms "treat", "treatment" and "treating" -refer to the inhibition of the progression of a proliferative disorder, either physically by, e.g., stabilization of a discernible symptom, physiologically by, e.g., stabilization of a physical parameter, or both. In other embodiments the terms "treat", "treatment" and "treating" refer to the reduction or stabilization of tumor size or cancerous cell count.

The term "signal transduction pathway" refers to the biochemical relationship between a variety of signal transduction molecules that play a role in the transmission of a signal from one portion of a cell to another portion of a cell. The phrase "cell surface receptor" includes molecules and complexes of molecules capable of receiving a signal and transmitting signal across the membrane of a cell.

The term "subject" is intended to include living organisms in which an immune response can be elicited (e.g., mammals, human).

The term, a "substantially purified" cell refers to a cell that is essentially free of other cell types. A substantially purified cell also refers to a cell which has been separated from other cell types with which it is normally associated in its naturally occurring state. In some instances, a population of substantially purified cells refers to a homogenous population of cells. In other instances, this term refers simply to cell that have been separated from the cells with which they are naturally associated in their natural state. In some aspects, the cells are cultured in vitro. In other aspects, the cells are not cultured in vitro.

The term "therapeutic" as used herein means a treatment. A therapeutic effect is obtained by reduction, suppression, remission, or eradication of a disease state.

The term "prophylaxis" as used herein means the prevention of or protective treatment for a disease or disease state.

The term "transfected" or "transformed" or "transduced" refers to a process by which exogenous nucleic acid is transferred or introduced into the host cell. A "transfected" or "transformed" or "transduced" cell is one which has been transfected, transformed or transduced with exogenous nucleic acid. The cell includes the primary subject cell and its progeny.

The term "specifically binds," refers to an antibody, or a ligand, which recognizes and binds with a binding partner (e.g., a tumor antigen) protein present in a sample, but which antibody or ligand does not substantially recognize or bind other molecules in the sample.

"Refractory" as used herein refers to a disease, e.g., cancer, that does not respond to a treatment. In embodiments, a refractory cancer can be resistant to a treatment before or at the beginning of the treatment. In other embodiments, the refractory cancer can become resistant during a treatment. A refractory cancer is also called a resistant cancer.

"Relapsed" as used herein refers to the return of a disease (e.g., cancer) or the signs and symptoms of a disease such as cancer after a period of improvement, e.g., after prior treatment of a therapy, e.g., cancer therapy

A "system" as the term is used herein in connection with, for example, gene editing, refers to a group of molecules, e.g., one or more molecules, which together act to produce a desired function.

A "gene editing system" as the term is used herein, refers to a system, e.g., one or more molecules, that direct and effect an alteration, e.g., a deletion, of one or more nucleic acids at or near a site of genomic DNA targeted by said system. Gene editing systems are known in the art, and are described more fully below.

A "dominant negative" gene product or protein is one that interferes with the function of a gene product or protein. The gene product affected can be the same or different from the dominant negative protein. Dominant negative gene products can be of many forms, including truncations, full length proteins with point mutations or fragments thereof, or fusions of full-length wild type or mutant proteins or fragments thereof with other proteins. The level of inhibition observed can be very low. For example, it may require a large excess of the dominant negative protein compared to the functional protein or proteins involved in a process in order to see an effect. It may be difficult to see effects under normal biological assay conditions.

The term "proportion" refers to the ratio of the specified molecule to the total number of molecules in a population. In an exemplary embodiment, a proportion of T cells having a specific phenotype (e.g., T_{SCM} cells) refers to the ratio of the number of T cells having that phenotype relative to the total number of T cells in a population. In an exemplary embodiment, a proportion of T cells having a specific phenotype (e.g., CD45RA+CD62L+ cells) refers to the ratio of the number of T cells having that phenotype relative to the total number of T cells in a

population. It will be understood that such proportions may be measured against certain subsets of cells, where indicted. For example, the proportion of CD4+ T_{SCM} cells may be measured against the total number of CD4+ T cells.

The term "population of immune effector cells" as used herein refers to a composition comprising at least two, e.g., two or more, e.g., more than one, immune effector cell, and does not denote any level of purity or the presence or absence of other cell types. In an exemplary embodiment, the population is substantially free of other cell types. In another exemplary embodiment, the population comprises at least two cells of the specified cell type or having the specified function or property.

As used herein, the term "biomaterial" refers to a substance engineered to interact with a biological system for a therapeutic purpose. A "hydrogel" is such a substance comprised of a network of polymer chain that may be hydrated to adopt a gel form – typically as a result of cross-linking between the polymer chains. A "cryogel" is a form of hydrogel that has been formed by freezing. In some embodiments, a cryogel is formed by allowing crosslinking to occur in a partially frozen state, resulting in a hydrogel network.

The terms "T_{SCM}-like cell," "naive T Cell' and "naïve T cell" are used interchangeably and refer to a less differentiated T cell state, that is characterized by surface expression of CD45RA and CD62L (e.g., is CD45RA positive and CD62L positive (sometimes written as CD45RA+CD62L+)). In general, T cell differentiation proceeds, from most "naive" to most "exhausted," T_{SCM}-like (e.g., a CD45RA+CD62L+ cell) >T_{CM} (e.g., a CD45RA-CD62L+ cell)>T_{EM} (e.g., a CD45RA-CD62L- cell)>T_{EFF}. Naive T cells may be characterized, for example, as having increased self-renewal, anti-tumor efficacy, proliferation and/or survival, relative to a more exhausted T cell phenotype. In an exemplary embodiment, a naive T cell refers to a CD45RA+CD62L+ T cell. In another exemplary embodiment, a naive T cell refers to a T_{SCM} cell, e.g., a CD45RA+CD62L+CCR7+CD27+CD95+ T cell.

The term "T_{SCM}" refers to a T cell having a stem cell memory phenotype, characterized in that it expresses CD45RA, CD62L, CCR7, CD27 and CD95 on its cell surface (e.g., is CD45RA positive, CD62L positive, CCR7 positive, CD27 positive and CD95 positive (sometimes written as CD45RA+CD62L+CCR7+CD27+CD95+)). A T_{SCM} cell is an example of a naive T cell. The T cell may be CD4+ and/or CD8+ T cell.

For specific proteins described herein (e.g., VEGF-C), the named protein includes any of the protein's naturally occurring forms, variants or homologs (e.g., within at least 50%, 80%, 90%, 95%, 96%, 97%, 98%, 99% or 100% activity compared to the native protein). In some embodiments, variants or homologs have at least 90%, 95%, 96%, 97%, 98%, 99% or 100% amino acid sequence identity across the whole sequence or a portion of the sequence (e.g. a 50, 100, 150 or 200 continuous amino acid portion) compared to a naturally occurring form. In some embodiments, the protein is the protein as identified by its NCBI sequence reference (e.g., NP_005420.1). In some embodiments, the protein is the protein as identified by its NCBI sequence reference, homolog or functional fragment thereof.

As used herein, the term "alkyl" refers to a fully saturated branched or unbranched (or straight chain or linear) hydrocarbon moiety, comprising 1 to 20 carbon atoms. Preferably the alkyl comprises 1 to 6 carbon atoms, and more preferably 1 to 4 carbon atoms. Representative examples of alkyl include methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, iso-butyl, vert-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, 3-methylhexyl, 2,2-dimethylpentyl, 2,3-dimethylpentyl, n-heptyl. For example, the term "C_{1-6}alkyl" refers to a hydrocarbon having from one to six carbon atoms, and the term "C_{1-7}alkyl" refers to a hydrocarbon having from one to seven carbon atoms.

As used herein, the term "haloalkyl" refers to an alkyl as defined herein, that is substituted by one or more halo groups as defined herein. Preferably the haloalkyl can be monohaloalkyl, dihaloalkyl or polyhaloalkyl including perhaloalkyl. A monohaloalkyl can have one iodo, bromo, chloro or fluoro within the alkyl group. Dihaloalky and polyhaloalkyl groups can have two or more of the same halo atoms or a combination of different halo groups within the alkyl. Preferably, the polyhaloalkyl contains up to 12, or 10, or 8, or 6, or 4, or 3, or 2 halo groups. Representative examples of haloalkyl are fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl and dichloropropyl. A perhaloalkyl refers to an alkyl having all hydrogen atoms replaced with halo atoms. For example, the term "halo-C_{1-6}alkyl" refers to a hydrocarbon having one to six carbon atoms and being substituted by one or more halo groups, and the term "halo-C_{1-7}alkyl" refers to a hydrocarbon having one to seven carbon atoms and being substituted by one or more halo groups.

As used herein, "salts" includes pharmaceutically acceptable acid addition salts that can be formed with inorganic acids and organic acids, e.g., acetate, aspartate, benzoate, besylate, bromide/hydrobromide, bicarbonate/carbonate, bisulfate/sulfate, camphorsulformate, chloride/hydrochloride, chlortheophyllonate, citrate, ethandisulfonate, fumarate, gluceptate, gluconate, glucuronate, hippurate, hydroiodide/iodide, isethionate, lactate, lactobionate, laurylsulfate, malate, maleate, malonate, mandelate, mesylate, methylsulphate, naphthoate, napsylate, nicotinate, nitrate, octadecanoate, oleate, oxalate, palmitate, pamoate, phosphate/hydrogen phosphate/dihydrogen phosphate, polygalacturonate, propionate, stearate, succinate, sulfosalicylate, tartrate, tosylate and trifluoroacetate salts.

Inorganic acids from which salts can be derived include, for example, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like. Organic acids from which salts can be derived include, for example, acetic acid, propionic acid, glycolic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, toluenesulfonic acid, sulfosalicylic acid, and the like. Pharmaceutically acceptable base addition salts can be formed with inorganic and organic bases.

Inorganic bases from which salts can be derived include, for example, ammonium salts and metals from columns I to XII of the periodic table. In certain embodiments, the salts are derived from sodium, potassium, ammonium, calcium, magnesium, iron, silver, zinc, and copper; particularly suitable salts include ammonium, potassium, sodium, calcium and magnesium salts. Organic bases from which salts can be derived include, for example, primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines, basic ion exchange resins, and the like. Certain organic amines include isopropylamine, benzathine, cholinate, diethanolamine, diethylamine, lysine, meglumine, piperazine and tromethamine.

Ranges: throughout this disclosure, various aspects of the invention can be presented in a range format. It should be understood that the description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation on the scope of the invention. Accordingly, the description of a range should be considered to have specifically disclosed all the possible subranges as well as individual numerical values within that range. For example, description of a range such as from 1 to 6 should be considered to have specifically

disclosed subranges such as from 1 to 3, from 1 to 4, from 1 to 5, from 2 to 4, from 2 to 6, from 3 to 6 etc., as well as individual numbers within that range, for example, 1, 2, 2.7, 3, 4, 5, 5.3, and 6. As another example, a range such as 95-99% identity, includes something with 95%, 96%, 97%, 98% or 99% identity, and includes subranges such as 96-99%, 96-98%, 96-97%, 97-99%, 97-98% and 98-99% identity. This applies regardless of the breadth of the range.

The terms "B cell antigen" or "B-Cell antigen" are used interchangeably, and refer to a molecule (typically a protein, carbohydrate or lipid) that is preferentially or specifically expressed on the surface of a B cell which can be targeted with an agent which binds thereto. The B cell antigen of particular interest is preferentially expressed on B cells compared to other non-B cell tissues of a mammal. The B cell antigen may be expressed on one particular B cell population, e.g., B cell precursors or mature B cells, or on more than one particular B cell population, e.g., both precursor B cells and mature B cells. Exemplary B cell surface markers include: CD5, CD10, CD19, CD20, CD21, CD22, CD23, CD24, CD25, CD27, CD30, CD34, CD37, CD38, CD40, CD53, CD69, CD72, CD73, CD74, CD75, CD77, CD79a, CD79b, CD80, CD81, CD82, CD83, CD84, CD85, CD86, CD123, CD135, CD138, CD179, CD269, Flt3, ROR1, BCMA, FcRn5, FcRn2, CS-1, CXCR4, 5, 7, IL-7/3R, IL7/4/3R, and IL4R. In some embodiments, the B-Cell antigen is: CD19, CD20, CD22, FcRn5, FcRn2, BCMA, CS-1 or CD138. In embodiments, the B-Cell antigen is CD19. In embodiments, the B-Cell antigen is CD20. In embodiments, the B-Cell antigen is CD22. In embodiments, the B-Cell antigen is BCMA. In embodiments, the B-Cell antigen is FcRn5. In embodiments, the B-Cell antigen is FcRn2. In embodiments, the B-Cell antigen is CS-1. In embodiments, the B-Cell antigen is CD138.

The terms "solid tumor antigen" or "solid tumor cell antigen" refer to a molecule (typically a protein, carbohydrate or lipid) that is preferentially or specifically expressed on the surface of a solid tumor cell which can be targeted with an agent which binds thereto. The solid tumor antigen of particular interest is preferentially expressed on a solid tumor cell compared to other non-tumor tissues of a mammal. The solid tumor antigen may be expressed on one particular solid tumor cell population, e.g., on mesothelioma tumor cells, or on more than one particular solid tumor cell population, e.g., both mesothelioma tumor cells and ovarian cancer cells. Exemplary solid tumor antigens include: EGFRvIII, mesothelin, GD2, Tn Ag, PSMA, TAG72, CD44v6, CEA, EPCAM, KIT, IL-13Ra2, leguman , GD3, CD171, IL-11Ra, PSCA,

MAD-CT-1, MAD-CT-2, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, folate receptor alpha, ERBBs (e.g., ERBB2), Her2/neu, MUC1, EGFR, NCAM, Ephrin B2, CAIX, LMP2, sLe, HMWMAA, o-acetyl-GD2, folate receptor beta, TEM1/CD248, TEM7R, FAP, Legumain, HPV E6 or E7, ML-IAP, CLDN6, TSHR, GPRC5D, ALK, Polysialic acid, Fos-related antigen, neutrophil elastase, TRP-2, CYP1B1, sperm protein 17, beta human chorionic gonadotropin, AFP, thyroglobulin, PLAC1, globoH, RAGE1, MN-CA IX, human telomerase reverse transcriptase, intestinal carboxyl esterase, mut hsp 70-2, NA-17, NY-BR-1, UPK2, HAVCR1, ADRB3, PANX3, GPR20, Ly6k, OR51E2, TARP, GFRα4, and a peptide of any of these antigens presented on MHC. In some embodiments, the solid tumor antigen is CLDN6, mesothelin or EGFRvIII.

The terms "myeloid tumor antigen" or "myeloid tumor cell antigen" refer to a molecule (typically a protein, carbohydrate or lipid) that is preferentially or specifically expressed on the surface of a myeloid tumor cell which can be targeted with an agent which binds thereto. The myeloid tumor antigen of particular interest is preferentially expressed on a myeloid tumor cell compared to other non-tumor tissues of a mammal. The myeloid tumor antigen may be expressed on one particular myeloid tumor cell population, e.g., on acute myeloid leukemia (AML) tumor cells, or on more than one particular myeloid tumor cell population. Exemplary myeloid tumor antigens include: CD33 and CLL-1.

The term "antigen of a hematological tumor not of B-Cell lineage" refers to a molecule (typically a protein, carbohydrate or lipid) that is preferentially or specifically expressed on the surface of a tumor or cancer of hematopoietic or lymphoid tissue origin, other than of B-Cell origin. These include tumors of myeloid lineage origin, e.g., tumors derived from granulocyte, erythrocyte, thrombocyte, macrophage and/or mast cell origin, or any of their precursor cell populations, and tumors of lymphoid origin other than B-Cell origin, e.g., T cell, NK cell and/or plasma cell origin, or any of their precursor cell populations.

Headings, sub-headings or numbered or lettered elements, e.g., (a), (b), (i) etc., are presented merely for ease of reading. The use of headings or numbered or lettered elements in this document does not require the steps or elements be performed in alphabetical order or that the steps or elements are necessarily discrete from one another.

All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety.

Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

Description

Contemplated herein is a first composition comprising a biomaterial and a cell recruitment factor and/or a second composition comprising a viral vector, optionally with a particle, e.g., a mesoporous silica particle (MSP), and a cell activation agent, e.g., a multispecific binding molecule described herein.

Also, contemplated herein is a composition comprising a biomaterial comprising a cell recruitment factor; a first population of mesoporous silica particles; a viral vector; and, optionally, a cell activation agent, and methods of use thereof. Also, contemplated herein is a composition and a biomaterial comprising a cell recruitment factor; a first population of mesoporous silica particles; a viral vector; and, optionally, a cell activation agent, and methods of use thereof.

The elements of these compositions and methods of use thereof are described herein below. Not to be bound by theory, Applicants contemplate that the compositions are able to be delivered locally, e.g., under the skin, and through use of a cell recruitment factor, cells are recruited to the defined site of delivery and are able to be transduced by the viral vector. In embodiments where the vector encodes a CAR, the transduced cells are CAR expressing and, thus, may be used to target a particular antigen to treat a disease, disorder, or condition.

Biomaterials

In some embodiments, the biomaterial comprises a hydrogel, optionally a cryogel. In some embodiments, the cryogel comprises gelatin, hyaluronic acid (HA), collagen, alginate, laminin, chitosan, silk fibroin, agarose, poly(ethylene glycol), poly-vinyl alcohol, and/or hydroxyethyl methylacrylate. In some embodiments, the biomaterial comprises an alginate hydrogel, e.g., an alginate cryogel. In some embodiments, the biomaterial comprises a hyaluronic acid hydrogel (HA hydrogel). In some embodiments, the biomaterial comprises a hyaluronic acid cryogel.

In some embodiments, alginate hydrogel, e.g., an alginate cryogel further comprises norbornene and/or tetrazine. In some embodiments, the norbornene and/or tetrazine is covalently

associated with, e.g., chemically linked to the alginate. In some embodiments, the norbornene and/or tetrazine is non-covalently associated with, e.g., adsorbed on, the alginate.

In some embodiments, a composition comprising the cryogel, e.g., an alginate cryogel, and a cell recruitment factor further comprises laponite. In some embodiments, a composition comprising the hydrogel, e.g., an HA hydrogel, and a cell recruitment factor further comprises laponite. Without wishing to be bound by theory, in some embodiments, use of laponite allows for a slow and/or controlled release of the cell recruitment factor from the composition. In some embodiments, the laponite is present at a concentration of about 0.1 to about 0.5 mg/mL, e.g., about 0.1 to 0.4 mg/mL, about 0.1 to 0.35 mg/mL, about 0.1 to 0.3 mg/mL, about 0.1 to 0.25 mg/mL, about 0.1 to 0.15 mg/mL, about 0.15 to 0.5 mg/mL, about 0.15 to 0.4 mg/mL, about 0.15 to 0.35 mg/mL, about 0.15 to 0.3 mg/mL, about 0.15 to 0.25 mg/mL, about 1.5 mg/mL to 0.2 mg/mL, about 0.2 to 0.5 mg/mL, about 0.2 to 0.4 mg/mL, about 0.2 to 0.35 mg/mL, about 0.2 to 0.3 mg/mL, about 0.2 to 0.25 mg/mL, about 0.25 to 0.5 mg/mL, about 0.25 to 0.4 mg/mL, about 0.25 to about 0.35 mg/mL, about 0.25 to 0.3 mg/mL, about 0.3 to 0.5 mg/mL, about 0.3 to 0.4 mg/mL, about 0.35 to 0.5 mg/mL, about 0.35 to 0.4 mg/mL, about 0.4 to 0.5 mg/mL, about 0.1 mg/mL, about 0.15 mg/mL, about 0.2 mg/mL, about 0.25 mg/mL, 0.3 mg/mL, about 0.35 mg/mL, or about 0.5 mg/mL. In some embodiments, the laponite is present at a concentration of about 0.25 mg/mL.

In some embodiments, the cryogel comprises pores between about 10 to 300 μm in diameter, e.g., between about 10 to 20 μm, about 10 to 30 μm, about 10 to 40 μm, about 10 to 50 μm, about 10 to 100 μm, about 10 to 150 μm, about 10 to 200 μm, about 10 to 250 μm, about 20 to 30 μm, about 20 to 40 μm, about 20 to 50 μm, about 20 to 100 μm, about 20 to 150 μm, about 20 to 200 μm, about 20 to 250 μm, about 20 to 300 μm, about 50 to 300 μm, about 50 to 100 μm, 50 to about 150 μm, 50 to about 200 μm, 50 to about 250 μm, 100 to about 150 μm, 100 to about 200 μm, 100 to about 250 μm, about 100 to 300 μm, about 150 to 200 μm, about 150 to 250 μm, about 150 to 300 μm, about 200 to 250 μm, about 200 to 300 μm, or about 250 to 300 μm. In some embodiments, the cryogel does not comprise pores. In some embodiments, the cryogel comprises pores of substantially the same size. In some embodiments, the biomaterial comprises pores of different sizes. In some embodiments, the cryogel is chemically crosslinked.

Methods of manufacturing biomaterials are well known in the art. See, e.g., Koshy, S. T., Zhang, D., Grolman, J. M., Stafford, A. G., & Mooney, D. J. (2018). Injectable nanocomposite

cryogels for versatile protein drug delivery. Acta biomaterialia, 65, 36–43 (describing the manufacture of an alginate cryogel). Additionally, biomaterials and components thereof may be commercially purchased, e.g., Partek SLC (silica from EMD Millipore) or TruTag silica particles.

In some embodiments, the cryogel, e.g., the alginate cryogel, is administered to a high subcutaneous space or a subcutaneous space adjacent to the dermis. In some embodiments, the hydrogel, e.g., the HA hydrogel, is administered to a high subcutaneous space or a subcutaneous space adjacent to the dermis.

Cell recruitment factors

In some embodiments, a cell recruitment factor is to be used in a composition or method described herein.

In some embodiments, the cell recruitment factor induces lymphangiogenesis. In some embodiments, induction of lymphangiogenesis comprises an increase in the level and/or activation of lymphatic endothelial cells (LECs) (for example, CD45-CD31+PDPN+ cells). In some embodiments, the level of LECs (e.g., CD45-CD31+PDPN+ cells) is increased by at least 10%, 20%, 30%, 40%, 50%, 60, 70%, 75%, 80%, 85%, 90%, 95%, 100%, or 200%.

In some embodiments, the cell recruitment factor recruits, e.g., selectively recruits immune cells, optionally T-cells and/or NK-cells. In some embodiments, the cell recruitment factor recruits cells (e.g., immune cells, e.g., T cells) directly. In some embodiments, the cell recruitment factor recruits cells (e.g., immune cells, e.g., T cells) indirectly. In some embodiments, the cell recruitment factor induces lymphangiogenesis, which in turn recruits cells, e.g., immune cells, e.g., T cells.

In some embodiments, the cell recruitment factor recruits (for example, directly or indirectly) T cells, e.g., naïve T cells (for example, CD45RA+CD62L+ T cells or CD45RA+CD62L+CCR7+CD27+CD95+ T cells). In some embodiments, recruitment of T cells comprises an increase in the level of T cells. In some embodiments, the level of T cells is increased by at least 10%, 20%, 30%, 40%, 50%, 60, 70%, 75%, 80%, 85%, 90%, 95%, 100%, 200%, 250%, or 300%.

In some embodiments, the cell recruitment factor is selected from the group consisting of CCL19, CXCL9, CXCL10, XCL1, IL-2, IL-7, CCL21, GM-CSF, CCL17, CCL22, CCL20,

CCL27, IL-15 (for example, hetIL-15 (IL15/sIL-15Ra)), lymphotoxin alpha, lymphotoxin beta, VEGF-C, FLT3L, G-CSF, PDGF, S100A8/A9, CSF-1, CXCL8, CCL20, CCL17, CCR5, CCR6, CCL2, VEGF, Angiopoietin-2, PGE2, LTB4, CXC3L1, CCL19, CCL21, CXCL10, CXCL11, and/or CXCL12. In some embodiments, the cell recruitment factor comprises VEGF-C or a functional variant thereof.

Without wishing to be bound by theory, in some embodiments, the release of the cell recruitment factor, e.g., a VEGF-C or variant thereof, from a cryogel described herein induces lymphangiogenesis of pre-existing skin lymphatic capillaries, activating lymphatic endothelial cells (LEC), which in turn secrete chemokines such as CCL21, recruiting T cells, e.g., naïve T cells, to the site of administration of the cryogel, e.g., to the site in the dermis on top of the gel. In some embodiments, the time to induce lymphangiogenesis and recruit immune cells, e.g., T cells, by a cell recruitment factor described herein comprises about 5 to about 28 days, e.g., about 5 to 21 days, about 5 to 15 days, about 5 to 14 days, about 5 to 10 days , about 7 to about 28 days, about 7 to about 21 days, about 7 to 15 days, about 7 to 14 days, about 7 to 10 days, about 10 to 28 days, about 10 to 21 days, about 10 to 15 days, about 10 to 14 days, about 14 to 28 days, about 14 to 21 days, about 15 to 28 days, about 15 to 21 days, about 21 to 28 days, about 7 days, about 10 days, about 14 days, about 15 days, or about 20 days, about 21 days, about 28 days. In some embodiments, the time to induce lymphangiogenesis and recruit immune cells, e.g., T cells, by a cell recruitment factor described herein comprises 14 days (e.g., two weeks). In some embodiments, the time to induce lymphangiogenesis and recruit immune cells, e.g., T cells, by a cell recruitment factor described herein comprises 21 days (e.g., three weeks). In some embodiments, the time to induce lymphangiogenesis and recruit immune cells, e.g., T cells, by a cell recruitment factor described herein comprises 28 days (e.g., four weeks or one month).

Methods of producing, formulating, and/or procuring these various cell recruitment factors are known in the art. See, e.g., Leppänen VM, Prota AE, Jeltsch M, et al. Structural determinants of growth factor binding and specificity by VEGF receptor 2. Proc Natl Acad Sci U S A. 2010;107(6):2425-2430. doi:10.1073/pnas.0914318107; Leppänen VM, Tvorogov D, Kisko K, et al. Structural and mechanistic insights into VEGF receptor 3 ligand binding and activation. Proc Natl Acad Sci U S A. 2013;110(32):12960-12965. doi:10.1073/pnas.1301415110; Joyce Chiu, Jason W. H. Wong, Michael Gerometta, and Philip J. Hogg. Mechanism of Dimerization

of a Recombinant Mature Vascular Endothelial Growth Factor C Biochemistry 2013 53 (1), 7-9. doi: 10.1021/bi401518b; Broggi, M. A. S., Schmaler, M., Lagarde, N., Rossi, S. W. Isolation of Murine Lymph Node Stromal Cells. J. Vis. Exp. (90), e51803, doi:10.3791/51803 (2014); Fankhauser, M., M.A. Broggi, L. Potin, N. Bordry, L. Jeanbart, A.W. Lund, E. Da Costa, S. Hauert, M. Rincon-Restrepo, and C. Tremblay. 2017. Tumor lymphangiogenesis promotes T cell infiltration and potentiates immunotherapy in melanoma. Science translational medicine. 9:eaal4712; US 2019 / 0099485 A1: "Lymphangiogenesis for therapeutic immunomodulation" (2017); and Vokali, E., S.Y. Shann, S. Hirosue, M. Rincon-Restrepo, F.V. Duraes, S. Scherer, P. Corthésy-Henrioud, W.W. Kilarski, A. Mondino, and D. Zehn. 2020. Lymphatic endothelial cells prime naïve CD8+ T cells into memory cells under steady-state conditions. Nature communications. 11:1–18.

In some embodiments, the VEGF-C is selected from the group consisting of immature VEGF-C peptide or mature VEGF-C peptide. In some embodiments, the mature VEGF-C peptide is the minor mature form or major mature form. In some embodiments, the mature VEGF-C peptide is a wild type minor mature form or a wild type major mature form. In some embodiments, the mature VEGF-C peptide is a modified minor mature form or a modified major mature form. In some embodiments, the mature VEGF-C peptide is a modified minor mature form comprising a mutation at Cysteine 137 (e.g., C137A) or a modified major mature form comprising a mutation at Cysteine 137 (e.g., C137A), numbered according to SEQ ID NO: 725. In some embodiments, the mature VEGF-C peptide is a modified minor mature form comprising a C137A mutation or a modified major mature form comprising a C137A mutation. In some embodiments, the mature VEGF-C peptide is present as a dimer or monomer. In some embodiments, the VEGF-C is a dimer of the major mature form further comprising a C137A mutation in each monomer. In some embodiments, the VEGF-C is a dimer of the minor mature form further comprising a C137A mutation in each monomer. In some embodiments, the VEGF-C is selected from a sequence provided in Table 18 below. In some embodiments, the VEGF-C is selected from a sequence provided in Table 18 or a sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity thereto. In some embodiments, the VEGF-C sequence comprises or does not comprise a linker (e.g., a glycine-serine linker) and/or a his tag.

In some embodiments, the VEGF-C comprises the amino acid sequence of SEQ ID NO: 731, 732, 733, or 734, or a sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity thereto. In some embodiments, the VEGF-C comprises the amino acid sequence of SEQ ID NO: 741, or a sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity thereto, provided that position 26 is not Cysteine (C), e.g., is Alanine (A). In some embodiments, the VEGF-C comprises the amino acid sequence of SEQ ID NO: 737 or 738, or a sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity thereto.

In some embodiments, the VEGF-C comprises the amino acid sequence of SEQ ID NO: 743, or a sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity thereto. In some embodiments, the VEGF-C further comprises the amino acid sequence of SEQ ID NO: 740 or a sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity thereto.

In some embodiments, the VEGF-C comprises the amino acid sequence of SEQ ID NO: 736 or an amino acid sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity thereto. In some embodiments, the VEGF-C comprises the amino acid sequence of SEQ ID NO: 735 or an amino acid sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity thereto.

Table 18 – VEGF-C Variants

The sequences below correspond to a monomer. When a dimer is formed, 2 of the same sequences are assembled together via cysteine bridges. It is noted that the his tag is used for experimental purposes but may not be necessary in all embodiments.

SEQ ID NO:	DESCRIPTOR	SEQUENCE	KEY
725	**>sp|P49767|VEGFC_HUMAN Vascular endothelial growth factor C OS=Homo sapiens OX=9606 GN=VEGFC PE=1 SV=1**	MHLLGFFSVACSLLAAALLPGPREAPAAAAA**FESGLDLSDAEPDAGEATAYASKDLEEQLRSVSSVDELMTVLYPEYWKMYKCQLRKGGWQHNREQANLNSRTEETIKFAA**AHYNTEILKSIDNEWRKTQCMPREVCIDVGKEFGVATNTFFKPPCVSVYRCGGCCNSEGLQCMNTSTSYLSKTLFEITVPLSQGPKPVTISFANHTSCRCMSKLDVYRQVHSIIRRSLPATLPQCQAANKTCPTNYMWNNHICRCLAQEDFMFSSDAGDDSTDGFHDICGPNKELDEETCQCVCRAGLRPASCGPHKELDRNSCQCVCKNKLFPSQCGANREFDENTCQCVCKRTCPRNQPLNPGK	Underlined: cleaved residues **Bold:** propeptide

		CACECTESPQKCLLKGKKFHHQTCSCYRRPCTN RQKACEPGFSYSEEVCRCVPSYWKRPQMS	
727	**>1 immature peptide (32-227)-VEGFC_His**	FESGLDLSDAEPDAGEATAYASKDLEEQLRSVS SVDELMTVLYPEYWKMYKCQLRKGGWQHNRE QANLNSRTEETIKFAAAHYNTEILKSIDNEWRKT QCMPREVCIDVGKEFGVATNTFFKPPCVSVYRC GGCCNSEGLQCMNTSTSYLSKTLFEITVPLSQGP KPVTISFANHTSCRCMSKLDVYRQVHSIIRRGS**H HHHHH**	Underlined: propeptide Double underlined: GS linker **Bold**: his tag
729	**>1 immature peptide (32-227)-VEGFC**	FESGLDLSDAEPDAGEATAYASKDLEEQLRSVS SVDELMTVLYPEYWKMYKCQLRKGGWQHNRE QANLNSRTEETIKFAAAHYNTEILKSIDNEWRKT QCMPREVCIDVGKEFGVATNTFFKPPCVSVYRC GGCCNSEGLQCMNTSTSYLSKTLFEITVPLSQGP KPVTISFANHTSCRCMSKLDVYRQVHSIIRR	Underlined: propeptide
731	**>2 major mature (112-227)-VEGFC_His**	AHYNTEILKSIDNEWRKTQCMPREVCIDVGKEF GVATNTFFKPPCVSVYRCGGCCNSEGLQCMNT STSYLSKTLFEITVPLSQGPKPVTISFANHTSCRC MSKLDVYRQVHSIIRRGS**HHHHHH**	Double underlined: GS linker **Bold**: his tag
732	**>2 major mature (112-227)-VEGFC**	AHYNTEILKSIDNEWRKTQCMPREVCIDVGKEF GVATNTFFKPPCVSVYRCGGCCNSEGLQCMNT STSYLSKTLFEITVPLSQGPKPVTISFANHTSCRC MSKLDVYRQVHSIIRR	
733	**>7 minor mature (103-227)-VEGFC_His**	TEETIKFAAahynteilksidnewrktqcmprevcidvgkefgvat ntffkppcvsvyrcggccnseglqcmntstsylsktlfeitvplsqgpkpv tisfanhtscrcmskldvyrqvhsiirrgs**hhhhhh**	Capital: fragment of propeptide Double underlined: GS linker **Bold**: his tag
734	**>7 minor mature (103-227)-VEGFC**	TEETIKFAAahynteilksidnewrktqcmprevcidvgkefgvat ntffkppcvsvyrcggccnseglqcmntstsylsktlfeitvplsqgpkpv tisfanhtscrcmskldvyrqvhsiirr	Capital: fragment of propeptide
735	**>8 minor mature with mutation (103-227)-VEGFC_C137A_His**	TEETIKFAAahynteilksidnewrktqcmprev**A**idvgkefgva tntffkppcvsvyrcggccnseglqcmntstsylsktlfeitvplsqgpkp vtisfanhtscrcmskldvyrqvhsiirrgs**hhhhhh**	Capital: fragment of propeptide Capital, **bold** A: C to A mutation Double underlined: GS linker **Bold**: his tag
736	**>8 minor mature with mutation**	TEETIKFAAahynteilksidnewrktqcmprev**A**idvgkefgva tntffkppcvsvyrcggccnseglqcmntstsylsktlfeitvplsqgpkp vtisfanhtscrcmskldvyrqvhsiirr	Capital: fragment of propeptide

	(103-227)-VEGFC_C137A		Capital, **bold** A: C to A mutation
737	**>9 major mature with mutation (112-227)-VEGFC_C137A_His**	ahynteilksidnewrktqcmprev**A**idvgkefgvatntffkppcvsvyrcggccnseglqcmntstsylsktlfeitvplsqgpkpvtisfanhtscrcmskldvyrqvhsiirrgs**hhhhhh**	Capital, **bold** A: C to A mutation Double underlined: GS linker **Bold**: his tag
738	**>9 major mature with mutation (112-227)-VEGFC_C137A**	ahynteilksidnewrktqcmprev**A**idvgkefgvatntffkppcvsvyrcggccnseglqcmntstsylsktlfeitvplsqgpkpvtisfanhtscrcmskldvyrqvhsiirr	Capital, **bold** A: C to A mutation
739	**Propeptide**	FESGLDLSDAEPDAGEATAYASKDLEEQLRSVSSVDELMTVLYPEYWKMYKCQLRKGGWQHNREQANLNSRTEETIKFAA	
740	**Fragment of Propeptide**	TEETIKFAA	
741	**VEGF-C consensus**	ahynteilksidnewrktqcmprev**X**idvgkefgvatntffkppcvsvyrcggccnseglqcmntstsylsktlfeitvplsqgpkpvtisfanhtscrcmskldvyrqvhsiirr	wherein X is C or A
742	**VEGF-C**	ahynteilksidnewrktqcmprevcidvgkefgvatntffkppcvsvyrcggccnseglqcmntstsylsktlfeitvplsqgpkpvtisfanhtscrcmskldvyrqvhsiirr	
743	**VEGF-C with mutation**	ahynteilksidnewrktqcmprev**A**idvgkefgvatntffkppcvsvyrcggccnseglqcmntstsylsktlfeitvplsqgpkpvtisfanhtscrcmskldvyrqvhsiirr	Capital, **bold** A: C to A mutation

In some embodiments, the VEGF-C is present in an effective amount, optionally in an amount of less than or about 1 mg, less than or about 10 mg, greater than or about 10 µg, greater than or about 1 µg, between about 1 µg and 1 mg, between about 10 µg and 1 mg, between about 1 µg and 10 mg, or between about 10 µg and 10 mg.

In some embodiments, the cell recruitment factor can induce, e.g., promote, migration of immune cells, e.g., T cells. In some embodiments, the cell recruitment factor can increase the expansion or proliferation of a population of immune cells, e.g., T cells. In some embodiments, the cell recruitment factor comprises IL-15 (for example, hetIL-15 (IL15/sIL-15Ra)) or a functional variant thereof. Without wishing to be bound by theory, it is believed that use of a cell recruitment factor, e.g., IL-15 (for example hetIL-15 (IL15/sIL-15Ra)) or a variant thereof, in combination with a cryogel induces immune cell expansion or proliferation, resulting in

localized activation as well as promotion and enhancement of migration of immune cells, e.g., T cells, into the cryogel.

In some embodiments, the cell recruitment factor enhances immune cell, e.g., T cell, survival. In some embodiments, the cell recruitment factor comprises IL-7 or a functional variant thereof. Without wishing to be bound by theory, it is believed that use of a cell recruitment factor, e.g., IL-7 or functional variant thereof, in combination with a cryogel enhances immune cell, e.g., T cell survival, and proliferation.

In some embodiments, one, two, three, or more cell recruitment factors are to be used in a composition or method described herein. In some embodiments, the cell recruitment factor comprises VEGF-C or a functional variant thereof; IL-15 (for example, hetIL-15 (IL15/sIL-15Ra)) or a functional variant thereof; IL-7 or a functional variant thereof; or a combination thereof. In some embodiments, the cell recruitment factor comprises VEGF-C or a functional variant thereof and IL-15 (for example, hetIL-15 (IL15/sIL-15Ra)) or a functional variant thereof. In some embodiments, the cell recruitment factor comprises VEGF-C or a functional variant thereof and IL-7 or a functional variant. In some embodiments, the cell recruitment factor comprises VEGF-C or a functional variant thereof; IL-15 (for example, hetIL-15 (IL15/sIL-15Ra)) or a functional variant thereof; and IL-7 or a functional variant thereof. In some embodiments, the cell recruitment factor comprises IL-15 (for example, hetIL-15 (IL15/sIL-15Ra)) or a functional variant thereof; and IL-7 or a functional variant thereof.

Agent to Promote T cell Function

In some embodiments, a composition or method described herein utilizes an agent that promotes immune cell, e.g. T cell, function. In some embodiments, the agent to promote T cell, function reduces T cell exhaustion and/or prevents T cell dysfunction.

In some embodiments, the agent to promote T cell function comprises an inhibitor of a Tet2 gene, e.g., a Tet2 inhibitor. While not wishing to be bound by the theory, disruption of a single allele of a Tet gene (e.g., a Tet1, Tet2, or Tet3) leads to decreased total levels of 5-hydroxymethylcytosine in association with enhanced proliferation, regulation of effector cytokine production and degranulation, and thereby increases CAR T cell proliferation and/or function. In some embodiments, the Tet2 inhibitor comprises: (1) a gene editing system targeted to one or more sites within the gene encoding Tet2, or its corresponding regulatory elements; (2)

a nucleic acid (e.g., an siRNA or shRNA) that inhibits expression of Tet2; (3) a protein (e.g., a dominant negative, e.g., catalytically inactive) Tet2, or a binding partner of Tet2 (e.g., a dominant negative binding partner of Tet2); (4) a small molecule that inhibits expression and/or function of Tet2; (5) a nucleic acid encoding any of (1)-(3); or (6) any combination of (1) –(5). In some embodiments, the agent to promote T cell function comprises a Tet2 inhibitor as described in, e.g., WO2017/049166, WO2018/175733, and WO2019/210153, the contents of which are hereby incorporated by reference in their entirety.

In some embodiments, the agent to promote T cell function comprises an inhibitor of ZBTB32, e.g., a ZBTB32 inhibitor. Without wishing to be bound by theory, it is believed that in some embodiments, inhibition of ZBTB32 can enhance T cell-mediated anti-tumor response. In certain embodiments, inhiation of ZBTB32 enhances CART cell activity, e.g., cell expansion, cytokine production, persistence, resistance to exhaustion, and anti-tumor activity *in vivo*. In some embodiments, the ZBTB32 inhibitor comprises: (1) a gene editing system targeting the ZBTB32 gene or one or more components thereof; (2) a nucleic acid encoding one or more components of the gene editing system; or (3) a combination of (1) and (2). In an embodiment, the ZBTB32 inhibitor comprises: (1) a gene editing system targeting the ZBTB32 gene or one or more components thereof. In an embodiment, the ZBTB32 inhibitor comprises (2) a nucleic acid encoding one or more components of the gene editing system. In an embodiment, the ZBTB32 inhibitor comprises a combination of (1) and (2). In some embodiments, the agent to promote T cell function comprises a ZBTB32 inhibitor as described in PCT/US2021/037048, the contents of which are hereby incorporated by reference in their entirety.

Extended Release Agent

In some embodiments, a composition or method described herein utilizes an extended release agent. In some embodiments, the extended release agent can be used to provide extended release of a viral vector (e.g., a lentiviral vector, e.g., a lentiviral vector encoding a CAR), a cell activation agent, or both a viral vector and a cell activation agent. In some embodiments, the extended release agent is formulated for administration by injection. In some embodiments, the extended release agent comprises a particle, e.g., a silica particle, e.g., a mesoporous silica particle.

Surface modified mesoporous silica particles

In some embodiments, a composition or method described herein utilizes a mesoporous silica particle. Mesoporous silica particles comprise a porous body, for example, with hexagonal close-packed, cylinder-shaped, uniform pores. Mesoporous silica particles can be synthesized by using a rod-like micelle of a surfactant as a template, which is formed in water by dissolving and hydrolyzing a silica source such as alkoxysilane, sodium silicate solution, kanemite, silica fine particle in water or alcohol in the presence of acid or basic catalyst. See, e.g., US Pub. No. 2015-0072009 and Hoffmann et al., Angewandte Chemie International Edition, 45, 3216-3251, 2006. Many kinds of surfactants such as cationic, anionic, and nonionic surfactants have been examined as the surfactant and it has been known that generally, an alkyl trimethylammonium salt of cationic surfactant leads to a mesoporous silica having the greatest specific surface area and a pore volume. See, U.S. Publication No. 2013/0052117 and Katiyar et al. (Journal of Chromatography 1122 (1-2): 13-20).

The mesoporous silica particles may be provided in various forms, e.g., microspheres, irregular particles, rectangular rods, round nanorods. The mesoporous silica particles can have various predetermined shapes, including, e.g., a spheroid shape, an ellipsoid shape, a rod-like shape, or a curved cylindrical shape. In particular embodiments, the compositions and methods recited herein use mesoporous silica rods (MSR). Methods of assembling mesoporous silica to generate microrods are known in the art. See, Wang et al , *Journal of Nanoparticle Research*, 15: 1501, 2013. In some embodiments, mesoporous silica particles are synthesized by reacting tetraethyl orthosilicate with a template made of micellar rods. The result is a collection of mesoporous silica spheres or rods that are filled with a regular arrangement of pores. The template can then be removed by washing with a solvent adjusted to the proper pH. In this example, after removal of surfactant templates, the mesoporous silica particles are characterized by a uniform, ordered, and connected mesoporosity are prepared with a specific surface area of, for example, about 600 m^2/g to about 1200 m^2/g, particularly about 800 m^2/g to about 1000 m^2/g and especially about 850 m^2/g to about 950 m^2/g. In another embodiment, the mesoporous silica particles may be synthesized using a sol-gel method or a spray drying method. Tetraethyl orthosilicate is also used with an additional polymer monomer (as a template). In yet another embodiment, one or more tetraalkoxy-silanes and one or more (3-cyanopropyl)trialkoxy-silanes may be co-condensed to provide the mesoporous silicate particles as rods. See, US Publication

Nos. 2013-0145488, 2012-0264599 and 2012-0256336, the content of which are incorporated by reference in their entireties.

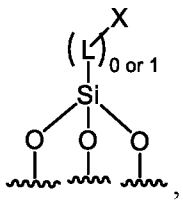
The mesoporous silica particles (MSPs) (e.g., MSRs) may comprise pores, which may be ordered or randomly distributed, of between 2 to 100 nm in diameter, or 2-50 nm in diameter, e.g., pores of between 2-5 nm, 10-20 nm, 10-30 nm, 10-40 nm, 20-30 nm, 30-50 nm, 30-40 nm, 40-50 nm. In some embodiments, the microrods comprise pores of approximately 5 nm, 6 nm, 7 nm, 8 nm, 9 nm, 10 nm, 11 nm, 12 nm, or more in diameter. The pore size may be altered depending on the type of application.

In some embodiments, the length of the MSRs is in the micrometer range, ranging from about 5 μm to about 500 μm. In one example, the MSRs comprise a length of 5-50 μm, e.g., 10-20 μm, 10-30 μm, 10-40 μm, 20-30 μm, 30-50 μm, 30-40 μm, 40-50 μm. In some embodiments, the MSRs comprise length of 50 μm to 250 μm, e.g., about 60 μm, 70 μm, 80 μm, 90 μm, 100 μm, 120 μm, 150 μm, 180 μm, 200 μm, 225 μm, or more. In some embodiments, the MSRs having a higher aspect ratio, e.g., with rods comprising a length of 50 μm to 200 μm, particularly a length of 80 μm to 120 μm, especially a length of about 100 μm or more, are used.
In yet another embodiment, the MSPs (e.g., MSRs) provide a high surface area for attachment and/or binding to target cells, e.g., T-cells. Methods of obtaining high surface area mesoporous silicates are known in the art. See, e.g., US patent No. 8,883,308 and US Publication No. 2011-0253643, the entire contents of which are incorporated by reference herein. In some embodiments, the high surface area is due to the fibrous morphology of the nanoparticles, which makes it possible to obtain a high concentration of highly dispersed and easily accessible moieties on the surface. In certain embodiments, the high surface area MSPs (e.g., MSRs) have a surface area of at least about 100 m^2/g, at least 150 m^2/g, or at least 300 m^2/g. In other embodiments, the high surface area MSPs (e.g., MSRs) have a surface area from about 100 m^2/g to about 1000 m^2/g, including all values or sub-ranges in between, e.g., 50 m^2/g, 100 m^2/g, 200 m^2/g, 300 m^2/g, 400 m^2/g, 600 m^2/g, 800 m^2/g, 100-500 m^2/g, 100-300 m^2/g, 500-800 m^2/g or 500-1000 m^2/g.

In some embodiments, the mesoporous silica particles may include a surface modification. As used herein, "surface modification" means attaching or appending functional groups on to the surface of the MSPs (e.g., MSRs). In some embodiments, the functional groups are adsorbed or covalently bonded onto the surfaces lining the pores and/or nanochannels or the

surface of the MSPs (e.g., MSRs). As used herein, the "functional group" defines a chemical moiety linked to the MSR. In some embodiments, the functional group is a –OH (hydroxyl), amine, carboxylic acid, phosphonate, halide, azide, alkyne, epoxide, sulfhydryl, disulfide, polyethyleneimine, hydrophobic moiety, or salts thereof. In some embodiments, the functional group (i.e. –OH (hydroxyl), amine, carboxylic acid, phosphonate, halide, azide, alkyne, epoxide, sulfhydryl, disulfide, polyethyleneimine, hydrophobic moiety, or salts thereof) may be separated from the silica surface by a linker. In some embodiments, the functional group is covalently bonded to the MSP or MSR surface via a C_1 to C_{20} alkyl linker. In other embodiments, the functional group is covalently bonded to the MSP or MSR surface via a polyethyleneglycol linker. In particular embodiments, the polyethylene glycol linker has the formula $(-O(CH_2\text{-}CH_2\text{-})_{1\text{-}25}$. In particular embodiments, the surface modification is a C_1 to C_{20} alkyl perhaloalkyl or a C_1 to C_{20} alkyl perfluoroalkyl.

A general structure of surface modifications may be as follows:



wherein L is a linker, and X is a functional group.

In some embodiments, L may be C_1 to C_{20} alkyl group or a polyethylene glycol group, and X may be –OH (hydroxyl), primary, secondary, tertiary or quaternary amine, carboxylic acid, phosphonate, halide, azide, alkyne, epoxide, sulfhydryl, disulfide, polyethyleneimine, or hydrophobic moiety, or salts thereof.

As used herein, surface modification having a phosphonate (also known as phosphonate-modified nanoparticles) have at least one phosphonic acid (—$P(O)(OH)_2$) group or phosphinic acid (—P(O)(OH)R, where R is an C_1 to C_{20} alkyl group). The phosphonic or phosphinic acid may be charged or uncharged, depending on the pH. At physiological pH, phosphonic acids and phosphinic acids are negatively charged, or anionic. Phosphonate modifications may be prepared, for example, by treating the silica body surface with a phosphonate bearing trialkylsiloxane compound or phosphonate-bearing trihydroxylsilyl compound, such as (trihydroxylsilyl)propyl methylphosphonate.

In some embodiments, the mesoporous silica particles (e.g., MSRs) are surface modified with a primary, secondary, tertiary, or quaternary amine. Secondary, tertiary, and quaternary amines may be substituted with C_1 to C_{20} alkyl groups and may be charged. In some embodiments, the amine group may be in the salt form. In some embodiments, the primary, secondary, tertiary, or quaternary amine may be separated from the MSP surface by a linker. In particular embodiments, the mesoporous silica particles are modified with polyethyleneimine. In specific embodiments, the polyethyleneimine is branched or unbranched. In alternate embodiments, the polyethyleneimine group has an average molecular weight in the range of about 1000 to 100,000 Daltons (Da), as measured by gel permeation chromatography (GPC). In some embodiments, the polyethyleneimine group has an average molecular weight of about 1,200 to 15,000 Da, about 1,500 to 12,000 Da, about 2,000 Da, about 3,000 Da, about 4,000 Da, about 5,000 Da, about 6,000 Da, about 7,000 Da, about 8,000 Da, about 9,000 Da, about 10,000 Da, or about 20,000 Da, as measured by gel permeation chromatography (GPC). Structures of various exemplary surface modified mesoporous silica particles are shown in FIG. 1.

The MSPs (e.g., MSRs) recited herein are prepared by methods known to those of skill in the art, as noted herein. Generally, MSPs with surface modification may be prepared by the following method.

In general, any reaction capable of reacting with the silyl hydroxide surface of the MSPs (e.g., MSRs) may be used to covalently modify the surface. For example, the surface of the MSP (e.g. MSR) may be treated with a trialkoxysilyl compound or trihydroxysilyl compound. In some embodiments mesoporous silica particles are suspended in a suitable reaction solvent. In some embodiments, the reaction solvent may be aqueous solvents or buffers of a pH from 0-14. Additional co-mixture of aqueous solutions with 1 or more organic solvents, including but not limited to tetrahydrofuran, 2-methyl tetrahydrofuran, ethyl acetate, toluene, triethylamine, dimethylformamide, dimethylacetamide, dimethylsulfoxide, methanol, ethanol, methylene chloride, or dichloroethane, may be used. In some embodiments, the suspended mesoporous silica particles are reacted with a trialkoxysilyl or trihydroxysilyl reagent having the desired functional group as described herein. Amine modifications may be prepared, for example, by treating the MSPs with an amine bearing trialkoxysilane compound, such as aminopropyltriethoxysilane, 3-(2-aminoethylamino)propyl-trimethoxysilane, or 3-

trimethoxysilylpropyl ethylenediamine. In certain embodiments, the trialkoxysilyl is a trimethoxysilyl or triethoxysilyl group. In alternate embodiments, the trialkoxysilyl reagent is a trialkoxy alkylamine. In some embodiments, the trialkoxy alkylamine includes a primary, secondary, tertiary, or quaternary amine.

In certain embodiments, the trialkoxysilyl reagent includes a polyethyleneimine group. In specific embodiments, the polyethyleneimine is branched or unbranched. In alternate embodiments, the polyethyleneimine group has an average molecular weight of about 1000 to 20,000 Da, about 1,200 to 15,000 Da, about 1,500 to 12,000 Da, about 2,000 Da, about 3,000 Da, about 4,000 Da, about 5,000 Da, about 6,000 Da, about 7,000 Da, about 8,000 Da, about 9,000 Da, or about 10,000 Da, as measured by gel permeation chromatography (GPC). In some embodiments, the trialkoxysilyl reagent includes an C_{1-20} alkylazide group. In certain embodiments, the trialkoxysilyl reagent includes an C_{1-20} alkylcarboxylic acid group. In other embodiments, the trialkoxysilyl reagent includes a C_{1-20} alkyl group.

A sulfhydryl modification on a MSP (e.g., MSR) may be prepared, for example, by treating the MSP with a sulfhydryl bearing trialkoxysilane compound, such as 3-mercaptopropyltriethoxysilane.

A disulfide modification on a MSP (e.g., MSR) may be prepared, for example, by treating the surface of the nanoparticle with a disulfide bearing trialkoxysilane compound, or by treating a sulfhydryl modified surface with 2,2′-dithiodipyridine or other disulfide.

MSP (e.g., MSR) surface modifications to include a carboxylic acid group may be prepared, for example, by treating the surface with a carboxylic acid bearing trialkoxysilane compound, or by treating the MSP with a trialkoxysilane compound bearing a functional group that may be converted chemically into a carboxylic acid. For example, the MSP may be treated with 3-cyanopropyltriethoxysilane, followed by hydrolysis with sulfuric acid.

MSP (e.g., MSR) surface modifications to include an epoxide will have at least one epoxide may be prepared, for example, by treating the MSP with an epoxide bearing trialkoxysilane compound, such as glycidoxypropyltriethoxysilane.

Surface modifications having a hydrophobic moiety will have at least one moiety intended to reduce the solubility in water, or increase the solubility in organic solvents. Examples of hydrophobic moieties include long chain alkyl groups (e.g., C_8-C_{20} alkyl groups), fatty acid esters (e.g., C_1-C_{22} alkyl acid esters), and aromatic rings having C_6-C_{10} carbon atoms.

In some embodiments, the reaction of the MSPs (e.g., MSRs) with the trialkoxysilyl reagent is carried out at ambient or room temperature. In other embodiments, the reaction is carried out at elevated temperatures. In further embodiments, the temperature of the reaction is from about 40 °C to about 120 °C, about 50 °C to about 100 °C, about 60 °C to about 80 °C, about 70 °C to about 80 °C, or about 50 °C, about 55 °C, about 60 °C, about 65 °C, about 70 °C, about 75 °C, about 80 °C, about 85 °C, about 90 °C, about 95 °C, or about 100 °C.

Viral vectors

In some embodiments, the compositions described herein can include an extended release agent, e.g., a mesoporous silica particle as described herein and a viral vector.

The viral vector can be any viral vector. Viral vector technology is well known in the art and is described, for example, in Sambrook et al., 2012, MOLECULAR CLONING: A LABORATORY MANUAL, volumes 1 -4, Cold Spring Harbor Press, NY), and in other virology and molecular biology manuals. By way of example, the viral vector can be an adenovirus, a lentivirus, a retrovirus, an adeno-associated virus, or a herpesvirus. In some embodiments, the viral vector is a lentivirus vector or an adenovirus vector.

Vectors derived from retroviruses such as the lentivirus are suitable tools to achieve long-term gene transfer since they allow long-term, stable integration of a transgene and its propagation in daughter cells. Lentiviral vectors have the added advantage over vectors derived from onco-retroviruses such as murine leukemia viruses in that they can transduce non-proliferating cells, such as hepatocytes. They also have the added advantage of low immunogenicity. A retroviral vector may also be, e.g., a gammaretroviral vector. A gammaretroviral vector may include, e.g., a promoter, a packaging signal (ψ), a primer binding site (PBS), one or more (e.g., two) long terminal repeats (LTR), and a transgene of interest, e.g., a gene encoding a CAR. A gammaretroviral vector may lack viral structural gens such as gag, pol, and env. Exemplary gammaretroviral vectors include Murine Leukemia Virus (MLV), Spleen-Focus Forming Virus (SFFV), and Myeloproliferative Sarcoma Virus (MPSV), and vectors derived therefrom. Other gammaretroviral vectors are described, e.g., in Tobias Maetzig et al., "Gammaretroviral Vectors: Biology, Technology and Application" Viruses. 2011 Jun; 3(6): 677–713.

In another embodiment, the vector comprising the nucleic acid encoding the desired CAR of the invention is an adenoviral vector (A5/35). In another embodiment, the expression of nucleic acids encoding CARs can be accomplished using of transposons such as sleeping beauty, CRISPR, CAS9, and zinc finger nucleases. See June et al. 2009 *Nature Reviews Immunology* 9.10: 704-716, is incorporated herein by reference.

In some embodiments, the viral vector comprises an expression vector comprising a recombinant polynucleotide comprising an expression control sequence operatively linked to a nucleotide sequence to be expressed. In some embodiments, the nucleotide sequence expresses a chimeric antigen receptor (CAR), engineered TCR, cytokines, chemokines, shRNA to block an inhibitory molecule, or mRNA to induce expression of protein. In some embodiments, the protein is a CAR that comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region, and a signaling domain. In some embodiments, the signaling domain is a CD3 zeta signaling domain.

In some embodiments, the nucleotide sequence in the viral vector express a peptide engineered to target a tumor antigen. In some embodiments, the peptide targets a tumor antigen selected from the group consisting of: TSHR, CD19, CD123, CD22, CD30, CD171, CS-1, CLL-1, CD33, EGFRvIII , GD2, GD3, BCMA, Tn Ag, PSMA, ROR1, FLT3, FAP, TAG72, CD38, CD44v6, CEA, EPCAM, B7H3, KIT, IL-13Ra2, Mesothelin, IL-11Ra, PSCA, PRSS21, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, CD20, Folate receptor alpha, ERBB2 (Her2/neu), MUC1, EGFR, NCAM, Prostase, PAP, ELF2M, Ephrin B2, IGF-I receptor, CAIX, LMP2, gp100, bcr-abl, tyrosinase, EphA2, Fucosyl GM1, sLe, GM3, TGS5, HMWMAA, o-acetyl-GD2, Folate receptor beta, TEM1/CD248, TEM7R, CLDN6, GPRC5D, CXORF61, CD97, CD179a, ALK, Polysialic acid, PLAC1, GloboH, NY-BR-1, UPK2, HAVCR1, ADRB3, PANX3, GPR20, LY6K, OR51E2, TARP, WT1, NY-ESO-1, LAGE-1a, MAGE-A1, legumain, HPV E6,E7, MAGE A1, ETV6-AML, sperm protein 17, XAGE1, Tie 2, MAD-CT-1, MAD-CT-2, Fos-related antigen 1, p53, p53 mutant, prostein, survivin and telomerase, PCTA-1/Galectin 8, MelanA/MART1, Ras mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, TRP-2, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP-4, SSX2, RAGE-1, human telomerase reverse transcriptase, RU1, RU2, intestinal carboxyl esterase, mut hsp70-2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3,

FCRL5, IGLL1, and any combination thereof. In some embodiments, the peptide is a chimeric antigen receptor (CAR) or an engineered TCR. Such peptides are described in greater detail herein below in the section entitled General Description of Chimeric Antigen Receptor Technology.

In some embodiments, the nucleotide sequence in the vector expresses a protein engineered to target a tumor antigen. In some embodiments, the tumor antigen is chosen from one or more of: CD19; CD123; CD22; CD30; CD171; CS-1 (also referred to as CD2 subset 1, CRACC, SLAMF7, CD319, and 19A24); C-type lectin-like molecule-1 (CLL-1 or CLECL1); CD33; epidermal growth factor receptor variant III (EGFRvIII); ganglioside G2 (GD2); ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); TNF receptor family member B cell maturation (BCMA); Tn antigen ((Tn Ag) or (GalNAcα-Ser/Thr)); prostate-specific membrane antigen (PSMA); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Fms-Like Tyrosine Kinase 3 (FLT3); Tumor-associated glycoprotein 72 (TAG72); CD38; CD44v6; Carcinoembryonic antigen (CEA); Epithelial cell adhesion molecule (EPCAM); B7H3 (CD276); KIT (CD117); Interleukin-13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Mesothelin; Interleukin 11 receptor alpha (IL-11Ra); prostate stem cell antigen (PSCA); Protease Serine 21 (Testisin or PRSS21); vascular endothelial growth factor receptor 2 (VEGFR2); Lewis(Y) antigen; CD24; Platelet-derived growth factor receptor beta (PDGFR-beta); Stage-specific embryonic antigen-4 (SSEA-4); CD20; Folate receptor alpha; Receptor tyrosine-protein kinase ERBB2 (Her2/neu); Mucin 1, cell surface associated (MUC1); epidermal growth factor receptor (EGFR); neural cell adhesion molecule (NCAM); Prostase; prostatic acid phosphatase (PAP); elongation factor 2 mutated (ELF2M); Ephrin B2; fibroblast activation protein alpha (FAP); insulin-like growth factor 1 receptor (IGF-I receptor), carbonic anhydrase IX (CAIX); Proteasome (Prosome, Macropain) Subunit, Beta Type, 9 (LMP2); glycoprotein 100 (gp100); oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); tyrosinase; ephrin type-A receptor 2 (EphA2); Fucosyl GM1; sialyl Lewis adhesion molecule (sLe); ganglioside GM3 (aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); transglutaminase 5 (TGS5); high molecular weight-melanoma-associated antigen (HMWMAA); o-acetyl-GD2 ganglioside (OAcGD2); Folate receptor beta; tumor endothelial marker 1 (TEM1/CD248); tumor endothelial marker 7-related (TEM7R); claudin 6 (CLDN6); thyroid stimulating hormone receptor (TSHR); G protein-coupled receptor

class C group 5, member D (GPRC5D); chromosome X open reading frame 61 (CXORF61); CD97; CD179a; anaplastic lymphoma kinase (ALK); Polysialic acid; placenta-specific 1 (PLAC1); hexasaccharide portion of globoH glycoceramide (GloboH); mammary gland differentiation antigen (NY-BR-1); uroplakin 2 (UPK2); Hepatitis A virus cellular receptor 1 (HAVCR1); adrenoceptor beta 3 (ADRB3); pannexin 3 (PANX3); G protein-coupled receptor 20 (GPR20); lymphocyte antigen 6 complex, locus K 9 (LY6K); Olfactory receptor 51E2 (OR51E2); TCR Gamma Alternate Reading Frame Protein (TARP); Wilms tumor protein (WT1); Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-1a); Melanoma-associated antigen 1 (MAGE-A1); ETS translocation-variant gene 6, located on chromosome 12p (ETV6-AML); sperm protein 17 (SPA17); X Antigen Family, Member 1A (XAGE1); angiopoietin-binding cell surface receptor 2 (Tie 2); melanoma cancer testis antigen-1 (MAD-CT-1); melanoma cancer testis antigen-2 (MAD-CT-2); Fos-related antigen 1; tumor protein p53 (p53); p53 mutant; prostein; surviving; telomerase; prostate carcinoma tumor antigen-1 (PCTA-1 or Galectin 8), melanoma antigen recognized by T cells 1 (MelanA or MART1); Rat sarcoma (Ras) mutant; human Telomerase reverse transcriptase (hTERT); sarcoma translocation breakpoints; melanoma inhibitor of apoptosis (ML-IAP); ERG (transmembrane protease, serine 2 (TMPRSS2) ETS fusion gene); N-Acetyl glucosaminyl-transferase V (NA17); paired box protein Pax-3 (PAX3); Androgen receptor; Cyclin B1; v-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Ras Homolog Family Member C (RhoC); Tyrosinase-related protein 2 (TRP-2); Cytochrome P450 1B1 (CYP1B1); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites), Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Paired box protein Pax-5 (PAX5); proacrosin binding protein sp32 (OY-TES1); lymphocyte-specific protein tyrosine kinase (LCK); A kinase anchor protein 4 (AKAP-4); synovial sarcoma, X breakpoint 2 (SSX2); Receptor for Advanced Glycation End products (RAGE-1); renal ubiquitous 1 (RU1); renal ubiquitous 2 (RU2); legumain; human papilloma virus E6 (HPV E6); human papilloma virus E7 (HPV E7); intestinal carboxyl esterase; heat shock protein 70-2 mutated (mut hsp70-2); CD79a; CD79b; CD72; Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Fc fragment of IgA receptor (FCAR or CD89); Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); CD300 molecule-like family member f (CD300LF); C-type lectin domain family 12 member A (CLEC12A); bone marrow stromal cell antigen 2 (BST2); EGF-like module-

containing mucin-like hormone receptor-like 2 (EMR2); lymphocyte antigen 75 (LY75); Glypican-3 (GPC3); Fc receptor-like 5 (FCRL5); and immunoglobulin lambda-like polypeptide 1 (IGLL1).

A CAR described herein can comprise an antigen binding domain (e.g., antibody or antibody fragment, TCR or TCR fragment) that binds to a tumor-supporting antigen (e.g., a tumor-supporting antigen as described herein). In some embodiments, the tumor-supporting antigen is an antigen present on a stromal cell or a myeloid-derived suppressor cell (MDSC). Stromal cells can secrete growth factors to promote cell division in the microenvironment. MDSC cells can inhibit T cell proliferation and activation. Without wishing to be bound by theory, in some embodiments, the CAR-expressing cells destroy the tumor-supporting cells, thereby indirectly inhibiting tumor growth or survival.

In some embodiments, the stromal cell antigen is chosen from one or more of: bone marrow stromal cell antigen 2 (BST2), fibroblast activation protein (FAP) and tenascin. In some embodiments, the FAP-specific antibody is, competes for binding with, or has the same CDRs as, sibrotuzumab. In embodiments, the MDSC antigen is chosen from one or more of: CD33, CD11b, C14, CD15, and CD66b. Accordingly, in some embodiments, the tumor-supporting antigen is chosen from one or more of: bone marrow stromal cell antigen 2 (BST2), fibroblast activation protein (FAP) or tenascin, CD33, CD11b, C14, CD15, and CD66b.

In some embodiments, the antigen binding domain of the encoded CAR molecule comprises an antibody, an antibody fragment, an scFv, a Fv, a Fab, a (Fab')2, a single domain antibody (SDAB), a VH or VL domain, a camelid VHH domain or a bi-functional (e.g. bi-specific) hybrid antibody (e.g., Lanzavecchia et al., Eur. J. Immunol. 17, 105 (1987)).

In some instances, scFvs can be prepared according to method known in the art (see, for example, Bird et al., (1988) Science 242:423-426 and Huston et al., (1988) Proc. Natl. Acad. Sci. USA 85:5879-5883). ScFv molecules can be produced by linking VH and VL regions together using flexible polypeptide linkers. The scFv molecules comprise a linker (e.g., a Ser-Gly linker) with an optimized length and/or amino acid composition. The linker length can greatly affect how the variable regions of a scFv fold and interact. In fact, if a short polypeptide linker is employed (e.g., between 5-10 amino acids) intrachain folding is prevented. Interchain folding is also required to bring the two variable regions together to form a functional epitope binding site. For examples of linker orientation and size see, e.g., Hollinger et al. 1993 Proc Natl Acad. Sci.

U.S.A. 90:6444-6448, U.S. Patent Application Publication Nos. 2005/0100543, 2005/0175606, 2007/0014794, and PCT publication Nos. WO2006/020258 and WO2007/024715, is incorporated herein by reference.

An scFv can comprise a linker of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30, 35, 40, 45, 50, or more amino acid residues between its VL and VH regions. The linker sequence may comprise any naturally occurring amino acid. In some embodiments, the linker sequence comprises amino acids glycine and serine. In another embodiment, the linker sequence comprises sets of glycine and serine repeats such as $(Gly_4Ser)n$, where n is a positive integer equal to or greater than 1 (SEQ ID NO: 22). In some embodiments, the linker can be $(Gly_4Ser)_4$ (SEQ ID NO:29) or $(Gly_4Ser)_3$(SEQ ID NO:30). Variation in the linker length may retain or enhance activity, giving rise to superior efficacy in activity studies.
In another aspect, the antigen binding domain is a T cell receptor ("TCR"), or a fragment thereof, for example, a single chain TCR (scTCR). Methods to make such TCRs are known in the art. See, e.g., Willemsen RA et al, Gene Therapy 7: 1369–1377 (2000); Zhang T et al, Cancer Gene Ther 11: 487–496 (2004); Aggen et al, Gene Ther. 19(4):365-74 (2012) (references are incorporated herein by its entirety). For example, scTCR can be engineered that contains the Vα and Vβ genes from a T cell clone linked by a linker (e.g., a flexible peptide). This approach is very useful to cancer associated target that itself is intracellular, however, a fragment of such antigen (peptide) is presented on the surface of the cancer cells by MHC.
In certain embodiments, the encoded antigen binding domain has a binding affinity KD of 10^{-4} M to 10^{-8} M.

In some embodiments, the encoded CAR molecule comprises an antigen binding domain that has a binding affinity KD of 10^{-4} M to 10^{-8} M, e.g., 10^{-5} M to 10^{-7} M, e.g., 10^{-6} M or 10^{-7} M, for the target antigen. In some embodiments, the antigen binding domain has a binding affinity that is at least five-fold, 10-fold, 20-fold, 30-fold, 50-fold, 100-fold or 1,000-fold less than a reference antibody, e.g., an antibody described herein. In some embodiments, the encoded antigen binding domain has a binding affinity at least 5-fold less than a reference antibody (e.g., an antibody from which the antigen binding domain is derived). In some aspects such antibody fragments are functional in that they provide a biological response that can include, but is not limited to, activation of an immune response, inhibition of signal-transduction origination from

its target antigen, inhibition of kinase activity, and the like, as will be understood by a skilled artisan.

In some aspects, the antigen binding domain of the CAR is a scFv antibody fragment that is humanized compared to the murine sequence of the scFv from which it is derived.
In some aspects, the antigen binding domain of a CAR of the invention (e.g., a scFv) is encoded by a nucleic acid molecule whose sequence has been codon optimized for expression in a mammalian cell. In some aspects, entire CAR construct of the invention is encoded by a nucleic acid molecule whose entire sequence has been codon optimized for expression in a mammalian cell. Codon optimization refers to the discovery that the frequency of occurrence of synonymous codons (i.e., codons that code for the same amino acid) in coding DNA is biased in different species. Such codon degeneracy allows an identical polypeptide to be encoded by a variety of nucleotide sequences. A variety of codon optimization methods is known in the art, and include, e.g., methods disclosed in at least US Patent Numbers 5,786,464 and 6,114,148.

In some embodiments involving immune effector cells engineered to express a CAR molecule, e.g., as described herein, it is understood that the treatment method may further include any of the steps, aspects or features described below in the section relating to Chimeric Antigen Receptors.

The cells are preferably immune effector cells. In some embodiments, the cells are T cells. In some embodiments, the cells are NK cells. In embodiments, the invention relates to a population of cells of the invention, e.g., a population of immune effector cells of the invention. In embodiments, the population of cells of the invention comprises cells of the type indicated, and may comprise other types (e.g., a population of immune effector cells, e.g., T cells, engineered to express a CAR molecule, e.g., as described herein, may include T cells engineered to express a CAR molecule as well as T cells (or other cell types) that have not been engineered to express a CAR molecule). In embodiments, the population of cells used in the methods of the invention consists essentially of cells of the type indicated. In embodiments, the population of cells of the invention is substantially free of other cell types. In embodiments, the population of cells of the invention consists of the indicated cell type.

In any of the foregoing aspects and embodiments, the cells and/or population of cells are or include immune effector cells, e.g., the population of immune effector cells includes, e.g.,

consists of, T cells or NK cells. In embodiments the cells are T cells, e.g., CD8+ T cells, CD4+ T cells, or a combination thereof. In embodiments the cells are NK cells.
In embodiments the cells are human cells. In embodiments, the cells are autologous, e.g., to the subject to be administered the cells. In embodiments, the cells are allogeneic, e.g., to the subject to be administered the cells.

In general, in the methods described herein, the compositions described herein may be administered in therapeutically effective amounts as described above via any of the usual and acceptable modes known in the art, either singly or in combination with one or more therapeutic agents. In particular embodiments, the compositions are administered by injection. In still particular embodiments, for in vivo administration, the compositions are administered subcutaneously to a subject in need thereof. In other embodiments, the compositions may be administered in the form of an implant at the desired site of action. The site of action may be determined by a person of skill in the art in accordance with the needs of the subject.

CAR Targets

Described herein are viral vectors to transduce immune effector cells (e.g., T cells, NK cells) that are engineered to contain one or more CARs that direct the immune effector cells to undesired cells (e.g., cancer cells). This is achieved through an antigen binding domain on the CAR that is specific for a cancer associated antigen. There are two classes of cancer associated antigens (tumor antigens) that can be targeted by the CARs of the instant invention: (1) cancer associated antigens that are expressed on the surface of cancer cells; and (2) cancer associated antigens that itself is intracellular, however, a fragment of such antigen (peptide) is presented on the surface of the cancer cells by MHC (major histocompatibility complex).

In some embodiments, the tumor antigen is chosen from one or more of: CD19; CD123; CD22; CD30; CD171; CS-1 (also referred to as CD2 subset 1, CRACC, SLAMF7, CD319, and 19A24); C-type lectin-like molecule-1 (CLL-1 or CLECL1); CD33; epidermal growth factor receptor variant III (EGFRvIII); ganglioside G2 (GD2); ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); TNF receptor family member B cell maturation (BCMA); Tn antigen ((Tn Ag) or (GalNAcα-Ser/Thr)); prostate-specific membrane antigen (PSMA); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Fms-Like Tyrosine Kinase 3 (FLT3); Tumor-associated glycoprotein 72 (TAG72); CD38; CD44v6; Carcinoembryonic

antigen (CEA); Epithelial cell adhesion molecule (EPCAM); B7H3 (CD276); KIT (CD117); Interleukin-13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Mesothelin; Interleukin 11 receptor alpha (IL-11Ra); prostate stem cell antigen (PSCA); Protease Serine 21 (Testisin or PRSS21); vascular endothelial growth factor receptor 2 (VEGFR2); Lewis(Y) antigen; CD24; Platelet-derived growth factor receptor beta (PDGFR-beta); Stage-specific embryonic antigen-4 (SSEA-4); CD20; Folate receptor alpha; Receptor tyrosine-protein kinase ERBB2 (Her2/neu); Mucin 1, cell surface associated (MUC1); epidermal growth factor receptor (EGFR); neural cell adhesion molecule (NCAM); Prostase; prostatic acid phosphatase (PAP); elongation factor 2 mutated (ELF2M); Ephrin B2; fibroblast activation protein alpha (FAP); insulin-like growth factor 1 receptor (IGF-I receptor), carbonic anhydrase IX (CAIX); Proteasome (Prosome, Macropain) Subunit, Beta Type, 9 (LMP2); glycoprotein 100 (gp100); oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); tyrosinase; ephrin type-A receptor 2 (EphA2); Fucosyl GM1; sialyl Lewis adhesion molecule (sLe); ganglioside GM3 (aNeu5Ac(2-3)bDGalp(1-4)bDGlcp(1-1)Cer); transglutaminase 5 (TGS5); high molecular weight-melanoma-associated antigen (HMWMAA); o-acetyl-GD2 ganglioside (OAcGD2); Folate receptor beta; tumor endothelial marker 1 (TEM1/CD248); tumor endothelial marker 7-related (TEM7R); claudin 6 (CLDN6); thyroid stimulating hormone receptor (TSHR); G protein-coupled receptor class C group 5, member D (GPRC5D); chromosome X open reading frame 61 (CXORF61); CD97; CD179a; anaplastic lymphoma kinase (ALK); Polysialic acid; placenta-specific 1 (PLAC1); hexasaccharide portion of globoH glycoceramide (GloboH); mammary gland differentiation antigen (NY-BR-1); uroplakin 2 (UPK2); Hepatitis A virus cellular receptor 1 (HAVCR1); adrenoceptor beta 3 (ADRB3); pannexin 3 (PANX3); G protein-coupled receptor 20 (GPR20); lymphocyte antigen 6 complex, locus K 9 (LY6K); Olfactory receptor 51E2 (OR51E2); TCR Gamma Alternate Reading Frame Protein (TARP); Wilms tumor protein (WT1); Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-1a); Melanoma-associated antigen 1 (MAGE-A1); ETS translocation-variant gene 6, located on chromosome 12p (ETV6-AML); sperm protein 17 (SPA17); X Antigen Family, Member 1A (XAGE1); angiopoietin-binding cell surface receptor 2 (Tie 2); melanoma cancer testis antigen-1 (MAD-CT-1); melanoma cancer testis antigen-2 (MAD-CT-2); Fos-related antigen 1; tumor protein p53 (p53); p53 mutant; prostein; surviving; telomerase; prostate carcinoma tumor antigen-1 (PCTA-1 or Galectin 8), melanoma antigen

recognized by T cells 1 (MelanA or MART1); Rat sarcoma (Ras) mutant; human Telomerase reverse transcriptase (hTERT); sarcoma translocation breakpoints; melanoma inhibitor of apoptosis (ML-IAP); ERG (transmembrane protease, serine 2 (TMPRSS2) ETS fusion gene); N-Acetyl glucosaminyl-transferase V (NA17); paired box protein Pax-3 (PAX3); Androgen receptor; Cyclin B1; v-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Ras Homolog Family Member C (RhoC); Tyrosinase-related protein 2 (TRP-2); Cytochrome P450 1B1 (CYP1B1); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites), Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Paired box protein Pax-5 (PAX5); proacrosin binding protein sp32 (OY-TES1); lymphocyte-specific protein tyrosine kinase (LCK); A kinase anchor protein 4 (AKAP-4); synovial sarcoma, X breakpoint 2 (SSX2); Receptor for Advanced Glycation End products (RAGE-1); renal ubiquitous 1 (RU1); renal ubiquitous 2 (RU2); legumain; human papilloma virus E6 (HPV E6); human papilloma virus E7 (HPV E7); intestinal carboxyl esterase; heat shock protein 70-2 mutated (mut hsp70-2); CD79a; CD79b; CD72; Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Fc fragment of IgA receptor (FCAR or CD89); Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); CD300 molecule-like family member f (CD300LF); C-type lectin domain family 12 member A (CLEC12A); bone marrow stromal cell antigen 2 (BST2); EGF-like module-containing mucin-like hormone receptor-like 2 (EMR2); lymphocyte antigen 75 (LY75); Glypican-3 (GPC3); Fc receptor-like 5 (FCRL5); and immunoglobulin lambda-like polypeptide 1 (IGLL1).

CD19

An non-limiting exemplary tumor antigen is CD19. CARs that bind to CD19 are known in the art. For example, those disclosed in WO2012/079000 and WO2014/153270. Any known CD19 CAR, for example, the CD19 antigen binding domain of any known CD19 CAR, in the art can be used in accordance with the present disclosure. For example, LG-740; CD19 CAR described in the US Pat. No. 8,399,645; US Pat. No. 7,446,190; Xu et al., Leuk Lymphoma. 2013 54(2):255-260(2012); Cruz et al., Blood 122(17):2965-2973 (2013); Brentjens et al., Blood, 118(18):4817-4828 (2011); Kochenderfer et al., Blood 116(20):4099-102 (2010); Kochenderfer et al., Blood 122 (25):4129-39(2013); and 16th Annu Meet Am Soc Gen Cell Ther (ASGCT) (May 15-18, Salt Lake City) 2013, Abst 10.

Non-limiting exemplary CD19 CARs include CD19 CARs described herein or an anti-CD19 CAR described in Xu et al. Blood 123.24(2014):3750-9; Kochenderfer et al. Blood 122.25(2013):4129-39, Cruz et al. Blood 122.17(2013):2965-73, NCT00586391, NCT01087294, NCT02456350, NCT00840853, NCT02659943, NCT02650999, NCT02640209, NCT01747486, NCT02546739, NCT02656147, NCT02772198, NCT00709033, NCT02081937, NCT00924326, NCT02735083, NCT02794246, NCT02746952, NCT01593696, NCT02134262, NCT01853631, NCT02443831, NCT02277522, NCT02348216, NCT02614066, NCT02030834, NCT02624258, NCT02625480, NCT02030847, NCT02644655, NCT02349698, NCT02813837, NCT02050347, NCT01683279, NCT02529813, NCT02537977, NCT02799550, NCT02672501, NCT02819583, NCT02028455, NCT01840566, NCT01318317, NCT01864889, NCT02706405, NCT01475058, NCT01430390, NCT02146924, NCT02051257, NCT02431988, NCT01815749, NCT02153580, NCT01865617, NCT02208362, NCT02685670, NCT02535364, NCT02631044, NCT02728882, NCT02735291, NCT01860937, NCT02822326, NCT02737085, NCT02465983, NCT02132624, NCT02782351, NCT01493453, NCT02652910, NCT02247609, NCT01029366, NCT01626495, NCT02721407, NCT01044069, NCT00422383, NCT01680991, NCT02794961, or NCT02456207, each of which is incorporated herein by reference in its entirety.

In some embodiments, the CD19 CAR comprises the fusion polypeptide sequence provided as SEQ ID NO: 12 in WO2012/079000, which provides an scFv fragment of murine origin that specifically binds to human CD19.

In some embodiments, the CD19 CAR comprises an amino acid sequence provided as SEQ ID NO: 12 in WO2012/079000.

In some embodiments, the CD19 CAR comprises the amino acid sequence: diqmtqttsslsaslgdrvtiscrasqdiskylnwyqqkpdgtvklliyhtsrlhsgvpsrfsgsgsgtdysltisnleqediatyfcqqgntl pytfgggtkleitggggsggggsggggsevklqesgpglvapsqslsvtctvsgvslpdygvswirqpprkglewlgviwgsettyyn salksrltiikdnsksqvflkmnslqtddtaiyycakhyyyggsyamdywgqgtsvtvsstttpaprpptpaptiasqplslrpeacrpa aggavhtrgldfacdiyiwaplagtcgvlllslvitlyckrgrkkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadap aykqgqnqlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmaeayseigmkgerrrgkghdglyqglstat kdtydalhmqalppr (SEQ ID NO: 757), or a sequence substantially homologous thereto.

In some embodiments, the CD19 CAR comprises the amino acid sequence: eivmtqspatlslspgeratlscrasqdiskylnwyqqkpgqaprlliyhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcqqgntl

pytfgqgtkleikggggsggggsggggsqvqlqesgpglvkpsetlsltctvsgvslpdygvswirqppgkglewigviwgsettyyq sslksrvtiskdnsknqvslklssvtaadtavyycakhyyyggsyamdywgqgtlvtvss (SEQ ID NO: 758)

In some embodiments, the CD19 CAR is a humanized CD19 CAR comprising the amino acid sequence:

eivmtqspatlslspgeratlscrasqdiskylnwyqqkpgqaprlliyhtsrlhsgiparfsgsgsgtdytltisslqpedfavyfcqqgntl pytfgqgtkleikggggsggggsggggsqvqlqesgpglvkpsetlsltctvsgvslpdygvswirqppgkglewigviwgsettyyq sslksrvtiskdnsknqvslklssvtaadtavyycakhyyyggsyamdywgqgtlvtvsstttpaprpptpaptiasqplslrpeacrpa aggavhtrgldfacdiyiwaplagtcgvlllslvitlyckrgrkkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsadap aykqgqnqlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmaeayseigmkgerrrgkghdglyqglstat kdtydalhmqalppr (SEQ ID NO: 759)

In some embodiments, CD19 CARs comprise a sequence, for example, a CDR, VH, VL, scFv, or full-CAR sequence, disclosed in Table 1 below, or a sequence having at least 80%, 85%, 90%, 95%, or 99% identity thereto.

Table 1. Amino acid sequences of exemplary anti-CD19 molecules

SEQ ID NO	Region	Sequence
CTL019		
760	HCDR1 (Kabat)	DYGVS
761	HCDR2 (Kabat)	VIWGSETTYYNSALKS
762	HCDR3 (Kabat)	HYYYGGSYAMDY
763	LCDR1 (Kabat)	RASQDISKYLN
764	LCDR2 (Kabat)	HTSRLHS
765	LCDR3 (Kabat)	QQGNTLPYT
766	CTL019 Full amino acid sequence	MALPVTALLLPLALLLHAARPdiqmtqttsslsaslgdrvtiscrasqdis kylnwyqqkpdgtvklliyhtsrlhsgvpsrfsgsgsgtdysltisnleqediatyfcqqg ntlpytfgggtkleitggggsggggsggggsevklqesgpglvapsqslsvtctvsgvsl pdygvswirqpprkglewlgviwgsettyynsalksrltiikdnsksqvflkmnslqtd dtaiyycakhyyyggsyamdywgqgtsvtvsstttpaprpptpaptiasqplslrpeac rpaaggavhtrgldfacdiyiwaplagtcgvlllslvitlyckrgrkkllyifkqpfmrpvq ttqeedgcscrfpeeeeggcelrvkfsrsadapaykqgqnqlynelnlgrreeydvldkr

		rgrdpemggkprrknpqeglynelqkdkmaeayseigmkgerrrgkghdglyqgls tatkdtydalhmqalppr
685	CTL019 Full nucleotide sequence	atggccttaccagtgaccgccttgctcctgccgctggccttgctgctccacgccgccaggc cggacatccagatgacacagactacatcctccctgtctgcctctctgggagacagagtcac catcagttgcagggcaagtcaggacattagtaaatatttaaattggtatcagcagaaaccag atggaactgttaaactcctgatctaccatacatcaagattacactcaggagtcccatcaaggt tcagtggcagtgggtctggaacagattattctctcaccattagcaacctggagcaagaagat attgccacttacttttgccaacagggtaatacgcttccgtacacgttcggaggggggaccaa gctggagatcacaggtggcggtggctcgggcggtggtgggtcgggtggcggcggatct gaggtgaaactgcaggagtcaggacctggcctggtggcgccctcacagagcctgtccgt cacatgcactgtctcaggggtctcattacccgactatggtgtaagctggattcgccagcctc cacgaaagggtctggagtggctgggagtaatatggggtagtgaaaccacatactataattc agctctcaaatccagactgaccatcatcaaggacaactccaagagccaagttttcttaaaaat gaacagtctgcaaactgatgacacagccatttactactgtgccaaacattattactacggtgg tagctatgctatggactactggggccaaggaacctcagtcaccgtctcctcaaccacgacg ccagcgccgcgaccaccaacaccggcgcccaccatcgcgtcgcagcccctgtccctgc gcccagaggcgtgccggccagcggcgggggggcgcagtgcacacgaggggctggac ttcgcctgtgatatctacatctgggcgcccttggccgggacttgtggggtccttctcctgtcac tggttatcacccctttactgcaaacggggcagaaagaaactcctgtatatattcaaacaaccat ttatgagaccagtacaaactactcaagaggaagatggctgtagctgccgatttccagaaga agaagaaggaggatgtgaactgagagtgaagttcagcaggagcgcagacgccccgcg tacaagcagggccagaaccagctctataacgagctcaatctaggacgaagagaggagta cgatgttttggacaagagacgtggccgggaccctgagatgggggaaagccgagaagg aagaaccctcaggaaggcctgtacaatgaactgcagaaagataagatggcggaggccta cagtgagattgggatgaaaggcgagcgccggaggggcaaggggcacgatggcctttac cagggtctcagtacagccaccaaggacacctacgacgcccttcacatgcaggccctgccc cctcgc
686	CTL019 scFv domain	Diqmtqttsslsaslgdrvtiscrasqdiskylnwyqqkpdgtvklliyhtsrlhsgvpsrf sgsgsgtdysltisnleqediatyfcqqgntlpytfgggtkleitggggsggggsggggse vklqesgpglvapsqslsvtctvsgvslpdygvswirqpprkglewlgviwgsettyyn salksrltiikdnsksqvflkmnslqtddtaiyycakhyyyggsyamdywgqgtsvtv ss
Humanized CAR2		
760	HCDR1 (Kabat)	DYGVS
687	HCDR2 (Kabat)	VIWGSETTYYQSSLKS
762	HCDR3 (Kabat)	HYYYGGSYAMDY
763	LCDR1 (Kabat)	RASQDISKYLN
764	LCDR2 (Kabat)	HTSRLHS
76–	LCDR3 (Kabat)	QQGNTLPYT

758	CAR2 scFv domain - aa (Linker is underlined)	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPED FAVYFCQQGNTLPYTFGQGTKLEIKGGGGSGGGGSGGGG SQVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYYQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAV– YCAKHYYYGGSYAMDYWGQGTLVTVSS
688	CAR2 scFv domain - nt	atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgctcggcc cgaaattgtgatgacccagtcacccgccactcttagcctttcacccggtgagcgcgcaacc ctgtcttgcagaggcctcccaagacatctcaaaataccttaattggtatcaacagaagcccgg acaggctcctcgccttctgatctaccacaccagccggctccattctggaatccctgccaggt tcagcggtagcggatctgggaccgactacaccctcactatcagctcactgcagccagagg acttcgctgtctatttctgtcagcaagggaacaccctgccctacacctttggacagggcacc aagctcgagattaaaggtggaggtggcagcggaggaggtgggtccggcggtggaggaa gccaggtccaactccaagaaagcggaccgggtcttgtgaagccatcagaaactctttcact gacttgtactgtgagcggagtgtctctccccgattacggggtgtcttggatcagacagccac cggggaagggtctggaatggattggagtgatttggggctctgagactacttactaccaatca tccctcaagtcacgcgtcaccatctcaaaggacaactctaagaatcaggtgtcactgaaact gtcatctgtgaccgcagccgacaccgccgtgtactattgcgctaagcattactattatggcg ggagctacgcaatggattactggggacagggtactctggtcaccgt– tccagccaccaccatcatcaccatcaccat
689	CAR 2 - Full - aa	MALPVTALLLPLALLLHAARPEIVMTQSPATLSLSPGERA TLSCRASQDISKYLNWYQQKPGQAPRLLIYHTSRLHSGIP ARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYTFG QGTKLEIKGGGGSGGGGSGGGGSQVQLQESGPGLVKPSE TLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSET TYYQSSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYC AKHYYYGGSYAMDYWGQGTLVTVSSTTTPAPRPPTPAP TIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLA GTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQE EDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGQNQLY NELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLY NELQKDKMAEAYSEIGMKGERR– GKGHDGLYQGLSTATKDTYDALHMQALPPR
690	CAR 2 - Full - nt	atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgctcggcc cgaaattgtgatgacccagtcacccgccactcttagcctttcacccggtgagcgcgcaacc ctgtcttgcagaggcctcccaagacatctcaaaataccttaattggtatcaacagaagcccgg acaggctcctcgccttctgatctaccacaccagccggctccattctggaatccctgccaggt tcagcggtagcggatctgggaccgactacaccctcactatcagctcactgcagccagagg acttcgctgtctatttctgtcagcaagggaacaccctgccctacacctttggacagggcacc aagctcgagattaaaggtggaggtggcagcggaggaggtgggtccggcggtggaggaa gccaggtccaactccaagaaagcggaccgggtcttgtgaagccatcagaaactctttcact gacttgtactgtgagcggagtgtctctccccgattacggggtgtcttggatcagacagccac cggggaagggtctggaatggattggagtgatttggggctctgagactacttactaccaatca tccctcaagtcacgcgtcaccatctcaaaggacaactctaagaatcaggtgtcactgaaact gtcatctgtgaccgcagccgacaccgccgtgtactattgcgctaagcattactattatggcg

		ggagctacgcaatggattactggggacagggtactctggtcaccgtgtccagcaccactac cccagcaccgaggccacccaccccggctcctaccatcgcctcccagcctctgtccctgcg tccggaggcatgtagacccgcagctggtggggccgtgcatacccggggtcttgacttcgc ctgcgatatctacatttgggcccctctggctggtacttgcggggtcctgctgctttcactcgtg atcactctttactgtaagcgcggtcggaagaagctgctgtacatctttaagcaacccttcatg aggcctgtgcagactactcaagaggaggacggctgttcatgccggttcccagaggagga ggaaggcggctgcgaactgcgcgtgaaattcagccgcagcgcagatgctccagcctaca agcaggggcagaaccagctctacaacgaactcaatcttggtcggagagaggagtacgac gtgctggacaagcggagaggacgggacccagaaatgggcgggaagccgcgcagaaa gaatccccaagagggcctgtacaacgagctccaaaaggataagatggcagaagcctata gcgagattggtatgaaaggggaacgcagaagaggcaaaggccacgacggactgtacca gggactcagcaccgccaccaaggacacctatgacgctcttcacatgcaggccctgccgcc tcgg
349	CAR 2A– Full amino acid sequence; signal peptide underlined	MALPVTALLLPLALLLHAARPEIVMTQSPATLSLSPGERATLSCRASQ DISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTIS SLQPEDFAVYFCQQGNTLPYTFGQGTKLEIKGGGGSGGGGSGGGGSQ VQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWIG VIWGSETTYYQSSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCA KHYYYGGSYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPLSLRP EACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKR GRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSA DAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKN PQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKD TYDALHMQALPPR
225	CAR 2A – amino acid sequence; no signal peptide	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLI YHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYT FGQGTKLEIKGGGGSGGGGSGGGGSQVQLQESGPGLVKPSETLSLTC TVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYQSSLKSRVTIS KDNSKNQVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGT LVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFA CDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTT QEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYS EIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
354	CAR 2A full nucleic acid sequence; signal peptide and stop codon underlined	atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgctcggcccgaaattgtgatg acccagtcacccgccactcttagcctttcacccggtgagcgcgcaaccctgtcttgcagagcctcccaagacat ctcaaaatacctaattggtatcaacagaagcccggacaggctcctcgccttctgatctaccacaccagccggc tccattctggaatccctgccaggttcagcggtagcggatctgggaccgactacaccctcactatcagctcactg cagccagaggacttcgctgtctatttctgtcagcaagggaacaccctgccctacacctttggacagggcaccaa gctcgagattaaaggtggaggtggcagcggaggaggtgggtccggcggtggaggaagccaggtccaactc caagaaagcggaccgggtcttgtgaagccatcagaaactctttcactgacttgtactgtgagcggagtgtctctc cccgattacggggtgtcttggatcagacagccaccggggaagggtctggaatggattggagtgatttggggct ctgagactacttactaccaatcatccctcaagtcacgcgtcaccatctcaaaggacaactctaagaatcaggtgt cactgaaactgtcatctgtgaccgcagccgacaccgccgtgtactattgcgctaagcattactattatggcggga gctacgcaatggattactggggacagggtactctggtcaccgtgtccagcaccactaccccagcaccgaggc cacccaccccggctcctaccatcgcctcccagcctctgtccctgcgtccggaggcatgtagacccgcagctg gtggggccgtgcatacccggggtcttgacttcgcctgcgatatctacatttgggcccctctggctggtacttgcg gggtcctgctgctttcactcgtgatcactctttactgtaagcgcggtcggaagaagctgctgtacatctttaagca acccttcatgaggcctgtgcagactactcaagaggaggacggctgttcatgccggttcccagaggaggagga aggcggctgcgaactgcgcgtgaaattcagccgcagcgcagatgctccagcctaccagcaggggcagaac cagctctacaacgaactcaatcttggtcggagagaggagtacgacgtgctggacaagcggagaggacgggga cccagaaatgggcgggaagccgcgcagaaagaatccccaagagggcctgtacaacgagctccaaaaggat aagatggcagaagcctatagcgagattggtatgaaaggggaacgcagaagaggcaaaggccacgacggac

		tgtaccagggactcagcaccgccaccaaggacacctatgacgctcttcacatgcaggccctgccgcctcggtaa
355	CAR 2A nucleic acid sequence; signal peptide underlined; no stop codon	atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgctcggcccgaaattgtgatgacccagtcacccgccactcttagcctttcacccggtgagcgcgcaaccctgtcttgcagagcctcccaagacatctcaaaatacctaattggtatcaacagaagcccggacaggctcctcgccttctgatctaccacaccagccggctccattctggaatccctgccaggttcagcggtagcggatctgggaccgactacaccctcactatcagctcactgcagccagaggacttcgctgtctatttctgtcagcaagggaacaccctgccctacacctttggacagggcaccaagctcgagattaaaggtggaggtggcagcggaggaggtgggtccggcggtggaggaagccaggtccaactccaagaaagcggaccgggtcttgtgaagccatcagaaactctttcactgacttgtactgtgagcggagtgtctctcccgattacggggtgtcttggatcagacagccaccggggaagggtctggaatggattggagtgatttggggctctgagactacttactaccaatcatccctcaagtcacgcgtcaccatctcaaaggacaactctaagaatcaggtgtcactgaaactgtcatctgtgaccgcagccgacaccgccgtgtactattgcgctaagcattactattatggcgggagctacgcaatggattactggggacagggtactctggtcaccgtgtccagcaccactaccccagcaccgaggccacccaccccggctcctaccatcgcctcccagcctctgtccctgcgtccggaggcatgtagacccgcagctggtggggccgtgcatacccggggtcttgacttcgcctgcgatatctacatttgggcccctctggctggtacttgcgggtcctgctgctttcactcgtgatcactctttactgtaagcgcggtcggaagaagctgctgtacatctttaagcaacccttcatgaggcctgtgcagactactcaagaggaggacggctgttcatgccggttcccagaggaggaggaggcggctgcgaactgcgcgtgaaattcagccgcagcgcagatgctccagcctaccagcaggggcagaaccagctctacaacgaactcaatcttggtcggagagaggagtacgacgtgctggacaagcggagaggacgggacccagaaatgggcgggaagccgcgcagaaagaatccccaagagggcctgtacaacgagctccaaaaggataagatggcagaagcctatagcgagattggtatgaaaggggaacgcagaagaggcaaaggccacgacggactgtaccagggactcagcaccgccaccaaggacacctatgacgctcttcacatgcaggccctgccgcctcgg
356	CAR 2A nucleic acid sequence; no signal peptide; stop codon underlined	gaaattgtgatgacccagtcacccgccactcttagcctttcacccggtgagcgcgcaaccctgtcttgcagagcctcccaagacatctcaaaataccttaattggtatcaacagaagcccggacaggctcctcgccttctgatctaccacaccagccggctccattctggaatccctgccaggttcagcggtagcggatctgggaccgactacaccctcactatcagctcactgcagccagaggacttcgctgtctatttctgtcagcaagggaacaccctgccctacacctttggacagggcaccaagctcgagattaaaggtggaggtggcagcggaggaggtgggtccggcggtggaggaagccaggtccaactccaagaaagcggaccgggtcttgtgaagccatcagaaactctttcactgacttgtactgtgagcggagtgtctctcccgattacggggtgtcttggatcagacagccaccggggaagggtctggaatggattggagtgatttggggctctgagactacttactaccaatcatccctcaagtcacgcgtcaccatctcaaaggacaactctaagaatcaggtgtcactgaaactgtcatctgtgaccgcagccgacaccgccgtgtactattgcgctaagcattactattatggcgggagctacgcaatggattactggggacagggtactctggtcaccgtgtccagcaccactaccccagcaccgaggccacccaccccggctcctaccatcgcctcccagcctctgtccctgcgtccggaggcatgtagacccgcagctggtggggccgtgcatacccggggtcttgacttcgcctgcgatatctacatttgggcccctctggctggtacttgcgggtcctgctgctttcactcgtgatcactctttactgtaagcgcggtcggaagaagctgctgtacatctttaagcaacccttcatgaggcctgtgcagactactcaagaggaggacggctgttcatgccggttcccagaggaggaggaaggcggctgcgaactgcgcgtgaaattcagccgcagcgcagatgctccagcctaccagcaggggcagaaccagctctacaacgaactcaatcttggtcggagagaggagtacgacgtgctggacaagcggagaggacgggacccagaaatgggcgggaagccgcgcagaaagaatccccaagagggcctgtacaacgagctccaaaaggataagatggcagaagcctatagcgagattggtatgaaaggggaacgcagaagaggcaaaggccacgacggactgtaccagggactcagcaccgccaccaaggacacctatgacgctcttcacatgcaggccctgccgcctcggtaa
417	CAR 2A nucleic acid sequence; no signal peptide; no stop codon	gaaattgtgatgacccagtcacccgccactcttagcctttcacccggtgagcgcgcaaccctgtcttgcagagcctcccaagacatctcaaaataccttaattggtatcaacagaagcccggacaggctcctcgccttctgatctaccacaccagccggctccattctggaatccctgccaggttcagcggtagcggatctgggaccgactacaccctcactatcagctcactgcagccagaggacttcgctgtctatttctgtcagcaagggaacaccctgccctacacctttggacagggcaccaagctcgagattaaaggtggaggtggcagcggaggaggtgggtccggcggtggaggaagccaggtccaactccaagaaagcggaccgggtcttgtgaagccatcagaaactctttcactgacttgtactgtgagcggagtgtctctcccgattacggggtgtcttggatcagacagccaccgggggaagggtctggaatggattggagtgatttggggctctgagactacttactaccaatcatccctcaagtcacgcgtcaccatctcaaaggacaactctaagaatcaggtgtcactgaaactgtcatctgtgaccgcagccgacaccgccgtgtactattgcgctaagcattactattatggcggg

		agctacgcaatggattactggggacagggtactctggtcaccgtgtccagcaccactaccc cagcaccgaggccacccaccccggctcctaccatcgcctcccagcctctgtccctgcgtc cggaggcatgtagacccgcagctggtggggccgtgcatacccggggtcttgacttcgcct gcgatatctacatttgggcccctctggctggtacttgcggggtcctgctgctttcactcgtgat cactctttactgtaagcgcggtcggaagaagctgctgtacatctttaagcaacccttcatgag gcctgtgcagactactcaagaggaggacggctgttcatgccggttcccagaggaggagg aaggcggctgcgaactgcgcgtgaaattcagccgcagcgcagatgctccagcctaccag caggggcagaaccagctctacaacgaactcaatcttggtcggagagaggagtacgacgt gctggacaagcggagaggacgggacccagaaatgggcgggaagccgcgcagaaaga atccccaagagggcctgtacaacgagctccaaaaggataagatggcagaagcctatagc gagattggtatgaaaggggaacgcagaagaggcaaaggccacgacggactgtaccagg gactcagcaccgccaccaaggacacctatgacgctcttcacatgcaggccctgccgcctc gg
250	Anti-CD19 VH	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWI GVIWGSETTYYQSSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYC AKHYYYGGSYAMDYWGQGTLVTVSS
251	Anti-CD19 VL	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLI YHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYT FGQGTKLEIK
331	VH	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKCLEWI GVIWGSETTYYQSSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYC AKHYYYGGSYAMDYWGQGTLVTVSS
332	VL	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLI YHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYT FGCGTKLEIK

BCMA

A non-limiting exemplary tumor antigen is BCMA. CARs that bind to BCMA are known in the art. For example, those disclosed WO2016/014565 or WO2019/241426. Any known BCMA CAR, for example, the BCMA antigen binding domain of any known BCMA CAR, in the art can be used in accordance with the present disclosure. For example, BCMA-1, BCMA-2, BCMA-3, BCMA-4, BCMA-5, BCMA-6, BCMA-7, BCMA-8, BCMA-9, BCMA-10, BCMA-11, BCMA-12, BCMA-13, BCMA-14, BCMA-15, 149362, 149363, 149364, 149365, 149366, 149367, 149368, 149369, BCMA_EBB-C1978-A4, BCMA_EBB-C1978-G1, BCMA_EBB-C1979-C1, BCMA_EBB-C1978-C7, BCMA_EBB-C1978-D10, BCMA_EBB-C1979-C12, BCMA_EBB-C1980-G4, BCMA_EBB-C1980-D2, BCMA_EBB-C1978-A10, BCMA_EBB-C1978-D4, BCMA_EBB-C1980-A2, BCMA_EBB-C1981-C3, BCMA_EBB-C1978-G4, A7D12.2, C11D5.3, C12A3.2, or C13F12.1, disclosed in WO2016/014565.

In some embodiments, the BCMA CAR comprises one or more CDRs, VH, VL, scFv, or full-length sequences of BCMA-1, BCMA-2, BCMA-3, BCMA-4, BCMA-5, BCMA-6, BCMA-

7, BCMA-8, BCMA-9, BCMA-10, BCMA-11, BCMA-12, BCMA-13, BCMA-14, BCMA-15, 149362, 149363, 149364, 149365, 149366, 149367, 149368, 149369, BCMA_EBB-C1978-A4, BCMA_EBB-C1978-G1, BCMA_EBB-C1979-C1, BCMA_EBB-C1978-C7, BCMA_EBB-C1978-D10, BCMA_EBB-C1979-C12, BCMA_EBB-C1980-G4, BCMA_EBB-C1980-D2, BCMA_EBB-C1978-A10, BCMA_EBB-C1978-D4, BCMA_EBB-C1980-A2, BCMA_EBB-C1981-C3, BCMA_EBB-C1978-G4, A7D12.2, C11D5.3, C12A3.2, or C13F12.1 disclosed in WO2016/014565, or a sequence substantially (for example, 95-99%) identical thereto.

In some embodiments, a BCMA CAR comprises a sequence, for example, a CDR, VH, VL, scFv, or full-CAR sequence, disclosed in Tables 2-14, or a sequence having at least 80%, 85%, 90%, 95%, or 99% identity thereto.

Table 2. Amino acid and nucleic acid sequences of exemplary PALLAS-derived anti-BCMA molecules

SEQ ID NO	Name/ Description	Sequence
R1B6		
SEQ ID NO: 44	HCDR1 (Kabat)	SYAMS
SEQ ID NO: 45	HCDR2 (Kabat)	AISGSGGSTYYADSVKG
SEQ ID NO: 46	HCDR3 (Kabat)	REWVPYDVSWYFDY
SEQ ID NO: 47	HCDR1 (Chothia)	GFTFSSY
SEQ ID NO: 48	HCDR2 (Chothia)	SGSGGS
SEQ ID NO: 46	HCDR3 (Chothia)	REWVPYDVSWYFDY
SEQ ID NO: 49	HCDR1 (IMGT)	GFTFSSYA
SEQ ID NO: 50	HCDR2 (IMGT)	ISGSGGST
SEQ ID NO: 51	HCDR3 (IMGT)	ARREWVPYDVSWYFDY
SEQ ID NO: 52	VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARREWVPYDVSWYFDYWGQGTLVTVSS

SEQ ID NO: 53	DNA VH	GAAGTGCAGTTGCTGGAGTCAGGCGGAGGACTGGTGCAG CCCGGAGGATCGCTTCGCTTGAGCTGCGCAGCCTCAGGCT TTACCTTCTCCTCCTACGCCATGTCCTGGGTCAGACAGGC TCCCGGGAAGGGACTGGAATGGGTGTCCGCCATTAGCGG TTCCGGCGGAAGCACTTACTATGCCGACTCTGTGAAGGG CCGCTTCACTATCTCCCGGGACAACTCCAAGAACACCCTG TATCTCCAAATGAATTCCCTGAGGGCCGAAGATACCGCG GTGTACTACTGCGCTAGACGGGAGTGGGTGCCCTACGAT GTCAGCTGGTACTTCGACTACTGGGGACAGGGCACTCTC GTGACTGTGTCCTCC
SEQ ID NO: 54	LCDR1 (Kabat)	RASQSISSYLN
SEQ ID NO: 55	LCDR2 (Kabat)	AASSLQS
SEQ ID NO: 56	LCDR3 (Kabat)	QQSYSTPLT
SEQ ID NO: 57	LCDR1 (Chothia)	SQSISSY
SEQ ID NO: 58	LCDR2 (Chothia)	AAS
SEQ ID NO: 59	LCDR3 (Chothia)	SYSTPL
SEQ ID NO: 60	LCDR1 (IMGT)	QSISSY
SEQ ID NO: 58	LCDR2 (IMGT)	AAS
SEQ ID NO: 56	LCDR3 (IMGT)	QQSYSTPLT
SEQ ID NO: 61	VL	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGK APKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFAT YYCQQSYSTPLTFGQGTKVEIK
SEQ ID NO: 62	DNA VL	GACATTCAAATGACTCAGTCCCCGTCCTCCCTCTCCGCCT CCGTGGGAGATCGCGTCACGATCACGTGCAGGGCCAGCC AGAGCATCTCCAGCTACCTGAACTGGTACCAGCAGAAGC CAGGGAAGGCACCGAAGCTCCTGATCTACGCCGCTAGCT CGCTGCAGTCCGGCGTCCCTTCACGGTTCTCGGGATCGGG CTCAGGCACCGACTTCACCCTGACCATTAGCAGCCTGCAG CCGGAGGACTTCGCGACATACTACTGTCAGCAGTCATACT CCACCCCTCTGACCTTCGGCCAAGGGACCAAAGTGGAGA TCAAG
SEQ ID NO: 63	Linker	GGGGSGGGGSGGGGSGGGGS
SEQ ID NO: 64	scFv (VH-linker-VL)	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARREWVPYDVSWYFDYWGQGTLVT VSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDR

		VTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGQGTK VEIK
SEQ ID NO: 65	DNA scFv	GAAGTGCAGTTGCTGGAGTCAGGCGGAGGACTGGTGCAG CCCGGAGGATCGCTTCGCTTGAGCTGCGCAGCCTCAGGCT TTACCTTCTCCTCCTACGCCATGTCCTGGGTCAGACAGGC TCCCGGGAAGGGACTGGAATGGGTGTCCGCCATTAGCGG TTCCGGCGGAAGCACTTACTATGCCGACTCTGTGAAGGG CCGCTTCACTATCTCCCGGGACAACTCCAAGAACACCCTG TATCTCCAAATGAATTCCCTGAGGGCCGAAGATACCGCG GTGTACTACTGCGCTAGACGGGAGTGGGTGCCCTACGAT GTCAGCTGGTACTTCGACTACTGGGGACAGGGCACTCTC GTGACTGTGTCCTCCGGTGGTGGTGGATCGGGGGGTGGT GGTTCGGGCGGAGGAGGATCTGGAGGAGGAGGGTCGGA CATTCAAATGACTCAGTCCCCGTCCTCCCTCTCCGCCTCC GTGGGAGATCGCGTCACGATCACGTGCAGGGCCAGCCAG AGCATCTCCAGCTACCTGAACTGGTACCAGCAGAAGCCA GGGAAGGCACCGAAGCTCCTGATCTACGCCGCTAGCTCG CTGCAGTCCGGCGTCCCTTCACGGTTCTCGGGATCGGGCT CAGGCACCGACTTCACCCTGACCATTAGCAGCCTGCAGC CGGAGGACTTCGCGACATACTACTGTCAGCAGTCATACTC CACCCCTCTGACCTTCGGCCAAGGGACCAAAGTGGAGAT CAAG
SEQ ID NO: 66	Full CAR amino acid sequence	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARREWVPYDVSWYFDYWGQGTLVT VSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDR VTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGQGTK VEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRG LDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFK QPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAP AYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPR RKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGL YQGLSTATKDTYDALHMQALPPR
SEQ ID NO: 67	Full CAR DNA sequence	GAAGTGCAGTTGCTGGAGTCAGGCGGAGGACTGGTGCAG CCCGGAGGATCGCTTCGCTTGAGCTGCGCAGCCTCAGGCT TTACCTTCTCCTCCTACGCCATGTCCTGGGTCAGACAGGC TCCCGGGAAGGGACTGGAATGGGTGTCCGCCATTAGCGG TTCCGGCGGAAGCACTTACTATGCCGACTCTGTGAAGGG CCGCTTCACTATCTCCCGGGACAACTCCAAGAACACCCTG TATCTCCAAATGAATTCCCTGAGGGCCGAAGATACCGCG GTGTACTACTGCGCTAGACGGGAGTGGGTGCCCTACGAT GTCAGCTGGTACTTCGACTACTGGGGACAGGGCACTCTC GTGACTGTGTCCTCCGGTGGTGGTGGATCGGGGGGTGGT GGTTCGGGCGGAGGAGGATCTGGAGGAGGAGGGTCGGA

		CATTCAAATGACTCAGTCCCCGTCCTCCCTCTCCGCCTCC GTGGGAGATCGCGTCACGATCACGTGCAGGGCCAGCCAG AGCATCTCCAGCTACCTGAACTGGTACCAGCAGAAGCCA GGGAAGGCACCGAAGCTCCTGATCTACGCCGCTAGCTCG CTGCAGTCCGGCGTCCCTTCACGGTTCTCGGGATCGGGCT CAGGCACCGACTTCACCCTGACCATTAGCAGCCTGCAGC CGGAGGACTTCGCGACATACTACTGTCAGCAGTCATACTC CACCCCTCTGACCTTCGGCCAAGGGACCAAAGTGGAGAT CAAGACCACTACCCCAGCACCGAGGCCACCCACCCCGGC TCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAG GCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGG GGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTC TGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGAT CACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTAC ATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTC AAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGG AGGAAGGCGGCTGCGAACTGCGCGTGAAATTCAGCCGCA GCGCAGATGCTCCAGCCTACCAGCAGGGGCAGAACCAGC TCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACG ACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATG GGCGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCT GTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTA TAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCA AAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCA CCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCC GCCTCGG
R1F2		
SEQ ID NO: 44	HCDR1 (Kabat)	SYAMS
SEQ ID NO: 45	HCDR2 (Kabat)	AISGSGGSTYYADSVKG
SEQ ID NO: 68	HCDR3 (Kabat)	REWWYDDWYLDY
SEQ ID NO: 47	HCDR1 (Chothia)	GFTFSSY
SEQ ID NO: 48	HCDR2 (Chothia)	SGSGGS
SEQ ID NO: 68	HCDR3 (Chothia)	REWWYDDWYLDY
SEQ ID NO: 49	HCDR1 (IMGT)	GFTFSSYA
SEQ ID NO: 50	HCDR2 (IMGT)	ISGSGGST
SEQ ID NO: 69	HCDR3 (IMGT)	ARREWWYDDWYLDY

SEQ ID NO: 70	VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARREWWYDDWYLDYWGQGTLVTVS S
SEQ ID NO: 71	DNA VH	GAAGTGCAGTTGCTGGAGTCAGGCGGAGGACTGGTGCAG CCCGGAGGATCGCTTCGCTTGAGCTGCGCAGCCTCAGGCT TTACCTTCTCCTCCTACGCCATGTCCTGGGTCAGACAGGC TCCCGGGAAGGGACTGGAATGGGTGTCCGCCATTAGCGG TTCCGGCGGAAGCACTTACTATGCCGACTCTGTGAAGGG CCGCTTCACTATCTCCCGGGACAACTCCAAGAACACCCTG TATCTCCAAATGAATTCCCTGAGGGCCGAAGATACCGCG GTGTACTACTGCGCTAGACGGGAGTGGTGGTACGACGAT TGGTACCTGGACTACTGGGGACAGGGCACTCTCGTGACT GTGTCCTCC
SEQ ID NO: 54	LCDR1 (Kabat)	RASQSISSYLN
SEQ ID NO: 55	LCDR2 (Kabat)	AASSLQS
SEQ ID NO: 56	LCDR3 (Kabat)	QQSYSTPLT
SEQ ID NO: 57	LCDR1 (Chothia)	SQSISSY
SEQ ID NO: 58	LCDR2 (Chothia)	AAS
SEQ ID NO: 59	LCDR3 (Chothia)	SYSTPL
SEQ ID NO: 60	LCDR1 (IMGT)	QSISSY
SEQ ID NO: 58	LCDR2 (IMGT)	AAS
SEQ ID NO: 56	LCDR3 (IMGT)	QQSYSTPLT
SEQ ID NO: 61	VL	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGK APKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFAT YYCQQSYSTPLTFGQGTKVEIK
SEQ ID NO: 62	DNA VL	GACATTCAAATGACTCAGTCCCCGTCCTCCCTCTCCGCCT CCGTGGGAGATCGCGTCACGATCACGTGCAGGGCCAGCC AGAGCATCTCCAGCTACCTGAACTGGTACCAGCAGAAGC CAGGGAAGGCACCGAAGCTCCTGATCTACGCCGCTAGCT CGCTGCAGTCCGGCGTCCCTTCACGGTTCTCGGGATCGGG CTCAGGCACCGACTTCACCCTGACCATTAGCAGCCTGCAG CCGGAGGACTTCGCGACATACTACTGTCAGCAGTCATACT CCACCCCTCTGACCTTCGGCCAAGGGACCAAAGTGGAGA TCAAG
SEQ ID NO: 63	Linker	GGGGSGGGGSGGGGSGGGGS

SEQ ID NO: 72	scFv (VH-linker-VL)	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARREWWYDDWYLDYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVT ITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRF SGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGQGTKV EIK
SEQ ID NO: 73	DNA scFv	GAAGTGCAGTTGCTGGAGTCAGGCGGAGGACTGGTGCAG CCCGGAGGATCGCTTCGCTTGAGCTGCGCAGCCTCAGGCT TTACCTTCTCCTCCTACGCCATGTCCTGGGTCAGACAGGC TCCCGGGAAGGGACTGGAATGGGTGTCCGCCATTAGCGG TTCCGGCGGAAGCACTTACTATGCCGACTCTGTGAAGGG CCGCTTCACTATCTCCCGGGACAACTCCAAGAACACCCTG TATCTCCAAATGAATTCCCTGAGGGCCGAAGATACCGCG GTGTACTACTGCGCTAGACGGGAGTGGTGGTACGACGAT TGGTACCTGGACTACTGGGGACAGGGCACTCTCGTGACT GTGTCCTCCGGTGGTGGTGGATCGGGGGGTGGTGGTTCG GGCGGAGGAGGATCTGGAGGAGGAGGGTCGGACATTCA AATGACTCAGTCCCCGTCCTCCCTCTCCGCCTCCGTGGGA GATCGCGTCACGATCACGTGCAGGGCCAGCCAGAGCATC TCCAGCTACCTGAACTGGTACCAGCAGAAGCCAGGGAAG GCACCGAAGCTCCTGATCTACGCCGCTAGCTCGCTGCAGT CCGGCGTCCCTTCACGGTTCTCGGGATCGGGCTCAGGCAC CGACTTCACCCTGACCATTAGCAGCCTGCAGCCGGAGGA CTTCGCGACATACTACTGTCAGCAGTCATACTCCACCCCT CTGACCTTCGGCCAAGGGACCAAAGTGGAGATCAAG
SEQ ID NO: 74	Full CAR amino acid sequence	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARREWWYDDWYLDYWGQGTLVTVS SGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVT ITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRF SGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGQGTKV EIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGL DFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQ PFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPA YQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRR KNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLY QGLSTATKDTYDALHMQALPPR
SEQ ID NO: 75	Full CAR DNA sequence	GAAGTGCAGTTGCTGGAGTCAGGCGGAGGACTGGTGCAG CCCGGAGGATCGCTTCGCTTGAGCTGCGCAGCCTCAGGCT TTACCTTCTCCTCCTACGCCATGTCCTGGGTCAGACAGGC TCCCGGGAAGGGACTGGAATGGGTGTCCGCCATTAGCGG TTCCGGCGGAAGCACTTACTATGCCGACTCTGTGAAGGG CCGCTTCACTATCTCCCGGGACAACTCCAAGAACACCCTG TATCTCCAAATGAATTCCCTGAGGGCCGAAGATACCGCG GTGTACTACTGCGCTAGACGGGAGTGGTGGTACGACGAT

		TGGTACCTGGACTACTGGGGACAGGGCACTCTCGTGACT GTGTCCTCCGGTGGTGGTGGATCGGGGGGTGGTGGTTCG GGCGGAGGAGGATCTGGAGGAGGAGGGTCGGACATTCA AATGACTCAGTCCCCGTCCTCCCTCTCCGCCTCCGTGGGA GATCGCGTCACGATCACGTGCAGGGCCAGCCAGAGCATC TCCAGCTACCTGAACTGGTACCAGCAGAAGCCAGGGAAG GCACCGAAGCTCCTGATCTACGCCGCTAGCTCGCTGCAGT CCGGCGTCCCTTCACGGTTCTCGGGATCGGGCTCAGGCAC CGACTTCACCCTGACCATTAGCAGCCTGCAGCCGGAGGA CTTCGCGACATACTACTGTCAGCAGTCATACTCCACCCCT CTGACCTTCGGCCAAGGGACCAAAGTGGAGATCAAGACC ACTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACC ATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTA GACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTG ACTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGG TACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCTTT ACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTA AGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGG AGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAG GCGGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAG ATGCTCCAGCCTACCAGCAGGGGCAGAACCAGCTCTACA ACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGC TGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGG AAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAAC GAGCTCCAAAAGGATAAGATGGCAGAAGCCTATAGCGAG ATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCA CGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGA CACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
R1G5		
SEQ ID NO: 44	HCDR1 (Kabat)	SYAMS
SEQ ID NO: 45	HCDR2 (Kabat)	AISGSGGSTYYADSVKG
SEQ ID NO: 76	HCDR3 (Kabat)	REWWGESWLFDY
SEQ ID NO: 47	HCDR1 (Chothia)	GFTFSSY
SEQ ID NO: 48	HCDR2 (Chothia)	SGSGGS
SEQ ID NO: 76	HCDR3 (Chothia)	REWWGESWLFDY
SEQ ID NO: 49	HCDR1 (IMGT)	GFTFSSYA
SEQ ID NO: 50	HCDR2 (IMGT)	ISGSGGST

SEQ ID NO: 77	HCDR3 (IMGT)	ARREWWGESWLFDY
SEQ ID NO: 78	VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARREWWGESWLFDYWGQGTLVTVSS
SEQ ID NO: 79	DNA VH	GAAGTGCAGTTGCTGGAGTCAGGCGGAGGACTGGTGCAG CCCGGAGGATCGCTTCGCTTGAGCTGCGCAGCCTCAGGCT TTACCTTCTCCTCCTACGCCATGTCCTGGGTCAGACAGGC TCCCGGGAAGGGACTGGAATGGGTGTCCGCCATTAGCGG TTCCGGCGGAAGCACTTACTATGCCGACTCTGTGAAGGG CCGCTTCACTATCTCCCGGGACAACTCCAAGAACACCCTG TATCTCCAAATGAATTCCCTGAGGGCCGAAGATACCGCG GTGTACTACTGCGCTAGACGGGAGTGGTGGGGAGAAAGC TGGCTGTTCGACTACTGGGGACAGGGCACTCTCGTGACTG TGTCCTCC
SEQ ID NO: 54	LCDR1 (Kabat)	RASQSISSYLN
SEQ ID NO: 55	LCDR2 (Kabat)	AASSLQS
SEQ ID NO: 56	LCDR3 (Kabat)	QQSYSTPLT
SEQ ID NO: 57	LCDR1 (Chothia)	SQSISSY
SEQ ID NO: 58	LCDR2 (Chothia)	AAS
SEQ ID NO: 59	LCDR3 (Chothia)	SYSTPL
SEQ ID NO: 60	LCDR1 (IMGT)	QSISSY
SEQ ID NO: 58	LCDR2 (IMGT)	AAS
SEQ ID NO: 56	LCDR3 (IMGT)	QQSYSTPLT
SEQ ID NO: 61	VL	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGK APKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLQPEDFAT YYCQQSYSTPLTFGQGTKVEIK
SEQ ID NO: 62	DNA VL	GACATTCAAATGACTCAGTCCCCGTCCTCCCTCTCCGCCT CCGTGGGAGATCGCGTCACGATCACGTGCAGGGCCAGCC AGAGCATCTCCAGCTACCTGAACTGGTACCAGCAGAAGC CAGGGAAGGCACCGAAGCTCCTGATCTACGCCGCTAGCT CGCTGCAGTCCGGCGTCCCTTCACGGTTCTCGGGATCGGG CTCAGGCACCGACTTCACCCTGACCATTAGCAGCCTGCAG CCGGAGGACTTCGCGACATACTACTGTCAGCAGTCATACT CCACCCCTCTGACCTTCGGCCAAGGGACCAAAGTGGAGA TCAAG

SEQ ID NO: 63	Linker	GGGGSGGGGSGGGGSGGGGS
SEQ ID NO: 80	scFv (VH-linker-VL)	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARREWWGESWLFDYWGQGTLVTVSS GGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTI TCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFS GSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGQGTKVEI K
SEQ ID NO: 81	DNA scFv	GAAGTGCAGTTGCTGGAGTCAGGCGGAGGACTGGTGCAG CCCGGAGGATCGCTTCGCTTGAGCTGCGCAGCCTCAGGCT TTACCTTCTCCTCCTACGCCATGTCCTGGGTCAGACAGGC TCCCGGGAAGGGACTGGAATGGGTGTCCGCCATTAGCGG TTCCGGCGGAAGCACTTACTATGCCGACTCTGTGAAGGG CCGCTTCACTATCTCCCGGGACAACTCCAAGAACACCCTG TATCTCCAAATGAATTCCCTGAGGGCCGAAGATACCGCG GTGTACTACTGCGCTAGACGGGAGTGGTGGGGAGAAAGC TGGCTGTTCGACTACTGGGGACAGGGCACTCTCGTGACTG TGTCCTCCGGTGGTGGTGGATCGGGGGGTGGTGGTTCGG GCGGAGGAGGATCTGGAGGAGGAGGGTCGGACATTCAA ATGACTCAGTCCCCGTCCTCCCTCTCCGCCTCCGTGGGAG ATCGCGTCACGATCACGTGCAGGGCCAGCCAGAGCATCT CCAGCTACCTGAACTGGTACCAGCAGAAGCCAGGGAAGG CACCGAAGCTCCTGATCTACGCCGCTAGCTCGCTGCAGTC CGGCGTCCCTTCACGGTTCTCGGGATCGGGCTCAGGCACC GACTTCACCCTGACCATTAGCAGCCTGCAGCCGGAGGAC TTCGCGACATACTACTGTCAGCAGTCATACTCCACCCCTC TGACCTTCGGCCAAGGGACCAAAGTGGAGATCAAG
SEQ ID NO: 82	Full CAR amino acid sequence	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAP GKGLEWVSAISGSGGSTYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCARREWWGESWLFDYWGQGTLVTVSS GGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTI TCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPSRFS GSGSGTDFTLTISSLQPEDFATYYCQQSYSTPLTFGQGTKVEI KTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLD FACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQP FMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAY QQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRK NPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQ GLSTATKDTYDALHMQALPPR
SEQ ID NO: 83	Full CAR DNA sequence	GAAGTGCAGTTGCTGGAGTCAGGCGGAGGACTGGTGCAG CCCGGAGGATCGCTTCGCTTGAGCTGCGCAGCCTCAGGCT TTACCTTCTCCTCCTACGCCATGTCCTGGGTCAGACAGGC TCCCGGGAAGGGACTGGAATGGGTGTCCGCCATTAGCGG TTCCGGCGGAAGCACTTACTATGCCGACTCTGTGAAGGG CCGCTTCACTATCTCCCGGGACAACTCCAAGAACACCCTG

		TATCTCCAAATGAATTCCCTGAGGGCCGAAGATACCGCG GTGTACTACTGCGCTAGACGGGAGTGGTGGGGAGAAAGC TGGCTGTTCGACTACTGGGGACAGGGCACTCTCGTGACTG TGTCCTCCGGTGGTGGTGGATCGGGGGGTGGTGGTTCGG GCGGAGGAGGATCTGGAGGAGGAGGGTCGGACATTCAA ATGACTCAGTCCCCGTCCTCCCTCTCCGCCTCCGTGGGAG ATCGCGTCACGATCACGTGCAGGGCCAGCCAGAGCATCT CCAGCTACCTGAACTGGTACCAGCAGAAGCCAGGGAAGG CACCGAAGCTCCTGATCTACGCCGCTAGCTCGCTGCAGTC CGGCGTCCCTTCACGGTTCTCGGGATCGGGCTCAGGCACC GACTTCACCCTGACCATTAGCAGCCTGCAGCCGGAGGAC TTCGCGACATACTACTGTCAGCAGTCATACTCCACCCCTC TGACCTTCGGCCAAGGGACCAAAGTGGAGATCAAGACCA CTACCCCAGCACCGAGGCCACCCACCCCGGCTCCTACCA TCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAG ACCCGCAGCTGGTGGGGCCGTGCATACCCGGGGTCTTGA CTTCGCCTGCGATATCTACATTTGGGCCCCTCTGGCTGGT ACTTGCGGGGTCCTGCTGCTTTCACTCGTGATCACTCTTT ACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACATCTTTA AGCAACCCTTCATGAGGCCTGTGCAGACTACTCAAGAGG AGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGAGGAAG GCGGCTGCGAACTGCGCGTGAAATTCAGCCGCAGCGCAG ATGCTCCAGCCTACCAGCAGGGGCAGAACCAGCTCTACA ACGAACTCAATCTTGGTCGGAGAGAGGAGTACGACGTGC TGGACAAGCGGAGAGGACGGGACCCAGAAATGGGCGGG AAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTACAAC GAGCTCCAAAAGGATAAGATGGCAGAAGCCTATAGCGAG ATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCA CGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGA CACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG

Table 3. Kabat CDRs of exemplary PALLAS-derived anti-BCMA molecules

Kabat	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3
R1B6	SYAMS (SEQ ID NO: 44)	AISGSGGSTY YADSVKG (SEQ ID NO: 45)	REWVPYDV SWYFDY (SEQ ID NO: 46)	RASQSISS YLN (SEQ ID NO: 54)	AASSL QS (SEQ ID NO: 55)	QQSYST PLT (SEQ ID NO: 56)
R1F2	SYAMS (SEQ ID NO: 44)	AISGSGGSTY YADSVKG (SEQ ID NO: 45)	REWWYDD WYLDY (SEQ ID NO: 68)	RASQSISS YLN (SEQ ID NO: 54)	AASSL QS (SEQ ID NO: 55)	QQSYST PLT (SEQ ID NO: 56)

R1G5	SYAMS (SEQ ID NO: 44)	AISGSGGSTYYADSVKG (SEQ ID NO: 45)	REWWGESWLFDY (SEQ ID NO: 76)	RASQSISSYLN (SEQ ID NO: 54)	AASSLQS (SEQ ID NO: 55)	QQSYSTPLT (SEQ ID NO: 56)
Consensus	SYAMS (SEQ ID NO: 44)	AISGSGGSTYYADSVKG (SEQ ID NO: 45)	REW$X_1X_2X_3$ $X_4X_5X_6WX_7$ X_8DY, wherein X_1 is absent or V; X_2 is absent or P; X_3 is W or Y; X_4 is G, Y, or D; X_5 is E, D, or V; X_6 is S or D; X_7 is L or Y; and X_8 is F or L (SEQ ID NO: 84)	RASQSISSYLN (SEQ ID NO: 54)	AASSLQS (SEQ ID NO: 55)	QQSYSTPLT (SEQ ID NO: 56)

Table 4. Chothia CDRs of exemplary PALLAS-derived anti-BCMA molecules

Chothia	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3
R1B6	GFTFSSY (SEQ ID NO: 47)	SGSGGS (SEQ ID NO: 48)	REWVPYDVSWYFDY (SEQ ID NO: 46)	SQSISSY (SEQ ID NO: 57)	AAS (SEQ ID NO: 58)	SYSTPL (SEQ ID NO: 59)
R1F2	GFTFSSY (SEQ ID NO: 47)	SGSGGS (SEQ ID NO: 48)	REWWYDDWYLDY (SEQ ID NO: 68)	SQSISSY (SEQ ID NO: 57)	AAS (SEQ ID NO: 58)	SYSTPL (SEQ ID NO: 59)
R1G5	GFTFSSY (SEQ ID NO: 47)	SGSGGS (SEQ ID NO: 48)	REWWGESWLFDY (SEQ ID NO: 76)	SQSISSY (SEQ ID NO: 57)	AAS (SEQ ID NO: 58)	SYSTPL (SEQ ID NO: 59)
Consensus	GFTFSSY (SEQ ID NO: 47)	SGSGGS (SEQ ID NO: 48)	REW$X_1X_2X_3$ $X_4X_5X_6WX_7$ X_8DY, wherein X_1 is absent or V; X_2 is absent or P; X_3 is W or Y; X_4 is G, Y, or D; X_5 is E, D, or V; X_6	SQSISSY (SEQ ID NO: 57)	AAS (SEQ ID NO: 58)	SYSTPL (SEQ ID NO: 59)

			is S or D; X_7 is L or Y; and X_8 is F or L (SEQ ID NO: 84)			

Table 5. IMGT CDRs of exemplary PALLAS-derived anti-BCMA molecules

IMGT	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3
R1B6	GFTFSSYA (SEQ ID NO: 49)	ISGSGGST (SEQ ID NO: 50)	ARREWVPYDVSWYFDY (SEQ ID NO: 51)	QSISSY (SEQ ID NO: 60)	AAS (SEQ ID NO: 58)	QQSYSTPLT (SEQ ID NO: 56)
R1F2	GFTFSSYA (SEQ ID NO: 49)	ISGSGGST (SEQ ID NO: 50)	ARREWWYDDWYLDY (SEQ ID NO: 69)	QSISSY (SEQ ID NO: 60)	AAS (SEQ ID NO: 58)	QQSYSTPLT (SEQ ID NO: 56)
R1G5	GFTFSSYA (SEQ ID NO: 49)	ISGSGGST (SEQ ID NO: 50)	ARREWWGESWLFDY (SEQ ID NO: 77)	QSISSY (SEQ ID NO: 60)	AAS (SEQ ID NO: 58)	QQSYSTPLT (SEQ ID NO: 56)
Consensus	GFTFSSYA (SEQ ID NO: 49)	ISGSGGST (SEQ ID NO: 50)	ARREW$X_1X_2X_3X_4X_5X_6$WX_7X_8DY, wherein X_1 is absent or V; X_2 is absent or P; X_3 is W or Y; X_4 is G, Y, or D; X_5 is E, D, or V; X_6 is S or D; X_7 is L or Y; and X_8 is F or L (SEQ ID NO: 85)	QSISSY (SEQ ID NO: 60)	AAS (SEQ ID NO: 58)	QQSYSTPLT (SEQ ID NO: 56)

Table 6. Amino acid and nucleic acid sequences of exemplary B cell-derived anti-BCMA molecules

SEQ ID NO	**Name/ Description**	**Sequence**
PI61		
SEQ ID NO: 86	HCDR1 (Kabat)	SYGMH

SEQ ID NO: 87	HCDR2 (Kabat)	VISYDGSNKYYADSVKG
SEQ ID NO: 88	HCDR3 (Kabat)	SGYALHDDYYGLDV
SEQ ID NO: 47	HCDR1 (Chothia)	GFTFSSY
SEQ ID NO: 89	HCDR2 (Chothia)	SYDGSN
SEQ ID NO: 88	HCDR3 (Chothia)	SGYALHDDYYGLDV
SEQ ID NO: 90	HCDR1 (IMGT)	GFTFSSYG
SEQ ID NO: 91	HCDR2 (IMGT)	ISYDGSNK
SEQ ID NO: 92	HCDR3 (IMGT)	GGSGYALHDDYYGLDV
SEQ ID NO: 93	VH	QVQLQESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAP GKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCGGSGYALHDDYYGLDVWGQGTLVTV SS
SEQ ID NO: 94	DNA VH	CAAGTGCAGCTGCAGGAATCCGGTGGCGGAGTCGTGCAG CCTGGAAGGAGCCTGAGACTCTCATGCGCCGCGTCAGGGT TCACCTTTTCCTCCTACGGGATGCATTGGGTCAGACAGGC CCCCGGAAAGGGACTCGAATGGGTGGCTGTGATCAGCTAC GACGGCTCCAACAAGTACTACGCCGACTCCGTGAAAGGCC GGTTCACTATCTCCCGGGACAACTCCAAGAACACGCTGTA TCTGCAAATGAATTCACTGCGCGCGGAGGATACCGCTGTG TACTACTGCGGTGGCTCCGGTTACGCCCTGCACGATGACT ATTACGGCCTTGACGTCTGGGGCCAGGGAACCCTCGTGAC TGTGTCCAGC
SEQ ID NO: 95	LCDR1 (Kabat)	TGTSSDVGGYNYVS
SEQ ID NO: 96	LCDR2 (Kabat)	DVSNRPS
SEQ ID NO: 97	LCDR3 (Kabat)	SSYTSSSTLYV
SEQ ID NO: 98	LCDR1 (Chothia)	TSSDVGGYNY
SEQ ID NO: 99	LCDR2 (Chothia)	DVS
SEQ ID NO: 100	LCDR3 (Chothia)	YTSSSTLY
SEQ ID NO: 101	LCDR1 (IMGT)	SSDVGGYNY

SEQ ID NO: 99	LCDR2 (IMGT)	DVS
SEQ ID NO: 97	LCDR3 (IMGT)	SSYTSSSTLYV
SEQ ID NO: 102	VL	QSALTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHP GKAPKLMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAED EADYYCSSYTSSSTLYVFGSGTKVTVL
SEQ ID NO: 103	DNA VL	CAGAGCGCACTGACTCAGCCGGCATCCGTGTCCGGTAGCC CCGGACAGTCGATTACCATCTCCTGTACCGGCACCTCCTC CGACGTGGGAGGGTACAACTACGTGTCGTGGTACCAGCA GCACCCAGGAAAGGCCCCTAAGTTGATGATCTACGATGTG TCAAACCGCCCGTCTGGAGTCTCCAACCGGTTCTCCGGCT CCAAGTCCGGCAACACCGCCAGCCTGACCATTAGCGGGCT GCAAGCCGAGGATGAGGCCGACTACTACTGCTCGAGCTAC ACATCCTCGAGCACCCTCTACGTGTTCGGCTCGGGGACTA AGGTCACCGTGCTG
SEQ ID NO: 104	Linker	GGGGSGGGGSGGGGS
SEQ ID NO: 105	scFv (VH-linker-VL)	QVQLQESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAP GKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCGGSGYALHDDYYGLDVWGQGTLVTV SSGGGGSGGGGSGGGGSQSALTQPASVSGSPGQSITISCTGTS SDVGGYNYVSWYQQHPGKAPKLMIYDVSNRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYYCSSYTSSSTLYVFGSGTKVT VL
SEQ ID NO: 106	DNA scFv	CAAGTGCAGCTGCAGGAATCCGGTGGCGGAGTCGTGCAG CCTGGAAGGAGCCTGAGACTCTCATGCGCCGCGTCAGGGT TCACCTTTTCCTCCTACGGGATGCATTGGGTCAGACAGGC CCCCGGAAAGGGACTCGAATGGGTGGCTGTGATCAGCTAC GACGGCTCCAACAAGTACTACGCCGACTCCGTGAAAGGCC GGTTCACTATCTCCCGGGACAACTCCAAGAACACGCTGTA TCTGCAAATGAATTCACTGCGCGCGGAGGATACCGCTGTG TACTACTGCGGTGGCTCCGGTTACGCCCTGCACGATGACT ATTACGGCCTTGACGTCTGGGGCCAGGGAACCCTCGTGAC TGTGTCCAGCGGTGGAGGAGGTTCGGGCGGAGGAGGATC AGGAGGGGGTGGATCGCAGAGCGCACTGACTCAGCCGGC ATCCGTGTCCGGTAGCCCCGGACAGTCGATTACCATCTCC TGTACCGGCACCTCCTCCGACGTGGGAGGGTACAACTACG TGTCGTGGTACCAGCAGCACCCAGGAAAGGCCCCTAAGTT GATGATCTACGATGTGTCAAACCGCCCGTCTGGAGTCTCC AACCGGTTCTCCGGCTCCAAGTCCGGCAACACCGCCAGCC TGACCATTAGCGGGCTGCAAGCCGAGGATGAGGCCGACT ACTACTGCTCGAGCTACACATCCTCGAGCACCCTCTACGT GTTCGGCTCGGGGACTAAGGTCACCGTGCTG

SEQ ID NO: 107	Full CAR amino acid sequence	QVQLQESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAP GKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCGGSGYALHDDYYGLDVWGQGTLVTV SSGGGGSGGGGSGGGGSQSALTQPASVSGSPGQSITISCTGTS SDVGGYNYVSWYQQHPGKAPKLMIYDVSNRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYYCSSYTSSSTLYVFGSGTKVT VLTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLD FACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPF MRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQ QGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNP QEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLS TATKDTYDALHMQALPPR
SEQ ID NO: 108	Full CAR DNA sequence	CAAGTGCAGCTGCAGGAATCCGGTGGCGGAGTCGTGCAG CCTGGAAGGAGCCTGAGACTCTCATGCGCCGCGTCAGGGT TCACCTTTTCCTCCTACGGGATGCATTGGGTCAGACAGGC CCCCGGAAAGGGACTCGAATGGGTGGCTGTGATCAGCTAC GACGGCTCCAACAAGTACTACGCCGACTCCGTGAAAGGCC GGTTCACTATCTCCCGGGACAACTCCAAGAACACGCTGTA TCTGCAAATGAATTCACTGCGCGCGGAGGATACCGCTGTG TACTACTGCGGTGGCTCCGGTTACGCCCTGCACGATGACT ATTACGGCCTTGACGTCTGGGGCCAGGGAACCCTCGTGAC TGTGTCCAGCGGTGGAGGAGGTTCGGGCGGAGGAGGATC AGGAGGGGGTGGATCGCAGAGCGCACTGACTCAGCCGGC ATCCGTGTCCGGTAGCCCCGGACAGTCGATTACCATCTCC TGTACCGGCACCTCCTCCGACGTGGGAGGGTACAACTACG TGTCGTGGTACCAGCAGCACCCAGGAAAGGCCCCTAAGTT GATGATCTACGATGTGTCAAACCGCCCGTCTGGAGTCTCC AACCGGTTCTCCGGCTCCAAGTCCGGCAACACCGCCAGCC TGACCATTAGCGGGCTGCAAGCCGAGGATGAGGCCGACT ACTACTGCTCGAGCTACACATCCTCGAGCACCCTCTACGT GTTCGGCTCGGGGACTAAGGTCACCGTGCTGACCACTACC CCAGCACCGAGGCCACCCACCCCGGCTCCTACCATCGCCT CCCAGCCTCTGTCCCTGCGTCCGGAGGCATGTAGACCCGC AGCTGGTGGGGCCGTGCATACCCGGGGTCTTGACTTCGCC TGCGATATCTACATTTGGGCCCCTCTGGCTGGTACTTGCGG GGTCCTGCTGCTTTCACTCGTGATCACTCTTTACTGTAAGC GCGGTCGGAAGAAGCTGCTGTACATCTTTAAGCAACCCTT CATGAGGCCTGTGCAGACTACTCAAGAGGAGGACGGCTG TTCATGCCGGTTCCCAGAGGAGGAGGAAGGCGGCTGCGA ACTGCGCGTGAAATTCAGCCGCAGCGCAGATGCTCCAGCC TACCAGCAGGGGCAGAACCAGCTCTACAACGAACTCAAT CTTGGTCGGAGAGAGGAGTACGACGTGCTGGACAAGCGG AGAGGACGGGACCCAGAAATGGGCGGGAAGCCGCGCAGA AAGAATCCCCAAGAGGGCCTGTACAACGAGCTCCAAAAG GATAAGATGGCAGAAGCCTATAGCGAGATTGGTATGAAA GGGGAACGCAGAAGAGGCAAAGGCCACGACGGACTGTAC

		CAGGGACTCAGCACCGCCACcaaggacacctatgacgctcttcacatgcaggccctgccgcctcgg
B61-02		
SEQ ID NO: 86	HCDR1 (Kabat)	SYGMH
SEQ ID NO: 109	HCDR2 (Kabat)	VISYKGSNKYYADSVKG
SEQ ID NO: 88	HCDR3 (Kabat)	SGYALHDDYYGLDV
SEQ ID NO: 47	HCDR1 (Chothia)	GFTFSSY
SEQ ID NO: 110	HCDR2 (Chothia)	SYKGSN
SEQ ID NO: 88	HCDR3 (Chothia)	SGYALHDDYYGLDV
SEQ ID NO: 90	HCDR1 (IMGT)	GFTFSSYG
SEQ ID NO: 111	HCDR2 (IMGT)	ISYKGSNK
SEQ ID NO: 92	HCDR3 (IMGT)	GGSGYALHDDYYGLDV
SEQ ID NO: 112	VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYKGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCGGSGYALHDDYYGLDVWGQGTLVTVSS
SEQ ID NO: 113	DNA VH	CAAGTGCAGCTTGTCGAATCGGGAGGCGGAGTGGTGCAGCCTGGACGATCGCTCCGGCTCTCATGTGCCGCGAGCGGATTCACCTTCTCGAGCTACGGCATGCACTGGGTCAGACAAGCCCCAGGAAAGGGCCTGGAATGGGTGGCTGTCATCTCGTACAAGGGCTCAAACAAGTACTACGCCGACTCCGTGAAGGGCCGGTTCACCATCTCCCGCGATAACTCCAAGAATACCCTCTATCTGCAAATGAACAGCCTGAGGGCCGAGGATACTGCAGTGTACTACTGCGGGGGTTCAGGCTACGCGCTGCACGACGACTACTACGGATTGGACGTCTGGGGCCAAGGAACTCTTGTGACCGTGTCCTCT
SEQ ID NO: 95	LCDR1 (Kabat)	TGTSSDVGGYNYVS
SEQ ID NO: 114	LCDR2 (Kabat)	EVSNRLR
SEQ ID NO: 115	LCDR3 (Kabat)	SSYTSSSALYV

SEQ ID NO: 98	LCDR1 (Chothia)	TSSDVGGYNY
SEQ ID NO: 116	LCDR2 (Chothia)	EVS
SEQ ID NO: 117	LCDR3 (Chothia)	YTSSSALY
SEQ ID NO: 101	LCDR1 (IMGT)	SSDVGGYNY
SEQ ID NO: 116	LCDR2 (IMGT)	EVS
SEQ ID NO: 115	LCDR3 (IMGT)	SSYTSSSALYV
SEQ ID NO: 118	VL	QSALTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHP GKAPKLMIYEVSNRLRGVSNRFSGSKSGNTASLTISGLQAED EADYYCSSYTSSSALYVFGSGTKVTVL
SEQ ID NO: 119	DNA VL	CAGAGCGCGCTGACTCAGCCTGCCTCCGTGAGCGGTTCGC CGGGACAGTCCATTACCATTTCGTGCACCGGGACCTCCTC CGACGTGGGAGGCTACAACTACGTGTCCTGGTACCAGCAG CATCCCGGAAAGGCCCCGAAGCTGATGATCTACGAAGTGT CGAACAGACTGCGGGGAGTCTCCAACCGCTTTTCCGGGTC CAAGTCCGGCAACACCGCCAGCCTGACCATCAGCGGGCTC CAGGCAGAAGATGAGGCTGACTATTACTGCTCCTCCTACA CGTCAAGCTCCGCCCTCTACGTGTTCGGGTCCGGGACCAA AGTCACTGTGCTG
SEQ ID NO: 63	Linker	GGGGSGGGGSGGGGSGGGGS
SEQ ID NO: 120	scFv (VH-linker-VL)	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAP GKGLEWVAVISYKGSNKYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCGGSGYALHDDYYGLDVWGQGTLVTV SSGGGGSGGGGSGGGGSGGGGSQSALTQPASVSGSPGQSITI SCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEVSNRLRGVS NRFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSALYVFGS GTKVTVL
SEQ ID NO: 121	DNA scFv	CAAGTGCAGCTTGTCGAATCGGGAGGCGGAGTGGTGCAG CCTGGACGATCGCTCCGGCTCTCATGTGCCGCGAGCGGAT TCACCTTCTCGAGCTACGGCATGCACTGGGTCAGACAAGC CCCAGGAAAGGGCCTGGAATGGGTGGCTGTCATCTCGTAC AAGGGCTCAAACAAGTACTACGCCGACTCCGTGAAGGGC CGGTTCACCATCTCCCGCGATAACTCCAAGAATACCCTCT ATCTGCAAATGAACAGCCTGAGGGCCGAGGATACTGCAG TGTACTACTGCGGGGGTTCAGGCTACGCGCTGCACGACGA

		CTACTACGGATTGGACGTCTGGGGCCAAGGAACTCTTGTG ACCGTGTCCTCTGGTGGAGGCGGATCAGGGGGTGGCGGAT CTGGGGGTGGTGGTTCCGGGGGAGGAGGATCGCAGAGCG CGCTGACTCAGCCTGCCTCCGTGAGCGGTTCGCCGGGACA GTCCATTACCATTTCGTGCACCGGGACCTCCTCCGACGTG GGAGGCTACAACTACGTGTCCTGGTACCAGCAGCATCCCG GAAAGGCCCCGAAGCTGATGATCTACGAAGTGTCGAACA GACTGCGGGGAGTCTCCAACCGCTTTTCCGGGTCCAAGTC CGGCAACACCGCCAGCCTGACCATCAGCGGGCTCCAGGC AGAAGATGAGGCTGACTATTACTGCTCCTCCTACACGTCA AGCTCCGCCCTCTACGTGTTCGGGTCCGGGACCAAAGTCA CTGTGCTG
SEQ ID NO: 122	Full CAR amino acid sequence	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAP GKGLEWVAVISYKGSNKYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCGGSGYALHDDYYGLDVWGQGTLVTV SSGGGGSGGGGSGGGGSGGGGSQSALTQPASVSGSPGQSITI SCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEVSNRLRGVS NRFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSALYVFGS GTKVTVLTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVH TRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYI FKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADA PAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPR RKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLY QGLSTATKDTYDALHMQALPPR
SEQ ID NO: 123	Full CAR DNA sequence	CAAGTGCAGCTTGTCGAATCGGGAGGCGGAGTGGTGCAG CCTGGACGATCGCTCCGGCTCTCATGTGCCGCGAGCGGAT TCACCTTCTCGAGCTACGGCATGCACTGGGTCAGACAAGC CCCAGGAAAGGGCCTGGAATGGGTGGCTGTCATCTCGTAC AAGGGCTCAAACAAGTACTACGCCGACTCCGTGAAGGGC CGGTTCACCATCTCCCGCGATAACTCCAAGAATACCCTCT ATCTGCAAATGAACAGCCTGAGGGCCGAGGATACTGCAG TGTACTACTGCGGGGGTTCAGGCTACGCGCTGCACGACGA CTACTACGGATTGGACGTCTGGGGCCAAGGAACTCTTGTG ACCGTGTCCTCTGGTGGAGGCGGATCAGGGGGTGGCGGAT CTGGGGGTGGTGGTTCCGGGGGAGGAGGATCGCAGAGCG CGCTGACTCAGCCTGCCTCCGTGAGCGGTTCGCCGGGACA GTCCATTACCATTTCGTGCACCGGGACCTCCTCCGACGTG GGAGGCTACAACTACGTGTCCTGGTACCAGCAGCATCCCG GAAAGGCCCCGAAGCTGATGATCTACGAAGTGTCGAACA GACTGCGGGGAGTCTCCAACCGCTTTTCCGGGTCCAAGTC CGGCAACACCGCCAGCCTGACCATCAGCGGGCTCCAGGC AGAAGATGAGGCTGACTATTACTGCTCCTCCTACACGTCA AGCTCCGCCCTCTACGTGTTCGGGTCCGGGACCAAAGTCA CTGTGCTGACCACTACCCCAGCACCGAGGCCACCCACCCC GGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGG AGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCG

		GGGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTC TGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGATC ACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACA TCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCA AGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGA GGAAGGCGGCTGCGAACTGCGCGTGAAATTCAGCCGCAG CGCAGATGCTCCAGCCTACCAGCAGGGGCAGAACCAGCT CTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGA CGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGG CGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTA CAACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTATAG CGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGG CCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAA GGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCT CGG
B61-10		
SEQ ID NO: 86	HCDR1 (Kabat)	SYGMH
SEQ ID NO: 109	HCDR2 (Kabat)	VISYKGSNKYYADSVKG
SEQ ID NO: 88	HCDR3 (Kabat)	SGYALHDDYYGLDV
SEQ ID NO: 47	HCDR1 (Chothia)	GFTFSSY
SEQ ID NO: 110	HCDR2 (Chothia)	SYKGSN
SEQ ID NO: 88	HCDR3 (Chothia)	SGYALHDDYYGLDV
SEQ ID NO: 90	HCDR1 (IMGT)	GFTFSSYG
SEQ ID NO: 111	HCDR2 (IMGT)	ISYKGSNK
SEQ ID NO: 92	HCDR3 (IMGT)	GGSGYALHDDYYGLDV
SEQ ID NO: 112	VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAP GKGLEWVAVISYKGSNKYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCGGSGYALHDDYYGLDVWGQGTLVTV SS
SEQ ID NO: 113	DNA VH	CAAGTGCAGCTTGTCGAATCGGGAGGCGGAGTGGTGCAG CCTGGACGATCGCTCCGGCTCTCATGTGCCGCGAGCGGAT TCACCTTCTCGAGCTACGGCATGCACTGGGTCAGACAAGC CCCAGGAAAGGGCCTGGAATGGGTGGCTGTCATCTCGTAC AAGGGCTCAAACAAGTACTACGCCGACTCCGTGAAGGGC

		CGGTTCACCATCTCCCGCGATAACTCCAAGAATACCCTCT ATCTGCAAATGAACAGCCTGAGGGCCGAGGATACTGCAG TGTACTACTGCGGGGGTTCAGGCTACGCGCTGCACGACGA CTACTACGGATTGGACGTCTGGGGCCAAGGAACTCTTGTG ACCGTGTCCTCT
SEQ ID NO: 95	LCDR1 (Kabat)	TGTSSDVGGYNYVS
SEQ ID NO: 114	LCDR2 (Kabat)	EVSNRLR
SEQ ID NO: 97	LCDR3 (Kabat)	SSYTSSSTLYV
SEQ ID NO: 98	LCDR1 (Chothia)	TSSDVGGYNY
SEQ ID NO: 116	LCDR2 (Chothia)	EVS
SEQ ID NO: 100	LCDR3 (Chothia)	YTSSSTLY
SEQ ID NO: 101	LCDR1 (IMGT)	SSDVGGYNY
SEQ ID NO: 116	LCDR2 (IMGT)	EVS
SEQ ID NO: 97	LCDR3 (IMGT)	SSYTSSSTLYV
SEQ ID NO: 124	VL	QSALTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHP GKAPKLMIYEVSNRLRGVSNRFSGSKSGNTASLTISGLQAED EADYYCSSYTSSSTLYVFGSGTKVTVL
SEQ ID NO: 125	DNA VL	CAGAGCGCGCTGACTCAGCCTGCCTCCGTGAGCGGTTCGC CGGGACAGTCCATTACCATTTCGTGCACCGGGACCTCCTC CGACGTGGGAGGCTACAACTACGTGTCCTGGTACCAGCAG CATCCCGGAAAGGCCCCGAAGCTGATGATCTACGAAGTGT CGAACAGACTGCGGGGAGTCTCCAACCGCTTTTCCGGGTC CAAGTCCGGCAACACCGCCAGCCTGACCATCAGCGGGCTC CAGGCAGAAGATGAGGCTGACTATTACTGCTCCTCCTACA CGTCAAGCTCCACCCTCTACGTGTTCGGGTCCGGGACCAA AGTCACTGTGCTG
SEQ ID NO: 63	Linker	GGGGSGGGGSGGGGSGGGGS
SEQ ID NO: 126	scFv (VH-linker-VL)	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAP GKGLEWVAVISYKGSNKYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCGGSGYALHDDYYGLDVWGQGTLVTV SSGGGGSGGGGSGGGGSGGGGSQSALTQPASVSGSPGQSITI

		SCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEVSNRLRGVS NRFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTLYVFGS GTKVTVL
SEQ ID NO: 127	DNA scFv	CAAGTGCAGCTTGTCGAATCGGGAGGCGGAGTGGTGCAG CCTGGACGATCGCTCCGGCTCTCATGTGCCGCGAGCGGAT TCACCTTCTCGAGCTACGGCATGCACTGGGTCAGACAAGC CCCAGGAAAGGGCCTGGAATGGGTGGCTGTCATCTCGTAC AAGGGCTCAAACAAGTACTACGCCGACTCCGTGAAGGGC CGGTTCACCATCTCCCGCGATAACTCCAAGAATACCCTCT ATCTGCAAATGAACAGCCTGAGGGCCGAGGATACTGCAG TGTACTACTGCGGGGGTTCAGGCTACGCGCTGCACGACGA CTACTACGGATTGGACGTCTGGGGCCAAGGAACTCTTGTG ACCGTGTCCTCTGGTGGAGGCGGATCAGGGGGTGGCGGAT CTGGGGGTGGTGGTTCCGGGGGAGGAGGATCGCAGAGCG CGCTGACTCAGCCTGCCTCCGTGAGCGGTTCGCCGGGACA GTCCATTACCATTTCGTGCACCGGGACCTCCTCCGACGTG GGAGGCTACAACTACGTGTCCTGGTACCAGCAGCATCCCG GAAAGGCCCCGAAGCTGATGATCTACGAAGTGTCGAACA GACTGCGGGGAGTCTCCAACCGCTTTTCCGGGTCCAAGTC CGGCAACACCGCCAGCCTGACCATCAGCGGGCTCCAGGC AGAAGATGAGGCTGACTATTACTGCTCCTCCTACACGTCA AGCTCCACCCTCTACGTGTTCGGGTCCGGGACCAAAGTCA CTGTGCTG
SEQ ID NO: 128	Full CAR amino acid sequence	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAP GKGLEWVAVISYKGSNKYYADSVKGRFTISRDNSKNTLYLQ MNSLRAEDTAVYYCGGSGYALHDDYYGLDVWGQGTLVTV SSGGGGSGGGGSGGGGSGGGGSQSALTQPASVSGSPGQSITI SCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEVSNRLRGVS NRFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTLYVFGS GTKVTVLTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVH TRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYI FKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADA PAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPR RKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLY QGLSTATKDTYDALHMQALPPR
SEQ ID NO: 129	Full CAR DNA sequence	CAAGTGCAGCTTGTCGAATCGGGAGGCGGAGTGGTGCAG CCTGGACGATCGCTCCGGCTCTCATGTGCCGCGAGCGGAT TCACCTTCTCGAGCTACGGCATGCACTGGGTCAGACAAGC CCCAGGAAAGGGCCTGGAATGGGTGGCTGTCATCTCGTAC AAGGGCTCAAACAAGTACTACGCCGACTCCGTGAAGGGC CGGTTCACCATCTCCCGCGATAACTCCAAGAATACCCTCT ATCTGCAAATGAACAGCCTGAGGGCCGAGGATACTGCAG TGTACTACTGCGGGGGTTCAGGCTACGCGCTGCACGACGA CTACTACGGATTGGACGTCTGGGGCCAAGGAACTCTTGTG ACCGTGTCCTCTGGTGGAGGCGGATCAGGGGGTGGCGGAT CTGGGGGTGGTGGTTCCGGGGGAGGAGGATCGCAGAGCG

		CGCTGACTCAGCCTGCCTCCGTGAGCGGTTCGCCGGGACA GTCCATTACCATTTCGTGCACCGGGACCTCCTCCGACGTG GGAGGCTACAACTACGTGTCCTGGTACCAGCAGCATCCCG GAAAGGCCCCGAAGCTGATGATCTACGAAGTGTCGAACA GACTGCGGGGAGTCTCCAACCGCTTTTCCGGGTCCAAGTC CGGCAACACCGCCAGCCTGACCATCAGCGGGCTCCAGGC AGAAGATGAGGCTGACTATTACTGCTCCTCCTACACGTCA AGCTCCACCCTCTACGTGTTCGGGTCCGGGACCAAAGTCA CTGTGCTGACCACTACCCCAGCACCGAGGCCACCCACCCC GGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGG AGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCG GGGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTC TGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGATC ACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTACA TCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTCA AGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGGA GGAAGGCGGCTGCGAACTGCGCGTGAAATTCAGCCGCAG CGCAGATGCTCCAGCCTACCAGCAGGGGCAGAACCAGCT CTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACGA CGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGG CGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTA CAACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTATAG CGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGG CCACGACGGACTGTACCAGGGACTCAGCACCGCCACCAA GGACACCTATGACGCTCTTCACATGCAGGCCCTGCCGCCT CGG

Table 7. Kabat CDRs of exemplary B cell-derived anti-BCMA molecules

Kabat	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3
PI61	SYGMH (SEQ ID NO: 86)	VISYDGSN KYYADSV KG (SEQ ID NO: 87)	SGYALHD DYYGLDV (SEQ ID NO: 88)	TGTSSD VGGYNY VS (SEQ ID NO: 95)	DVSNRPS (SEQ ID NO: 96)	SSYTSSS TLYV (SEQ ID NO: 97)
B61-02	SYGMH (SEQ ID NO: 86)	VISYKGSN KYYADSV KG (SEQ ID NO: 109)	SGYALHD DYYGLDV (SEQ ID NO: 88)	TGTSSD VGGYNY VS (SEQ ID NO: 95)	EVSNRLR (SEQ ID NO: 114)	SSYTSSS ALYV (SEQ ID NO: 115)
B61-10	SYGMH (SEQ ID NO: 86)	VISYKGSN KYYADSV KG (SEQ ID NO: 109)	SGYALHD DYYGLDV (SEQ ID NO: 88)	TGTSSD VGGYNY VS (SEQ ID NO: 95)	EVSNRLR (SEQ ID NO: 114)	SSYTSSS TLYV (SEQ ID NO: 97)

Consensus	SYGMH (SEQ ID NO: 86)	VISYXGSN KYYADSV KG, wherein X is D or K (SEQ ID NO: 130)	SGYALHD DYYGLDV (SEQ ID NO: 88)	TGTSSD VGGYNY VS (SEQ ID NO: 95)	X_1VSNRX_2X_3, wherein X_1 is D or E; X_2 is P or L; and X_3 is S or R (SEQ ID NO: 131)	SSYTSSS XLYV, wherein X is T or A (SEQ ID NO: 132)

Table 8. Chothia CDRs of exemplary B cell-derived anti-BCMA molecules

Chothia	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3
PI61	GFTFSS Y (SEQ ID NO: 47)	SYDGSN (SEQ ID NO: 89)	SGYALHDDY YGLDV (SEQ ID NO: 88)	TSSDVGG YNY (SEQ ID NO: 98)	DVS (SEQ ID NO: 99)	YTSSSTL Y (SEQ ID NO: 100)
B61-02	GFTFSS Y (SEQ ID NO: 47)	SYKGSN (SEQ ID NO: 110)	SGYALHDDY YGLDV (SEQ ID NO: 88)	TSSDVGG YNY (SEQ ID NO: 98)	EVS (SEQ ID NO: 116)	YTSSSAL Y (SEQ ID NO: 117)
B61-10	GFTFSS Y (SEQ ID NO: 47)	SYKGSN (SEQ ID NO: 110)	SGYALHDDY YGLDV (SEQ ID NO: 88)	TSSDVGG YNY (SEQ ID NO: 98)	EVS (SEQ ID NO: 116)	YTSSSTL Y (SEQ ID NO: 100)
Consensus	GFTFSS Y (SEQ ID NO: 47)	SYXGSN, wherein X is D or K (SEQ ID NO: 133)	SGYALHDDY YGLDV (SEQ ID NO: 88)	TSSDVGG YNY (SEQ ID NO: 98)	XVS, wherein X is D or E (SEQ ID NO: 134)	YTSSSXL Y, wherein X is T or A (SEQ ID NO: 135)

Table 9. IMGT CDRs of exemplary B cell-derived anti-BCMA molecules

IMGT	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3
PI61	GFTFSSY G (SEQ ID NO: 90)	ISYDGSN K (SEQ ID NO: 91)	GGSGYALHD DYYGLDV (SEQ ID NO: 92)	SSDVGGY NY (SEQ ID NO: 101)	DVS (SEQ ID NO: 99)	SSYTSSST LYV (SEQ ID NO: 97)
B61-02	GFTFSSY G (SEQ ID NO: 90)	ISYKGSN K (SEQ ID NO: 111)	GGSGYALHD DYYGLDV (SEQ ID NO: 92)	SSDVGGY NY (SEQ ID NO: 101)	EVS (SEQ ID NO: 116)	SSYTSSSA LYV (SEQ ID NO: 115)
B61-10	GFTFSSY G (SEQ ID NO: 90)	ISYKGSN K (SEQ ID NO: 111)	GGSGYALHD DYYGLDV (SEQ ID NO: 92)	SSDVGGY NY (SEQ ID NO: 101)	EVS (SEQ ID NO: 116)	SSYTSSST LYV (SEQ ID NO: 97)

Consensus	GFTFSSYG (SEQ ID NO: 90)	ISYXGSNK, wherein X is D or K (SEQ ID NO: 136)	GGSGYALHDDYYGLDV (SEQ ID NO: 92)	SSDVGGYNY (SEQ ID NO: 101)	XVS, wherein X is D or E (SEQ ID NO: 134)	SSYTSSSXLYV, wherein X is T or A (SEQ ID NO: 132)

Table 14. Amino acid and nucleic acid sequences of exemplary anti-BCMA molecules based on PI61

Identification	Protein sequence	DNA sequence (5'-3')
Signal peptide	MALPVTALLLPLALLLHAARP (SEQ ID NO: 2)	Atggccctccctgtcaccgctctgttgctgccgcttgctctgctgctccacgcagcgcgaccg (SEQ ID NO: 252)
ScFv PI61	QVQLQESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCGGSGYALHDDYYGLDVWGQGTLVTVSSGGGGSGGGGSGGGGSQSALTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTLYVFGSGTKVTVL (SEQ ID NO: 105)	CaggtacaattgcaggagtctggaggcggtgtgGtgcaacccggtcgcagcttgcgcctgagttgtGctgcgtctggatttacattttcatcttacggaAtgcattgggtacgccaggcaccggggaaaggcCttgaatgggtggctgtaatttcatacgatggtTccaacaaatactatgctgactcagtcaagggtCgatttacaattagtcgggacaactccaagaacAcccttttatcttcaaatgaattcccttagagcaGaggatacggcggtctattactgtggtggcagtGgttatgcacttcatgatgattactatggcttgGatgtctgggggcaagggacgcttgtaactgtaTcctctggtggtggtggtagtggtgggggaggcTccggcggtggcggctctcaatctgctctgactCaaccagcaagcgtatcagggtcaccgggacagAgtattaccataagttgcacggggacctctagcGatgtaggggggtataattatgtatcttggtatCaacaacaccccgggaaagccccctaaattgatgAtctacgacgtgagcaatcgacctagtggcgtaTcaaatcgcttctctggtagcaagagtgggaatAcggcgtcccttactattagcggattgcaagcaGaagatgaggccgattactactgcagctcctatActagctcttctacattgtacgtctttgggagcggaacaaaagtaacagtactc (SEQ ID NO: 253)
Transmembrane domain and hinge	TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC (SEQ ID NO: 202)	AcaacaacacctgccccgagaccgcctacaccaGccccgactattgccagccagcctctgagcctcAggcctgaggcctgtaggcccgcagcgggcggcGcagttcatacacggggcttggatttcgcttgtGatatttatatttgggctccttggcggggacaTgtggcgtgctgcttctgtcacttgttattacactgtactgt (SEQ ID NO: 254)
4-1BB	KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL (SEQ ID NO: 14)	AaacgcgggcgaaaaaaattgctgtatatttttAagcagccatttatgaggcccgttcagacgacgCaggaggaggacggttgctcttgcaggttcccagaagaggaagaagggggctgtgaattg (SEQ ID NO: 255)

CD3zeta	RVKFSRSADAPAYQQGQ NQLYNELNLGRREEYDV LDKRRGRDPEMGGKPRR KNPQEGLYNELQKDKMA EAYSEIGMKGERRRGKG HDGLYQGLSTATKDTYD ALHMQALPPR (SEQ ID NO: 20)	CgggttaaattttcaagatccgcagacgctccaGcatac caacagggacaaaaccaactctataacGagctgaatctt ggaagaagggaggaatatgatGtgctggataaacggcg cggtagagatccggagAtgggcggaaaaccaaggcg aaaaaaccctcagGagggactctacaacgaactgcaga aagacaaaAtggcggaggcttattccgaaataggcatg aagGgcgagcggaggcgagggaaagggcacgacgg aCtgtatcaaggcctctcaaccgcgactaaggatAcgta cgacgccctgcacatgcaggccctgcctccgaga (SEQ ID NO: 256)
PI61 full CAR construct	MALPVTALLLPLALLLHA ARPQVQLQESGGGVVQP GRSLRLSCAASGFTFSSY GMHWVRQAPGKGLEWV AVISYDGSNKYYADSVK GRFTISRDNSKNTLYLQM NSLRAEDTAVYYCGGSG YALHDDYYGLDVWGQG TLVTVSSGGGGSGGGGS GGGGSQSALTQPASVSGS PGQSITISCTGTSSDVGGY NYVSWYQQHPGKAPKL MIYDVSNRPSGVSNRFSG SKSGNTASLTISGLQAED EADYYCSSYTSSSTLYVF GSGTKVTVLTTTPAPRPP TPAPTIASQPLSLRPEACR PAAGGAVHTRGLDFACD IYIWAPLAGTCGVLLLSL VITLYCKRGRKKLLYIFK QPFMRPVQTTQEEDGCSC RFPEEEEGGCELRVKFSR SADAPAYQQGQNQLYNE LNLGRREEYDVLDKRRG RDPEMGGKPRRKNPQEG LYNELQKDKMAEAYSEI GMKGERRRGKGHDGLY QGLSTATKDTYDALHMQ ALPPR (SEQ ID NO: 257)	ATGGCCCTCCCTGTCACCGCTCTGT TGCTGCCGCTTGCTCTGCTGCTCCA CGCAGCGCGACCGCAGGTACAATT GCAGGAGTCTGGAGGCGGTGTGGT GCAACCCGGTCGCAGCTTGCGCCT GAGTTGTGCTGCGTCTGGATTTACA TTTTCATCTTACGGAATGCATTGGG TACGCCAGGCACCGGGGAAAGGCC TTGAATGGGTGGCTGTAATTTCATA CGATGGTTCCAACAAATACTATGCT GACTCAGTCAAGGGTCGATTTACA ATTAGTCGGGACAACTCCAAGAAC ACCCTTTATCTTCAAATGAATTCCC TTAGAGCAGAGGATACGGCGGTCT ATTACTGTGGTGGCAGTGGTTATGC ACTTCATGATGATTACTATGGCTTG GATGTCTGGGGGCAAGGGACGCTT GTAACTGTATCCTCTGGTGGTGGTG GTAGTGGTGGGGGAGGCTCCGGCG GTGGCGGCTCTCAATCTGCTCTGAC TCAACCAGCAAGCGTATCAGGGTC ACCGGGACAGAGTATTACCATAAG TTGCACGGGGACCTCTAGCGATGT AGGGGGGTATAATTATGTATCTTGG TATCAACAACACCCCGGGAAAGCC CCTAAATTGATGATCTACGACGTGA GCAATCGACCTAGTGGCGTATCAA ATCGCTTCTCTGGTAGCAAGAGTGG GAATACGGCGTCCCTTACTATTAGC GGATTGCAAGCAGAAGATGAGGCC GATTACTACTGCAGCTCCTATACTA GCTCTTCTACATTGTACGTCTTTGG GAGCGGAACAAAAGTAACAGTACT CACAACAACACCTGCCCCGAGACC GCCTACACCAGCCCCGACTATTGCC AGCCAGCCTCTGAGCCTCAGGCCT

		GAGGCCTGTAGGCCCGCAGCGGGC GGCGCAGTTCATACACGGGGCTTG GATTTCGCTTGTGATATTTATATTT GGGCTCCTTTGGCGGGGACATGTG GCGTGCTGCTTCTGTCACTTGTTAT TACACTGTACTGTAAACGCGGGCG AAAAAAATTGCTGTATATTTTTAAG CAGCCATTTATGAGGCCCGTTCAGA CGACGCAGGAGGAGGACGGTTGCT CTTGCAGGTTCCCAGAAGAGGAAG AAGGGGGCTGTGAATTGCGGGTTA AATTTTCAAGATCCGCAGACGCTCC AGCATACCAACAGGGACAAAACCA ACTCTATAACGAGCTGAATCTTGGA AGAAGGGAGGAATATGATGTGCTG GATAAACGGCGCGGTAGAGATCCG GAGATGGGCGGAAAACCAAGGCGA AAAAACCCTCAGGAGGGACTCTAC AACGAACTGCAGAAAGACAAAATG GCGGAGGCTTATTCCGAAATAGGC ATGAAGGGCGAGCGGAGGCGAGG GAAAGGGCACGACGGACTGTATCA AGGCCTCTCAACCGCGACTAAGGA TACGTACGACGCCCTGCACATGCA GGCCCTGCCTCCGAGA (SEQ ID NO: 258)
PI61 mature CAR protein	QVQLQESGGGVVQPGRS LRLSCAASGFTFSSYGMH WVRQAPGKGLEWVAVIS YDGSNKYYADSVKGRFT ISRDNSKNTLYLQMNSLR AEDTAVYYCGGSGYALH DDYYGLDVWGQGTLVT VSSGGGGSGGGGSGGGG SQSALTQPASVSGSPGQSI TISCTGTSSDVGGYNYVS WYQQHPGKAPKLMIYDV SNRPSGVSNRFSGSKSGN TASLTISGLQAEDEADYY CSSYTSSSTLYVFGSGTK VTVLTTTPAPRPPTPAPTI ASQPLSLRPEACRPAAGG AVHTRGLDFACDIYIWAP LAGTCGVLLLSLVITLYC KRGRKKLLYIFKQPFMRP VQTTQEEDGCSCRFPEEE	

	EGGCELRVKFSRSADAPA YQQGQNQLYNELNLGRR EEYDVLDKRRGRDPEMG GKPRRKNPQEGLYNELQ KDKMAEAYSEIGMKGER RRGKGHDGLYQGLSTAT KDTYDALHMQALPPR (SEQ ID NO: 107)	

Table 10. Amino acid and nucleic acid sequences of exemplary hybridoma-derived anti-BCMA molecules

SEQ ID NO	**Name/ Description**	**Sequence**
Hy03		
SEQ ID NO: 137	HCDR1 (Kabat)	GFWMS
SEQ ID NO: 138	HCDR2 (Kabat)	NIKQDGSEKYYVDSVRG
SEQ ID NO: 139	HCDR3 (Kabat)	ALDYYGMDV
SEQ ID NO: 140	HCDR1 (Chothia)	GFTFSGF
SEQ ID NO: 141	HCDR2 (Chothia)	KQDGSE
SEQ ID NO: 139	HCDR3 (Chothia)	ALDYYGMDV
SEQ ID NO: 142	HCDR1 (IMGT)	GFTFSGFW
SEQ ID NO: 143	HCDR2 (IMGT)	IKQDGSEK
SEQ ID NO: 144	HCDR3 (IMGT)	ARALDYYGMDV
SEQ ID NO: 145	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSGFWMSWVRQA PGKGLEWVANIKQDGSEKYYVDSVRGRFTISRDNAKNSLYL QMNSLRAEDTAVYYCARALDYYGMDVWGQGTTVTVSS

SEQ ID NO: 146	DNA VH	GAAGTGCAACTGGTGGAGAGCGGTGGAGGGCTTGTCCAG CCCGGAGGATCGCTGCGGCTGTCCTGTGCTGCGTCCGGGT TCACCTTCTCCGGCTTCTGGATGTCCTGGGTCAGACAGGC ACCGGGAAAGGGCCTCGAATGGGTGGCCAACATCAAGCA GGATGGCTCCGAGAAGTACTACGTCGACTCCGTGAGAGG CCGCTTCACCATCTCCCGGGACAACGCCAAGAACTCGCT GTACCTCCAAATGAATAGCCTCAGGGCGGAAGATACTGC TGTGTATTACTGCGCACGCGCCCTTGACTACTACGGCATG GACGTCTGGGGCCAAGGGACCACTGTGACCGTGTCTAGC
SEQ ID NO: 147	LCDR1 (Kabat)	RSSQSLLDSDDGNTYLD
SEQ ID NO: 148	LCDR2 (Kabat)	TLSYRAS
SEQ ID NO: 149	LCDR3 (Kabat)	TQRLEFPSIT
SEQ ID NO: 150	LCDR1 (Chothia)	SQSLLDSDDGNTY
SEQ ID NO: 151	LCDR2 (Chothia)	TLS
SEQ ID NO: 152	LCDR3 (Chothia)	RLEFPSI
SEQ ID NO: 153	LCDR1 (IMGT)	QSLLDSDDGNTY
SEQ ID NO: 151	LCDR2 (IMGT)	TLS
SEQ ID NO: 149	LCDR3 (IMGT)	TQRLEFPSIT
SEQ ID NO: 154	VL	DIVMTQTPLSLPVTPGEPASISCRSSQSLLDSDDGNTYLDWY LQKPGQSPRLLIYTLSYRASGVPDRFSGSGSGTDFTLKISRVE AEDVGLYYCTQRLEFPSITFGQGTRLEIK
SEQ ID NO: 155	DNA VL	GATATCGTGATGACCCAGACTCCCCTGTCCCTGCCTGTGA CTCCCGGAGAACCAGCCTCCATTTCCTGCCGGTCCTCCCA GTCCCTGCTGGACAGCGACGACGGCAACACTTACCTGGA CTGGTACTTGCAGAAGCCGGGCCAATCGCCTCGCCTGCTG ATCTATACCCTGTCATACCGGGCCTCAGGAGTGCCTGACC GCTTCTCGGGATCAGGGAGCGGGACCGATTTCACCCTGA AAATTTCCCGAGTGGAAGCCGAGGACGTCGGACTGTACT

		ACTGCACCCAGCGCCTCGAATTCCCGTCGATTACGTTTGG ACAGGGTACCCGGCTTGAGATCAAG
SEQ ID NO: 63	Linker	GGGGSGGGGSGGGGSGGGGS
SEQ ID NO: 156	scFv (VH-linker-VL)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSGFWMSWVRQA PGKGLEWVANIKQDGSEKYYVDSVRGRFTISRDNAKNSLYL QMNSLRAEDTAVYYCARALDYYGMDVWGQGTTVTVSSG GGGSGGGGSGGGGSGGGGSDIVMTQTPLSLPVTPGEPASISC RSSQSLLDSDDGNTYLDWYLQKPGQSPRLLIYTLSYRASGV PDRFSGSGSGTDFTLKISRVEAEDVGLYYCTQRLEFPSITFGQ GTRLEIK
SEQ ID NO: 157	DNA scFv	GAAGTGCAACTGGTGGAGAGCGGTGGAGGGCTTGTCCAG CCCGGAGGATCGCTGCGGCTGTCCTGTGCTGCGTCCGGGT TCACCTTCTCCGGCTTCTGGATGTCCTGGGTCAGACAGGC ACCGGGAAAGGGCCTCGAATGGGTGGCCAACATCAAGCA GGATGGCTCCGAGAAGTACTACGTCGACTCCGTGAGAGG CCGCTTCACCATCTCCCGGGACAACGCCAAGAACTCGCT GTACCTCCAAATGAATAGCCTCAGGGCGGAAGATACTGC TGTGTATTACTGCGCACGCGCCCTTGACTACTACGGCATG GACGTCTGGGGCCAAGGGACCACTGTGACCGTGTCTAGC GGAGGCGGAGGTTCAGGGGGCGGTGGATCAGGCGGAGG AGGATCGGGGGGTGGTGGATCGGATATCGTGATGACCCA GACTCCCCTGTCCCTGCCTGTGACTCCCGGAGAACCAGCC TCCATTTCCTGCCGGTCCTCCCAGTCCCTGCTGGACAGCG ACGACGGCAACACTTACCTGGACTGGTACTTGCAGAAGC CGGGCCAATCGCCTCGCCTGCTGATCTATACCCTGTCATA CCGGGCCTCAGGAGTGCCTGACCGCTTCTCGGGATCAGG GAGCGGGACCGATTTCACCCTGAAAATTTCCCGAGTGGA AGCCGAGGACGTCGGACTGTACTACTGCACCCAGCGCCT CGAATTCCCGTCGATTACGTTTGGACAGGGTACCCGGCTT GAGATCAAG
SEQ ID NO: 158	Full CAR amino acid sequence	EVQLVESGGGLVQPGGSLRLSCAASGFTFSGFWMSWVRQA PGKGLEWVANIKQDGSEKYYVDSVRGRFTISRDNAKNSLYL QMNSLRAEDTAVYYCARALDYYGMDVWGQGTTVTVSSG GGGSGGGGSGGGGSGGGGSDIVMTQTPLSLPVTPGEPASISC RSSQSLLDSDDGNTYLDWYLQKPGQSPRLLIYTLSYRASGV PDRFSGSGSGTDFTLKISRVEAEDVGLYYCTQRLEFPSITFGQ GTRLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVH TRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLY IFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSAD APAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHD GLYQGLSTATKDTYDALHMQALPPR
SEQ ID NO: 159	Full CAR DNA sequence	GAAGTGCAACTGGTGGAGAGCGGTGGAGGGCTTGTCCAG CCCGGAGGATCGCTGCGGCTGTCCTGTGCTGCGTCCGGGT TCACCTTCTCCGGCTTCTGGATGTCCTGGGTCAGACAGGC

		ACCGGGAAAGGGCCTCGAATGGGTGGCCAACATCAAGCA GGATGGCTCCGAGAAGTACTACGTCGACTCCGTGAGAGG CCGCTTCACCATCTCCCGGGACAACGCCAAGAACTCGCT GTACCTCCAAATGAATAGCCTCAGGGCGGAAGATACTGC TGTGTATTACTGCGCACGCGCCCTTGACTACTACGGCATG GACGTCTGGGGCCAAGGGACCACTGTGACCGTGTCTAGC GGAGGCGGAGGTTCAGGGGGCGGTGGATCAGGCGGAGG AGGATCGGGGGGTGGTGGATCGGATATCGTGATGACCCA GACTCCCCTGTCCCTGCCTGTGACTCCCGGAGAACCAGCC TCCATTTCCTGCCGGTCCTCCCAGTCCCTGCTGGACAGCG ACGACGGCAACACTTACCTGGACTGGTACTTGCAGAAGC CGGGCCAATCGCCTCGCCTGCTGATCTATACCCTGTCATA CCGGGCCTCAGGAGTGCCTGACCGCTTCTCGGGATCAGG GAGCGGGACCGATTTCACCCTGAAAATTTCCCGAGTGGA AGCCGAGGACGTCGGACTGTACTACTGCACCCAGCGCCT CGAATTCCCGTCGATTACGTTTGGACAGGGTACCCGGCTT GAGATCAAGACCACTACCCCAGCACCGAGGCCACCCACC CCGGCTCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTC CGGAGGCATGTAGACCCGCAGCTGGTGGGGCCGTGCATA CCCGGGGTCTTGACTTCGCCTGCGATATCTACATTTGGGC CCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTC GTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTG CTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGA CTACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAG AGGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAATTCA GCCGCAGCGCAGATGCTCCAGCCTACCAGCAGGGGCAGA ACCAGCTCTACAACGAACTCAATCTTGGTCGGAGAGAGG AGTACGACGTGCTGGACAAGCGGAGAGGACGGGACCCA GAAATGGGCGGGAAGCCGCGCAGAAAGAATCCCCAAGA GGGCCTGTACAACGAGCTCCAAAAGGATAAGATGGCAGA AGCCTATAGCGAGATTGGTATGAAAGGGGAACGCAGAAG AGGCAAAGGCCACGACGGACTGTACCAGGGACTCAGCAC CGCCACCAAGGACACCTATGACGCTCTTCACATGCAGGC CCTGCCGCCTCGG
Hy52		
SEQ ID NO: 160	HCDR1 (Kabat)	SFRMN
SEQ ID NO: 161	HCDR2 (Kabat)	SISSSSSYIYYADSVKG
SEQ ID NO: 162	HCDR3 (Kabat)	WLSYYGMDV

SEQ ID NO: 163	HCDR1 (Chothia)	GFTFSSF
SEQ ID NO: 164	HCDR2 (Chothia)	SSSSSY
SEQ ID NO: 162	HCDR3 (Chothia)	WLSYYGMDV
SEQ ID NO: 165	HCDR1 (IMGT)	GFTFSSFR
SEQ ID NO: 166	HCDR2 (IMGT)	ISSSSSYI
SEQ ID NO: 167	HCDR3 (IMGT)	ARWLSYYGMDV
SEQ ID NO: 168	VH	EVQLVESGGGLVKPGGSLRLSCAASGFTFSSFRMNWVRQAP GKGLEWVSSISSSSSYIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARWLSYYGMDVWGQGTTVTVSS
SEQ ID NO: 169	DNA VH	GAAGTGCAACTGGTGGAGAGCGGTGGAGGGCTTGTCAAG CCCGGAGGATCGCTGCGGCTGTCCTGTGCTGCGTCCGGGT TCACCTTCTCCTCGTTCCGCATGAACTGGGTCAGACAGGC ACCGGGAAAGGGCCTCGAATGGGTGTCCTCAATCTCATC GTCCTCGTCCTACATCTACTACGCCGACTCCGTGAAAGGC CGCTTCACCATCTCCCGGGACAACGCCAAGAACTCGCTGT ACCTCCAAATGAATAGCCTCAGGGCGGAAGATACTGCTG TGTATTACTGCGCACGCTGGCTTTCCTACTACGGCATGGA CGTCTGGGGCCAAGGGACCACTGTGACCGTGTCTAGC
SEQ ID NO: 147	LCDR1 (Kabat)	RSSQSLLDSDDGNTYLD
SEQ ID NO: 170	LCDR2 (Kabat)	TLSFRAS
SEQ ID NO: 171	LCDR3 (Kabat)	MQRIGFPIT
SEQ ID NO: 150	LCDR1 (Chothia)	SQSLLDSDDGNTY
SEQ ID NO: 151	LCDR2 (Chothia)	TLS

SEQ ID NO: 172	LCDR3 (Chothia)	RIGFPI
SEQ ID NO: 153	LCDR1 (IMGT)	QSLLDSDDGNTY
SEQ ID NO: 151	LCDR2 (IMGT)	TLS
SEQ ID NO: 171	LCDR3 (IMGT)	MQRIGFPIT
SEQ ID NO: 173	VL	DIVMTQTPLSLPVTPGEPASISCRSSQSLLDSDDGNTYLDWY LQKPGQSPQLLIYTLSFRASGVPDRFSGSGSGTDFTLKIRRVE AEDVGVYYCMQRIGFPITFGQGTRLEIK
SEQ ID NO: 174	DNA VL	GATATCGTGATGACCCAGACTCCCCTGTCCCTGCCTGTGA CTCCCGGAGAACCAGCCTCCATTTCCTGCCGGTCCTCCCA GTCCCTGCTGGACAGCGACGACGGCAACACTTACCTGGA CTGGTACTTGCAGAAGCCGGGCCAATCGCCTCAGCTGCT GATCTATACCCTGTCATTCCGGGCCTCAGGAGTGCCTGAC CGCTTCTCGGGATCAGGGAGCGGGACCGATTTCACCCTG AAAATTAGGCGAGTGGAAGCCGAGGACGTCGGAGTGTAC TACTGCATGCAGCGCATCGGCTTCCCGATTACGTTTGGAC AGGGTACCCGGCTTGAGATCAAG
SEQ ID NO: 63	Linker	GGGGSGGGGSGGGGSGGGGS
SEQ ID NO: 175	scFv (VH-linker-VL)	EVQLVESGGGLVKPGGSLRLSCAASGFTFSSFRMNWVRQAP GKGLEWVSSISSSSSYIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARWLSYYGMDVWGQGTTVTVSSGGGG SGGGGSGGGGSGGGGSDIVMTQTPLSLPVTPGEPASISCRSS QSLLDSDDGNTYLDWYLQKPGQSPQLLIYTLSFRASGVPDR FSGSGSGTDFTLKIRRVEAEDVGVYYCMQRIGFPITFGQGTR LEIK
SEQ ID NO: 176	DNA scFv	GAAGTGCAACTGGTGGAGAGCGGTGGAGGGCTTGTCAAG CCCGGAGGATCGCTGCGGCTGTCCTGTGCTGCGTCCGGGT TCACCTTCTCCTCGTTCCGCATGAACTGGGTCAGACAGGC ACCGGGAAAGGGCCTCGAATGGGTGTCCTCAATCTCATC GTCCTCGTCCTACATCTACTACGCCGACTCCGTGAAAGGC CGCTTCACCATCTCCCGGGACAACGCCAAGAACTCGCTGT ACCTCCAAATGAATAGCCTCAGGGCGGAAGATACTGCTG TGTATTACTGCGCACGCTGGCTTTCCTACTACGGCATGGA CGTCTGGGGCCAAGGGACCACTGTGACCGTGTCTAGCGG AGGCGGAGGTTCAGGGGGCGGTGGATCAGGCGGAGGAG GATCGGGGGGTGGTGGATCGGATATCGTGATGACCCAGA CTCCCCTGTCCCTGCCTGTGACTCCCGGAGAACCAGCCTC CATTTCCTGCCGGTCCTCCCAGTCCCTGCTGGACAGCGAC

		GACGGCAACACTTACCTGGACTGGTACTTGCAGAAGCCG GGCCAATCGCCTCAGCTGCTGATCTATACCCTGTCATTCC GGGCCTCAGGAGTGCCTGACCGCTTCTCGGGATCAGGGA GCGGGACCGATTTCACCCTGAAAATTAGGCGAGTGGAAG CCGAGGACGTCGGAGTGTACTACTGCATGCAGCGCATCG GCTTCCCGATTACGTTTGGACAGGGTACCCGGCTTGAGAT CAAG
SEQ ID NO: 177	Full CAR amino acid sequence	EVQLVESGGGLVKPGGSLRLSCAASGFTFSSFRMNWVRQAP GKGLEWVSSISSSSSYIYYADSVKGRFTISRDNAKNSLYLQM NSLRAEDTAVYYCARWLSYYGMDVWGQGTTVTVSSGGGG SGGGGSGGGGSGGGGSDIVMTQTPLSLPVTPGEPASISCRSS QSLLDSDDGNTYLDWYLQKPGQSPQLLIYTLSFRASGVPDR FSGSGSGTDFTLKIRRVEAEDVGVYYCMQRIGFPITFGQGTR LEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRG LDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFK QPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAP AYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPR RKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGL YQGLSTATKDTYDALHMQALPPR
SEQ ID NO: 178	Full CAR DNA sequence	GAAGTGCAACTGGTGGAGAGCGGTGGAGGGCTTGTCAAG CCCGGAGGATCGCTGCGGCTGTCCTGTGCTGCGTCCGGGT TCACCTTCTCCTCGTTCCGCATGAACTGGGTCAGACAGGC ACCGGGAAAGGGCCTCGAATGGGTGTCCTCAATCTCATC GTCCTCGTCCTACATCTACTACGCCGACTCCGTGAAAGGC CGCTTCACCATCTCCCGGGACAACGCCAAGAACTCGCTGT ACCTCCAAATGAATAGCCTCAGGGCGGAAGATACTGCTG TGTATTACTGCGCACGCTGGCTTTCCTACTACGGCATGGA CGTCTGGGGCCAAGGGACCACTGTGACCGTGTCTAGCGG AGGCGGAGGTTCAGGGGGCGGTGGATCAGGCGGAGGAG GATCGGGGGGTGGTGGATCGGATATCGTGATGACCCAGA CTCCCCTGTCCCTGCCTGTGACTCCCGGAGAACCAGCCTC CATTTCCTGCCGGTCCTCCCAGTCCCTGCTGGACAGCGAC GACGGCAACACTTACCTGGACTGGTACTTGCAGAAGCCG GGCCAATCGCCTCAGCTGCTGATCTATACCCTGTCATTCC GGGCCTCAGGAGTGCCTGACCGCTTCTCGGGATCAGGGA GCGGGACCGATTTCACCCTGAAAATTAGGCGAGTGGAAG CCGAGGACGTCGGAGTGTACTACTGCATGCAGCGCATCG GCTTCCCGATTACGTTTGGACAGGGTACCCGGCTTGAGAT CAAGACCACTACCCCAGCACCGAGGCCACCCACCCCGGC TCCTACCATCGCCTCCCAGCCTCTGTCCCTGCGTCCGGAG GCATGTAGACCCGCAGCTGGTGGGGCCGTGCATACCCGG GGTCTTGACTTCGCCTGCGATATCTACATTTGGGCCCCTC TGGCTGGTACTTGCGGGGTCCTGCTGCTTTCACTCGTGAT CACTCTTTACTGTAAGCGCGGTCGGAAGAAGCTGCTGTAC ATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGACTACTC AAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAGGAGG

		AGGAAGGCGGCTGCGAACTGCGCGTGAAATTCAGCCGCA GCGCAGATGCTCCAGCCTACCAGCAGGGGCAGAACCAGC TCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACG ACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATG GGCGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCT GTACAACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTA TAGCGAGATTGGTATGAAAGGGGAACGCAGAAGAGGCA AAGGCCACGACGGACTGTACCAGGGACTCAGCACCGCCA CCAAGGACACCTATGACGCTCTTCACATGCAGGCCCTGCC GCCTCGG

Table 11. Kabat CDRs of exemplary hybridoma-derived anti-BCMA molecules

Kabat	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3
Hy03	GFWMS (SEQ ID NO: 137)	NIKQDGSEK YYVDSVRG (SEQ ID NO: 138)	ALDYYGM DV (SEQ ID NO: 139)	RSSQSLLD SDDGNTY LD (SEQ ID NO: 147)	TLSYRA S (SEQ ID NO: 148)	TQRLEF PSIT (SEQ ID NO: 149)
Hy52	SFRMN (SEQ ID NO: 160)	SISSSSSYIY YADSVKG (SEQ ID NO: 161)	WLSYYGM DV (SEQ ID NO: 162)	RSSQSLLD SDDGNTY LD (SEQ ID NO: 147)	TLSFRA S (SEQ ID NO: 170)	MQRIGF PIT (SEQ ID NO: 171)
Consensus	$X_1FX_2MX_3$, wherein X_1 is G or S; X_2 is W or R; and X_3 is S or N (SEQ ID NO: 179)	$X_1IX_2X_3X_4X_5SX_6X_7YYX_8DSVX_9G$, wherein X_1 is N or S; X_2 is K or S; X_3 is Q or S; X_4 is D or S; X_5 is G or S; X_6 is E or Y; X_7 is K or I; X_8 is V or A; and X_9 is R or K (SEQ ID NO: 180)	$X_1LX_2YYGMDV$, wherein X_1 is A or W; and X_2 is D or S (SEQ ID NO: 181)	RSSQSLLD SDDGNTY LD (SEQ ID NO: 147)	TLSXRA S, wherein X is Y or F (SEQ ID NO: 182)	$X_1QRX_2X_3FPX_4IT$, wherein X_1 is T or M; X_2 is L or I; X_3 is E or G; and X_4 is S or absent (SEQ ID NO: 183)

Table 12. Chothia CDRs of exemplary hybridoma-derived anti-BCMA molecules

Chothia	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3
Hy03	GFTFSGF (SEQ ID NO: 140)	KQDGSE (SEQ ID NO: 141)	ALDYYGM DV (SEQ ID NO: 139)	SQSLLDS DDGNTY	TLS (SEQ	RLEFPSI (SEQ ID NO: 152)

				(SEQ ID NO: 150)	ID NO: 151)	
Hy52	GFTFSSF (SEQ ID NO: 163)	SSSSSY (SEQ ID NO: 164)	WLSYYGMDV (SEQ ID NO: 162)	SQSLLDSDDGNTY (SEQ ID NO: 150)	TLS (SEQ ID NO: 151)	RIGFPI (SEQ ID NO: 172)
Consensus	GFTFSXF, wherein X is G or S (SEQ ID NO: 184)	$X_1X_2X_3X_4SX_5$, wherein X_1 is K or S; X_2 is Q or S; X_3 is D or S; X_4 is G or S; and X_5 is E or Y (SEQ ID NO: 185)	$X_1LX_2YYGMDV$, wherein X_1 is A or W; and X_2 is D or S (SEQ ID NO: 181)	SQSLLDSDDGNTY (SEQ ID NO: 150)	TLS (SEQ ID NO: 151)	$RX_1X_2FPX_3I$, wherein X_1 is L or I; X_2 is E or G; and X_3 is S or absent (SEQ ID NO: 186)

Table 13. IMGT CDRs of exemplary hybridoma-derived anti-BCMA molecules

IMGT	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3
Hy03	GFTFSGFW (SEQ ID NO: 142)	IKQDGSEK (SEQ ID NO: 143)	ARALDYYGMDV (SEQ ID NO: 144)	QSLLDSDDGNTY (SEQ ID NO: 153)	TLS (SEQ ID NO: 151)	TQRLEFPSIT (SEQ ID NO: 149)
Hy52	GFTFSSFR (SEQ ID NO: 165)	ISSSSSYI (SEQ ID NO: 166)	ARWLSYYGMDV (SEQ ID NO: 167)	QSLLDSDDGNTY (SEQ ID NO: 153)	TLS (SEQ ID NO: 151)	MQRIGFPIT (SEQ ID NO: 171)
Consensus	$GFTFSX_1FX_2$, wherein X_1 is G or S; and X_2 is W or R (SEQ ID NO: 187)	$IX_1X_2X_3X_4SX_5X_6$, wherein X_1 is K or S; X_2 is Q or S; X_3 is D or S; X_4 is G or S; X_5 is E or Y; and X_6 is K or I (SEQ ID NO: 188)	$ARX_1LX_2YYGMDV$, wherein X_1 is A or W; and X_2 is D or S (SEQ ID NO: 189)	QSLLDSDDGNTY (SEQ ID NO: 153)	TLS (SEQ ID NO: 151)	$X_1QRX_2X_3FPX_4IT$, wherein X_1 is T or M; X_2 is L or I; X_3 is E or G; and X_4 is S or absent (SEQ ID NO: 183)

In some embodiments, BCMA CARs may be generated using the VH and VL sequences from WO2012/0163805 (the contents of which are hereby incorporated by reference in its entirety). In some embodiments, BCMA CARs may be generated using the CDRs, VHs, VLs,

scFvs, or full-CAR sequences from WO2019/241426 (the contents of which are hereby incorporated by reference in its entirety).

Other Exemplary Targets

Further non-limiting exemplary tumor antigens include CD20, CD22, EGFR, CD123, and CLL-1.

CARs that bind to CD20 are known in the art. For example, those disclosed in WO2018/067992 or WO2016/164731, incorporated by reference herein. Any known CD20 CAR, for example, the CD20 antigen binding domain of any known CD20 CAR, in the art can be used in accordance with the present disclosure. Exemplary CD20-binding sequences or CD20 CAR sequences are disclosed in, for example, Tables 1-5 of WO2018/067992, incorporated by reference. In some embodiments, the CD20 CAR comprises a CDR, variable region, scFv, or full-length sequence of a CD20 CAR disclosed in WO2018/067992 or WO2016/164731, both incorporated by reference herein. In some embodiments, CD20 CARs comprise a sequence, for example, a CDR, VH, VL, scFv, or full-CAR sequence, disclosed in Table 23 below, or a sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identity thereto.

Table 23. Amino acid sequences of exemplary anti-CD20 molecules

SEQ ID NO:	Region	Sequence
CD20-C3H2		
769	HCDR1 (Kabat)	NYNLH
770	HCDR2 (Kabat)	AIYPGNYDTSYNQKFKG
771	HCDR3 (Kabat)	VDFGHSRYWYFDV
772	HCDR1 (Chothia)	GYTFTNY
773	HCDR2 (Chothia)	YPGNYD
771	HCDR3 (Chothia)	VDFGHSRYWYFDV
774	HCDR1 (IMGT)	GYTFTNYN
775	HCDR2 (IMGT)	IYPGNYDT
776	HCDR3 (IMGT)	ARVDFGHSRYWYFDV
777	HCDR1	GYTFTNYNLH

	(Combined)	
770	HCDR2 (Combined)	AIYPGNYDTSYNQKFKG
771	HCDR3 (Combined)	VDFGHSRYWYFDV
778	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYNLHWVRQAP GQGLEWMGAIYPGNYDTSYNQKFKGRVTMTADKSTSTAYME LSSLRSEDTAVYYCARVDFGHSRYWYFDVWGQGTTVTVSS
779	DNA VH	CAAGTCCAACTCGTCCAGTCCGGTGCAGAAGTCAAGAAACC TGGAGCATCCGTGAAAGTGTCTTGCAAAGCCTCCGGCTACA CCTTCACCAACTACAACCTCCATTGGGTCAGACAGGCCCCC GGACAAGGACTCGAATGGATGGGAGCGATCTACCCGGGAA ACTACGACACCAGCTACAACCAGAAGTTCAAGGGCCGCGTG ACTATGACCGCCGATAAGAGCACCTCCACCGCCTACATGGA ACTGTCCTCGCTGAGGTCCGAGGACACTGCGGTGTACTACT GCGCCCGCGTGGACTTCGGACACTCACGGTATTGGTACTTC GACGTCTGGGGACAGGGCACTACCGTGACCGTGTCGAGC
780	LCDR1 (Kabat)	RATSSVSSMN
781	LCDR2 (Kabat)	ATSNLAS
782	LCDR3 (Kabat)	QQWTFNPPT
783	LCDR1 (Chothia)	TSSVSS
784	LCDR2 (Chothia)	ATS
785	LCDR3 (Chothia)	WTFNPP
786	LCDR1 (IMGT)	SSVSS
784	LCDR2 (IMGT)	ATS
782	LCDR3 (IMGT)	QQWTFNPPT
780	LCDR1 (Combined)	RATSSVSSMN
781	LCDR2 (Combined)	ATSNLAS
782	LCDR3 (Combined)	QQWTFNPPT
787	VL	DIQLTQSPSFLSASVGDRVTITCRATSSVSSMNWYQQKPGKAP KPLIHATSNLASGVPSRFSGSGSGTEYTLTISSLQPEDFATYYCQ QWTFNPPTFGQGTKLEIK
788	DNA VL	GATATCCAGCTGACTCAGTCCCCGTCATTCCTGTCCGCCTCC GTGGGAGACAGAGTGACCATCACCTGTCGGGCCACTTCCTC CGTGTCAAGCATGAACTGGTATCAGCAGAAGCCCGGGAAGG CCCCAAAGCCGCTGATTCACGCGACGTCCAACCTGGCTTCC GGCGTGCCGAGCCGGTTCTCCGGCTCGGGGAGCGGGACTGA GTACACCCTGACTATTTCCTCGCTTCAACCCGAGGACTTTGC

		TACCTACTACTGCCAACAGTGGACCTTCAATCCTCCGACATT CGGACAGGGTACCAAGTTGGAAATCAAG
789	scFv (VH-linker-VL)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYNLHWVRQAP GQGLEWMGAIYPGNYDTSYNQKFKGRVTMTADKSTSTAYME LSSLRSEDTAVYYCARVDFGHSRYWYFDVWGQGTTVTVSSGG GGSGGGGSGGGGSGGGGSDIQLTQSPSFLSASVGDRVTITCRA TSSVSSMNWYQQKPGKAPKPLIHATSNLASGVPSRFSGSGSGT EYTLTISSLQPEDFATYYCQQWTFNPPTFGQGTKLEIK
790	DNA scFv (VH-linker-VL)	caagtccaactcgtccagtccggtgcagaagtcaagaaacctggagcatccgtgaaagtgtcttgc aaagcctccggctacaccttcaccaactacaacctccattgggtcagacaggccccggacaagg actcgaatggatgggagcgatctacccgggaaactacgacaccagctacaaccagaagttcaagg gccgcgtgactatgaccgccgataagagcacctccaccgcctacatggaactgtcctcgctgaggt ccgaggacactgcggtgtactactgcgcccgcgtggacttcggacactcacggtattggtacttcga cgtctggggacagggcactaccgtgaccgtgtcgagcggcggaggaggttcgggaggggggcgg atcaggggcggcggcagcggtggaggggctcggatatccagctgactcagtccccgtcattcc tgtccgcctccgtgggagacagagtgaccatcacctgtcgggccacttcctccgtgtcaagcatgaa ctggtatcagcagaagcccgggaaggccccaaagccgctgattcacgcgacgtccaacctggctt ccggcgtgccgagccggttctccggctcggggagcgggactgagtacaccctgactatttcctcgc ttcaacccgaggactttgctacctactactgccaacagtggaccttcaatcctccgacattcggacag ggtaccaagttggaaatcaag
791	Full CAR amino acid sequence	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVKVS CKASGYTFTNYNLHWVRQAPGQGLEWMGAIYPGNYDTSYNQ KFKGRVTMTADKSTSTAYMELSSLRSEDTAVYYCARVDFGHS RYWYFDVWGQGTTVTVSSGGGGSGGGGSGGGGSGGGGSDIQ LTQSPSFLSASVGDRVTITCRATSSVSSMNWYQQKPGKAPKPLI HATSNLASGVPSRFSGSGSGTEYTLTISSLQPEDFATYYCQQWT FNPPTFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAA GGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRK KLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRS ADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGL YQGLSTATKDTYDALHMQALPPR
792	Full CAR nucleotide sequence	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTT CTGCTCCACGCCGCTCGGCCCCAAGTCCAACTCGTCCAGTCC GGTGCAGAAGTCAAGAAACCTGGAGCATCCGTGAAAGTGTC TTGCAAAGCCTCCGGCTACACCTTCACCAACTACAACCTCCA TTGGGTCAGACAGGCCCCCGGACAAGGACTCGAATGGATGG GAGCGATCTACCCGGGAAACTACGACACCAGCTACAACCAG AAGTTCAAGGGCCGCGTGACTATGACCGCCGATAAGAGCAC CTCCACCGCCTACATGGAACTGTCCTCGCTGAGGTCCGAGG ACACTGCGGTGTACTACTGCGCCCGCGTGGACTTCGGACAC TCACGGTATTGGTACTTCGACGTCTGGGGACAGGGCACTAC CGTGACCGTGTCGAGCGGCGGAGGAGGTTCGGGAGGGGGC GGATCAGGGGGCGGCGGCAGCGGTGGAGGGGGCTCGGATA TCCAGCTGACTCAGTCCCCGTCATTCCTGTCCGCCTCCGTGG GAGACAGAGTGACCATCACCTGTCGGGCCACTTCCTCCGTG TCAAGCATGAACTGGTATCAGCAGAAGCCCGGGAAGGCCCC AAAGCCGCTGATTCACGCGACGTCCAACCTGGCTTCCGGCG TGCCGAGCCGGTTCTCCGGCTCGGGGAGCGGGACTGAGTAC ACCCTGACTATTTCCTCGCTTCAACCCGAGGACTTTGCTACC

		TACTACTGCCAACAGTGGACCTTCAATCCTCCGACATTCGGA CAGGGTACCAAGTTGGAAATCAAGACCACTACCCCAGCACC GAGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCT GTCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGG CCGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACA TTTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTT CACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAG CTGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAG ACTACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGA GGAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAATTCAGC CGCAGCGCAGATGCTCCAGCCTACCAGCAGGGGCAGAACCA GCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACG ACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGG CGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTAC AACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTATAGCG AGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCA CGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACA CCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
CD20-C5H1		
793	HCDR1 (Kabat)	SYNMH
794	HCDR2 (Kabat)	AIYPGNGDTSYNPKFKG
795	HCDR3 (Kabat)	SYFYGSSSWYFDV
523	HCDR1 (Chothia)	GYTFTSY
796	HCDR2 (Chothia)	YPGNGD
795	HCDR3 (Chothia)	SYFYGSSSWYFDV
797	HCDR1 (IMGT)	GYTFTSYN
798	HCDR2 (IMGT)	IYPGNGDT
799	HCDR3 (IMGT)	ARSYFYGSSSWYFDV
800	HCDR1 (Combined)	GYTFTSYNMH
794	HCDR2 (Combined)	AIYPGNGDTSYNPKFKG
795	HCDR3 (Combined)	SYFYGSSSWYFDV
801	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAP GQGLEWMGAIYPGNGDTSYNPKFKGRVTMTADKSTRTAYME LSSLRSEDTAVYYCARSYFYGSSSWYFDVWGQGTTVTVSS
802	DNA VH	CAAGTGCAGCTCGTCCAGTCCGGTGCAGAAGTCAAGAAACC CGGTGCTTCAGTGAAAGTGTCCTGCAAGGCCTCCGGTTACA CCTTCACCTCCTACAACATGCACTGGGTCCGCCAAGCCCCG GGCCAGGGACTCGAATGGATGGGAGCCATCTACCCTGGCAA

		CGGGGACACCTCATACAACCCTAAGTTCAAGGGCAGAGTGA CCATGACTGCGGACAAGTCCACTAGAACAGCGTACATGGAG CTGAGCAGCCTGCGGTCCGAGGATACTGCCGTGTACTACTG CGCCCGCTCCTACTTCTACGGAAGCTCGTCGTGGTACTTCGA TGTCTGGGGACAGGGCACCACTGTGACTGTGTCCTCC
803	LCDR1 (Kabat)	RASSSVSSMH
781	LCDR2 (Kabat)	ATSNLAS
804	LCDR3 (Kabat)	QQWIFNPPT
805	LCDR1 (Chothia)	SSSVSS
784	LCDR2 (Chothia)	ATS
806	LCDR3 (Chothia)	WIFNPP
786	LCDR1 (IMGT)	SSVSS
784	LCDR2 (IMGT)	ATS
804	LCDR3 (IMGT)	QQWIFNPPT
803	LCDR1 (Combined)	RASSSVSSMH
781	LCDR2 (Combined)	ATSNLAS
804	LCDR3 (Combined)	QQWIFNPPT
807	VL	EIVLTQSPATLSLSPGERATLSCRASSSVSSMHWYQQKPGQAPR PLIFATSNLASGIPARFSGSGSGTDYTLTISSLEPEDAAVYYCQQ WIFNPPTFGGGTKVEIK
808	DNA VL	GAAATTGTGCTGACTCAGAGCCCCGCCACCCTGAGCTTGTC CCCCGGGGAAAGGGCAACGCTGTCATGCCGCGCCTCGTCAT CCGTGTCCTCCATGCATTGGTACCAGCAGAAGCCGGGACAG GCCCCTCGGCCGCTGATCTTCGCCACCTCCAATCTCGCTTCC GGCATTCCGGCCCGGTTCTCGGGAAGCGGGTCGGGGACCGA CTATACCCTGACCATCTCTAGCCTTGAACCTGAGGACGCCGC GGTGTACTATTGTCAACAGTGGATCTTTAACCCCCCAACCTT CGGTGGAGGCACCAAAGTGGAGATTAAG
809	scFv (VH-linker-VL)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAP GQGLEWMGAIYPGNGDTSYNPKFKGRVTMTADKSTRTAYME LSSLRSEDTAVYYCARSYFYGSSSWYFDVWGQGTTVTVSSGG GGSGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCRAS SSVSSMHWYQQKPGQAPRPLIFATSNLASGIPARFSGSGSGTDY TLTISSLEPEDAAVYYCQQWIFNPPTFGGGTKVEIK
810	DNA scFv (VH-linker-VL)	Caagtgcagctcgtccagtccggtgcagaagtcaagaaacccggtgcttcagtgaaagtgtcctgc aaggcctccggttacaccttcacctcctacaacatgcactgggtccgccaagccccgggccaggg actcgaatggatgggagccatctaccctggcaacggggacacctcatacaaccctaagttcaaggg cagagtgaccatgactgcggacaagtccactagaacagcgtacatggagctgagcagcctgcggt

		ccgaggatactgccgtgtactactgcgcccgctcctacttctacggaagctcgtcgtggtacttcgat gtctggggacagggcaccactgtgactgtgtcctccggtggcggaggctcgggcggaggcggaa gcggcggcgggggatcgggaggaggagggtccgaaattgtgctgactcagagccccgccaccc tgagcttgtcccccggggaaagggcaacgctgtcatgccgcgcctcgtcatccgtgtcctccatgc attggtaccagcagaagccgggacaggcccctcggccgctgatcttcgccacctccaatctcgctt ccggcattccggcccggttctcgggaagcgggtcggggaccgactataccctgaccatctctagcc ttgaacctgaggacgccgcggtgtactattgtcaacagtggatctttaacccccaaccttcggtgga ggcaccaaagtggagattaag
811	Full CAR amino acid sequence	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVKVS CKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNP KFKGRVTMTADKSTRTAYMELSSLRSEDTAVYYCARSYFYGS SSWYFDVWGQGTTVTVSSGGGGSGGGGSGGGGSGGGGSEIVL TQSPATLSLSPGERATLSCRASSSVSSMHWYQQKPGQAPRPLIF ATSNLASGIPARFSGSGSGTDYTLTISSLEPEDAAVYYCQQWIF NPPTFGGGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAA GGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRK KLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRS ADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGL YQGLSTATKDTYDALHMQALPPR
812	Full CAR nucleotide sequence	ATGGCCCTCCCTGTCACCGCCCTGCTGCTTCCGCTGGCTCTT CTGCTCCACGCCGCTCGGCCCCAAGTGCAGCTCGTCCAGTCC GGTGCAGAAGTCAAGAAACCCGGTGCTTCAGTGAAAGTGTC CTGCAAGGCCTCCGGTTACACCTTCACCTCCTACAACATGCA CTGGGTCCGCCAAGCCCCGGGCCAGGGACTCGAATGGATGG GAGCCATCTACCCTGGCAACGGGGACACCTCATACAACCCT AAGTTCAAGGGCAGAGTGACCATGACTGCGGACAAGTCCAC TAGAACAGCGTACATGGAGCTGAGCAGCCTGCGGTCCGAGG ATACTGCCGTGTACTACTGCGCCCGCTCCTACTTCTACGGAA GCTCGTCGTGGTACTTCGATGTCTGGGGACAGGGCACCACT GTGACTGTGTCCTCCGGTGGCGGAGGCTCGGGCGGAGGCGG AAGCGGCGGCGGGGGATCGGGAGGAGGAGGGTCCGAAATT GTGCTGACTCAGAGCCCCGCCACCCTGAGCTTGTCCCCCGG GGAAAGGGCAACGCTGTCATGCCGCGCCTCGTCATCCGTGT CCTCCATGCATTGGTACCAGCAGAAGCCGGGACAGGCCCCT CGGCCGCTGATCTTCGCCACCTCCAATCTCGCTTCCGGCATT CCGGCCCGGTTCTCGGGAAGCGGGTCGGGGACCGACTATAC CCTGACCATCTCTAGCCTTGAACCTGAGGACGCCGCGGTGT ACTATTGTCAACAGTGGATCTTTAACCCCCCAACCTTCGGTG GAGGCACCAAAGTGGAGATTAAGACCACTACCCCAGCACCG AGGCCACCCACCCCGGCTCCTACCATCGCCTCCCAGCCTCTG TCCCTGCGTCCGGAGGCATGTAGACCCGCAGCTGGTGGGGC CGTGCATACCCGGGGTCTTGACTTCGCCTGCGATATCTACAT TTGGGCCCCTCTGGCTGGTACTTGCGGGGTCCTGCTGCTTTC ACTCGTGATCACTCTTTACTGTAAGCGCGGTCGGAAGAAGC TGCTGTACATCTTTAAGCAACCCTTCATGAGGCCTGTGCAGA CTACTCAAGAGGAGGACGGCTGTTCATGCCGGTTCCCAGAG GAGGAGGAAGGCGGCTGCGAACTGCGCGTGAAATTCAGCC GCAGCGCAGATGCTCCAGCCTACCAGCAGGGGCAGAACCA GCTCTACAACGAACTCAATCTTGGTCGGAGAGAGGAGTACG ACGTGCTGGACAAGCGGAGAGGACGGGACCCAGAAATGGG

		CGGGAAGCCGCGCAGAAAGAATCCCCAAGAGGGCCTGTAC AACGAGCTCCAAAAGGATAAGATGGCAGAAGCCTATAGCG AGATTGGTATGAAAGGGGAACGCAGAAGAGGCAAAGGCCA CGACGGACTGTACCAGGGACTCAGCACCGCCACCAAGGACA CCTATGACGCTCTTCACATGCAGGCCCTGCCGCCTCGG
CD20-C3H1		
896	HCDR1 (Kabat)	NYNLH
897	HCDR2 (Kabat)	AIYPGNYDTSYNQKFKG
898	HCDR3 (Kabat)	VDFGHSRYWYFDV
899	HCDR1 (Chothia)	GYTFTNY
900	HCDR2 (Chothia)	YPGNYD
901	HCDR3 (Chothia)	VDFGHSRYWYFDV
903	HCDR1 (IMGT)	GYTFTNYN
904	HCDR2 (IMGT)	IYPGNYDT
905	HCDR3 (IMGT)	ARVDFGHSRYWYFDV
906	HCDR1 (Combined)	GYTFTNYNLH
907	HCDR2 (Combined)	AIYPGNYDTSYNQKFKG
908	HCDR3 (Combined)	VDFGHSRYWYFDV
909	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYNLHWVRQAP GQGLEWMGAIYPGNYDTSYNQKFKGRVTMTADKSTSTAYME LSSLRSEDTAVYYCARVDFGHSRYWYFDVWGQGTTVTVSS
910	LCDR1 (Kabat)	RATSSVSSMN
911	LCDR2 (Kabat)	ATSNLAS
912	LCDR3 (Kabat)	QQWTFNPPT
913	LCDR1 (Chothia)	TSSVSS
914	LCDR2 (Chothia)	ATS
915	LCDR3 (Chothia)	WTFNPP
916	LCDR1 (IMGT)	SSVSS
917	LCDR2 (IMGT)	ATS
918	LCDR3	QQWTFNPPT

	(IMGT)	
919	LCDR1 (Combined)	RATSSVSSMN
920	LCDR2 (Combined)	ATSNLAS
921	LCDR3 (Combined)	QQWTFNPPT
922	VL	EIVLTQSPATLSLSPGERATLSCRATSSVSSMNWYQQKPGQAPR PLIHATSNLASGIPARFSGSGSGTDYTLTISSLEPEDAAVYYCQQ WTFNPPTFGQGTKLEIK
923	scFv (VH-linker-VL)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYNLHWVRQAP GQGLEWMGAIYPGNYDTSYNQKFKGRVTMTADKSTSTAYME LSSLRSEDTAVYYCARVDFGHSRYWYFDVWGQGTTVTVSSGG GGSGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCRAT SSVSSMNWYQQKPGQAPRPLIHATSNLASGIPARFSGSGSGTD YTLTISSLEPEDAAVYYCQQWTFNPPTFGQGTKLEIK
924	Full CAR	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVKVS CKASGYTFTNYNLHWVRQAPGQGLEWMGAIYPGNYDTSYNQ KFKGRVTMTADKSTSTAYMELSSLRSEDTAVYYCARVDFGHS RYWYFDVWGQGTTVTVSSGGGGSGGGGSGGGGSGGGGSEIV LTQSPATLSLSPGERATLSCRATSSVSSMNWYQQKPGQAPRPLI HATSNLASGIPARFSGSGSGTDYTLTISSLEPEDAAVYYCQQWT FNPPTFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAA GGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRK KLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRS ADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGL YQGLSTATKDTYDALHMQALPPR
CD20-3H3		
925	HCDR1 (Kabat)	NYNLH
926	HCDR2 (Kabat)	AIYPGNYDTSYNQKFKG
927	HCDR3 (Kabat)	VDFGHSRYWYFDV
928	HCDR1 (Chothia)	GYTFTNY
929	HCDR2 (Chothia)	YPGNYD
930	HCDR3 (Chothia)	VDFGHSRYWYFDV
931	HCDR1 (IMGT)	GYTFTNYN
932	HCDR2 (IMGT)	IYPGNYDT
933	HCDR3 (IMGT)	ARVDFGHSRYWYFDV
934	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTNYNLHWVRQAP GQGLEWMGAIYPGNYDTSYNQKFKGRVTITADKSTSTAYMEL SSLRSEDTAVYYCARVDFGHSRYWYFDVWGQGTTVTVSS

935	LCDR1 (Kabat)	RATSSVSSMN
936	LCDR2 (Kabat)	ATSNLAS
937	LCDR3 (Kabat)	QQWTFNPPT
938	LCDR1 (Chothia)	TSSVSS
939	LCDR2 (Chothia)	ATS
940	LCDR3 (Chothia)	WTFNPP
941	LCDR1 (IMGT)	SSVSS
942	LCDR2 (IMGT)	ATS
943	LCDR3 (IMGT)	QQWTFNPPT
944	LCDR1 (Combined)	RATSSVSSMN
945	LCDR2 (Combined)	ATSNLAS
946	LCDR3 (Combined)	QQWTFNPPT
947	VL	EIVLTQSPATLSLSPGERATLSCRATSSVSSMNWYQQKPGQAPR PLIHATSNLASGIPARFSGSGSGTDYTLTISSLEPEDAAVYYCQQ WTFNPPTFGQGTKLEIK
948	scFv (VH-linker-VL)	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTNYNLHWVRQAP GQGLEWMGAIYPGNYDTSYNQKFKGRVTITADKSTSTAYMEL SSLRSEDTAVYYCARVDFGHSRYWYFDVWGQGTTVTVSSGG GGSGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCRAT SSVSSMNWYQQKPGQAPRPLIHATSNLASGIPARFSGSGSGTD YTLTISSLEPEDAAVYYCQQWTFNPPTFGQGTKLEIK
949	Full CAR	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGSSVKVS CKASGYTFTNYNLHWVRQAPGQGLEWMGAIYPGNYDTSYNQ KFKGRVTITADKSTSTAYMELSSLRSEDTAVYYCARVDFGHSR YWYFDVWGQGTTVTVSSGGGGSGGGGSGGGGSGGGGSEIVL TQSPATLSLSPGERATLSCRATSSVSSMNWYQQKPGQAPRPLIH ATSNLASGIPARFSGSGSGTDYTLTISSLEPEDAAVYYCQQWTF NPPTFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAA GGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRK KLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRS ADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGL YQGLSTATKDTYDALHMQALPPR
CD20-C3H4		
950	HCDR1 (Kabat)	NYNLH
951	HCDR2 (Kabat)	AIYPGNYDTSYNQKFKG

952	HCDR3 (Kabat)	VDFGHSRYWYFDV
953	HCDR1 (Chothia)	GYTFTNY
954	HCDR2 (Chothia)	YPGNYD
955	HCDR3 (Chothia)	VDFGHSRYWYFDV
956	HCDR1 (IMGT)	GYTFTNYN
957	HCDR2 (IMGT)	IYPGNYDT
958	HCDR3 (IMGT)	ARVDFGHSRYWYFDV
959	HCDR1 (Combined)	GYTFTNYNLH
960	HCDR2 (Combined)	AIYPGNYDTSYNQKFKG
961	HCDR3 (Combined)	VDFGHSRYWYFDV
962	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTNYNLHWVRQAP GQGLEWMGAIYPGNYDTSYNQKFKGRVTITADKSTSTAYMEL SSLRSEDTAVYYCARVDFGHSRYWYFDVWGQGTTVTVSS
963	LCDR1 (Kabat)	RATSSVSSMN
964	LCDR2 (Kabat)	ATSNLAS
965	LCDR3 (Kabat)	QQWTFNPPT
966	LCDR1 (Chothia)	TSSVSS
967	LCDR2 (Chothia)	ATS
968	LCDR3 (Chothia)	WTFNPP
969	LCDR1 (IMGT)	SSVSS
970	LCDR2 (IMGT)	ATS
971	LCDR3 (IMGT)	QQWTFNPPT
972	LCDR1 (Combined)	RATSSVSSMN
973	LCDR2 (Combined)	ATSNLAS
974	LCDR3 (Combined)	QQWTFNPPT
975	VL	DIQLTQSPSFLSASVGDRVTITCRATSSVSSMNWYQQKPGKAP KPLIHATSNLASGVPSRFSGSGSGTEYTLTISSLQPEDFATYYCQ QWTFNPPTFGQGTKLEIK

976	scFv (VH-linker-VL)	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTNYNLHWVRQAP GQGLEWMGAIYPGNYDTSYNQKFKGRVTITADKSTSTAYMEL SSLRSEDTAVYYCARVDFGHSRYWYFDVWGQGTTVTVSSGG GGSGGGGSGGGGSGGGGSDIQLTQSPSFLSASVGDRVTITCRA TSSVSSMNWYQQKPGKAPKPLIHATSNLASGVPSRFSGSGSGT EYTLTISSLQPEDFATYYCQQWTFNPPTFGQGTKLEIK
977	Full CAR	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGSSVKVS CKASGYTFTNYNLHWVRQAPGQGLEWMGAIYPGNYDTSYNQ KFKGRVTITADKSTSTAYMELSSLRSEDTAVYYCARVDFGHSR YWYFDVWGQGTTVTVSSGGGGSGGGGSGGGGSGGGGSDIQL TQSPSFLSASVGDRVTITCRATSSVSSMNWYQQKPGKAPKPLIH ATSNLASGVPSRFSGSGSGTEYTLTISSLQPEDFATYYCQQWTF NPPTFGQGTKLEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAA GGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRK KLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRS ADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGL YQGLSTATKDTYDALHMQALPPR
CD20-C2H1		
978	HCDR1 (Kabat)	NYWMH
979	HCDR2 (Kabat)	FITPTTGYPEYNQKFKD
980	HCDR3 (Kabat)	RKVGKGVYYALDY
981	HCDR1 (Chothia)	GYTFTNY
982	HCDR2 (Chothia)	TPTTGY
983	HCDR3 (Chothia)	RKVGKGVYYALDY
984	HCDR1 (IMGT)	GYTFTNYW
985	HCDR2 (IMGT)	ITPTTGYP
986	HCDR3 (IMGT)	ARRKVGKGVYYALDY
987	HCDR1 (Combined)	GYTFTNYWMH
988	HCDR2 (Combined)	FITPTTGYPEYNQKFKD
989	HCDR3 (Combined)	RKVGKGVYYALDY
990	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYWMHWVRQA PGQGLEWMGFITPTTGYPEYNQKFKDRVTMTADKSTSTAYME LSSLRSEDTAVYYCARRKVGKGVYYALDYWGQGTTVTVSS
991	LCDR1 (Kabat)	RASGNIHNYLA
992	LCDR2 (Kabat)	NTKTLAD

993	LCDR3 (Kabat)	QHFWSSPWT
994	LCDR1 (Chothia)	SGNIHNY
995	LCDR2 (Chothia)	NTK
996	LCDR3 (Chothia)	FWSSPW
997	LCDR1 (IMGT)	GNIHNY
998	LCDR2 (IMGT)	NTK
999	LCDR3 (IMGT)	QHFWSSPWT
1000	LCDR1 (Combined)	RASGNIHNYLA
1001	LCDR2 (Combined)	NTKTLAD
1002	LCDR3 (Combined)	QHFWSSPWT
1003	VL	DIQMTQSPSSLSASVGDRVTITCRASGNIHNYLAWYQQKPGKV PKLLIYNTKTLADGVPSRFSGSGSGTDYTLTISSLQPEDVATYY CQHFWSSPWTFGGGTKVEIK
1004	scFv (VH-linker-VL)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYWMHWVRQA PGQGLEWMGFITPTTGYPEYNQKFKDRVTMTADKSTSTAYME LSSLRSEDTAVYYCARRKVGKGVYYALDYWGQGTTVTVSSG GGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCR ASGNIHNYLAWYQQKPGKVPKLLIYNTKTLADGVPSRFSGSGS GTDYTLTISSLQPEDVATYYCQHFWSSPWTFGGGTKVEIK
1005	Full CAR	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVKVS CKASGYTFTNYWMHWVRQAPGQGLEWMGFITPTTGYPEYNQ KFKDRVTMTADKSTSTAYMELSSLRSEDTAVYYCARRKVGKG VYYALDYWGQGTTVTVSSGGGGSGGGGSGGGGSGGGGSDIQ MTQSPSSLSASVGDRVTITCRASGNIHNYLAWYQQKPGKVPKL LIYNTKTLADGVPSRFSGSGSGTDYTLTISSLQPEDVATYYCQH FWSSPWTFGGGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACR PAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKR GRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVK FSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEM GGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGH DGLYQGLSTATKDTYDALHMQALPPR
CD20-C2H2		
1006	HCDR1 (Kabat)	NYWMH
1007	HCDR2 (Kabat)	FITPTTGYPEYNQKFKD
1008	HCDR3 (Kabat)	RKVGKGVYYALDY
1009	HCDR1 (Chothia)	GYTFTNY

1010	HCDR2 (Chothia)	TPTTGY
1011	HCDR3 (Chothia)	RKVGKGVYYALDY
1012	HCDR1 (IMGT)	GYTFTNYW
1013	HCDR2 (IMGT)	ITPTTGYP
1014	HCDR3 (IMGT)	ARRKVGKGVYYALDY
1015	HCDR1 (Combined)	GYTFTNYWMH
1016	HCDR2 (Combined)	FITPTTGYPEYNQKFKD
1017	HCDR3 (Combined)	RKVGKGVYYALDY
1018	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTNYWMHWVRQAP GQGLEWMGFITPTTGYPEYNQKFKDRVTITADKSTSTAYMELS SLRSEDTAVYYCARRKVGKGVYYALDYWGQGTTVTVSS
1019	LCDR1 (Kabat)	RASGNIHNYLA
1020	LCDR2 (Kabat)	NTKTLAD
1021	LCDR3 (Kabat)	QHFWSSPWT
1022	LCDR1 (Chothia)	SGNIHNY
1023	LCDR2 (Chothia)	NTK
1024	LCDR3 (Chothia)	FWSSPW
1025	LCDR1 (IMGT)	GNIHNY
1026	LCDR2 (IMGT)	NTK
1027	LCDR3 (IMGT)	QHFWSSPWT
1028	LCDR1 (Combined)	RASGNIHNYLA
1029	LCDR2 (Combined)	NTKTLAD
1030	LCDR3 (Combined)	QHFWSSPWT
1031	VL	DIQMTQSPSSLSASVGDRVTITCRASGNIHNYLAWYQQKPGKV PKLLIYNTKTLADGVPSRFSGSGSGTDYTLTISSLQPEDVATYY CQHFWSSPWTFGGGTKVEIK
1032	scFv (VH-linker-VL)	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTNYWMHWVRQAP GQGLEWMGFITPTTGYPEYNQKFKDRVTITADKSTSTAYMELS SLRSEDTAVYYCARRKVGKGVYYALDYWGQGTTVTVSSGGG GSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRAS

		GNIHNYLAWYQQKPGKVPKLLIYNTKTLADGVPSRFSGSGSGT DYTLTISSLQPEDVATYYCQHFWSSPWTFGGGTKVEIK
1033	Full CAR	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGSSVKVS CKASGYTFTNYWMHWVRQAPGQGLEWMGFITPTTGYPEYNQ KFKDRVTITADKSTSTAYMELSSLRSEDTAVYYCARRKVGKG VYYALDYWGQGTTVTVSSGGGGSGGGGSGGGGSGGGGSDIQ MTQSPSSLSASVGDRVTITCRASGNIHNYLAWYQQKPGKVPKL LIYNTKTLADGVPSRFSGSGSGTDYTLTISSLQPEDVATYYCQH FWSSPWTFGGGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACR PAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKR GRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVK FSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEM GGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGH DGLYQGLSTATKDTYDALHMQALPPR
CD20-C2H3		
1034	HCDR1 (Kabat)	NYWMH
1035	HCDR2 (Kabat)	FITPTTGYPEYNQKFKD
1036	HCDR3 (Kabat)	RKVGKGVYYALDY
1037	HCDR1 (Chothia)	GYTFTNY
1038	HCDR2 (Chothia)	TPTTGY
1039	HCDR3 (Chothia)	RKVGKGVYYALDY
1040	HCDR1 (IMGT)	GYTFTNYW
1041	HCDR2 (IMGT)	ITPTTGYP
1042	HCDR3 (IMGT)	ARRKVGKGVYYALDY
1043	HCDR1 (Combined)	GYTFTNYWMH
1044	HCDR2 (Combined)	FITPTTGYPEYNQKFKD
1045	HCDR3 (Combined)	RKVGKGVYYALDY
1046	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYWMHWVRQA PGQGLEWMGFITPTTGYPEYNQKFKDRVTMTADKSTSTAYME LSSLRSEDTAVYYCARRKVGKGVYYALDYWGQGTTVTVSS
1047	LCDR1 (Kabat)	RASGNIHNYLA
1048	LCDR2 (Kabat)	NTKTLAD
1049	LCDR3 (Kabat)	QHFWSSPWT
1050	LCDR1 (Chothia)	SGNIHNY

1051	LCDR2 (Chothia)	NTK
1052	LCDR3 (Chothia)	FWSSPW
1053	LCDR1 (IMGT)	GNIHNY
1054	LCDR2 (IMGT)	NTK
1055	LCDR3 (IMGT)	QHFWSSPWT
1056	LCDR1 (Combined)	RASGNIHNYLA
1057	LCDR2 (Combined)	NTKTLAD
1058	LCDR3 (Combined)	QHFWSSPWT
1059	VL	AIRMTQSPFSLSASVGDRVTITCRASGNIHNYLAWYQQKPAKA PKLFIYNTKTLADGVPSRFSGSGSGTDYTLTISSLQPEDFATYYC QHFWSSPWTFGGGTKVEIK
1060	scFv (VH-linker-VL)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYWMHWVRQA PGQGLEWMGFITPTTGYPEYNQKFKDRVTMTADKSTSTAYME LSSLRSEDTAVYYCARRKVGKGVYYALDYWGQGTTVTVSSG GGGSGGGGSGGGGSGGGGSAIRMTQSPFSLSASVGDRVTITCR ASGNIHNYLAWYQQKPAKAPKLFIYNTKTLADGVPSRFSGSGS GTDYTLTISSLQPEDFATYYCQHFWSSPWTFGGGTKVEIK
1061	Full CAR	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVKVS CKASGYTFTNYWMHWVRQAPGQGLEWMGFITPTTGYPEYNQ KFKDRVTMTADKSTSTAYMELSSLRSEDTAVYYCARRKVGKG VYYALDYWGQGTTVTVSSGGGGSGGGGSGGGGSGGGGSAIR MTQSPFSLSASVGDRVTITCRASGNIHNYLAWYQQKPAKAPKL FIYNTKTLADGVPSRFSGSGSGTDYTLTISSLQPEDFATYYCQH FWSSPWTFGGGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACR PAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKR GRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVK FSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEM GGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGH DGLYQGLSTATKDTYDALHMQALPPR
CD20-C2H4		
1062	HCDR1 (Kabat)	NYWMH
1063	HCDR2 (Kabat)	FITPTTGYPEYNQKFKD
1064	HCDR3 (Kabat)	RKVGKGVYYALDY
1065	HCDR1 (Chothia)	GYTFTNY
1066	HCDR2 (Chothia)	TPTTGY
1067	HCDR3 (Chothia)	RKVGKGVYYALDY

1068	HCDR1 (IMGT)	GYTFTNYW
1069	HCDR2 (IMGT)	ITPTTGYP
1070	HCDR3 (IMGT)	ARRKVGKGVYYALDY
1071	HCDR1 (Combined)	GYTFTNYWMH
1072	HCDR2 (Combined)	FITPTTGYPEYNQKFKD
1073	HCDR3 (Combined)	RKVGKGVYYALDY
1074	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTNYWMHWVRQAP GQGLEWMGFITPTTGYPEYNQKFKDRVTITADKSTSTAYMELS SLRSEDTAVYYCARRKVGKGVYYALDYWGQGTTVTVSS
1075	LCDR1 (Kabat)	RASGNIHNYLA
1076	LCDR2 (Kabat)	NTKTLAD
1077	LCDR3 (Kabat)	QHFWSSPWT
1078	LCDR1 (Chothia)	SGNIHNY
1079	LCDR2 (Chothia)	NTK
1080	LCDR3 (Chothia)	FWSSPW
1081	LCDR1 (IMGT)	GNIHNY
1082	LCDR2 (IMGT)	NTK
1083	LCDR3 (IMGT)	QHFWSSPWT
1084	LCDR1 (Combined)	RASGNIHNYLA
1085	LCDR2 (Combined)	NTKTLAD
1086	LCDR3 (Combined)	QHFWSSPWT
1087	VL	AIRMTQSPFSLSASVGDRVTITCRASGNIHNYLAWYQQKPAKA PKLFIYNTKTLADGVPSRFSGSGSGTDYTLTISSLQPEDFATYYC QHFWSSPWTFGGGTKVEIK
1088	scFv (VH-linker-VL)	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTNYWMHWVRQAP GQGLEWMGFITPTTGYPEYNQKFKDRVTITADKSTSTAYMELS SLRSEDTAVYYCARRKVGKGVYYALDYWGQGTTVTVSSGGG GSGGGGSGGGGSGGGGSAIRMTQSPFSLSASVGDRVTITCRAS GNIHNYLAWYQQKPAKAPKLFIYNTKTLADGVPSRFSGSGSGT DYTLTISSLQPEDFATYYCQHFWSSPWTFGGGTKVEIK
1089	Full CAR	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGSSVKVS CKASGYTFTNYWMHWVRQAPGQGLEWMGFITPTTGYPEYNQ

		KFKDRVTITADKSTSTAYMELSSLRSEDTAVYYCARRKVGKG VYYALDYWGQGTTVTVSSGGGGSGGGGSGGGGSGGGGSAIR MTQSPFSLSASVGDRVTITCRASGNIHNYLAWYQQKPAKAPKL FIYNTKTLADGVPSRFSGSGSGTDYTLTISSLQPEDFATYYCQH FWSSPWTFGGGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACR PAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKR GRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVK FSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEM GGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGH DGLYQGLSTATKDTYDALHMQALPPR
CD20-C5H2		
1090	HCDR1 (Kabat)	SYNMH
1091	HCDR2 (Kabat)	AIYPGNGDTSYNPKFKG
1092	HCDR3 (Kabat)	SYFYGSSSWYFDV
1093	HCDR1 (Chothia)	GYTFTSY
1094	HCDR2 (Chothia)	YPGNGD
1095	HCDR3 (Chothia)	SYFYGSSSWYFDV
1096	HCDR1 (IMGT)	GYTFTSYN
1097	HCDR2 (IMGT)	IYPGNGDT
1098	HCDR3 (IMGT)	ARSYFYGSSSWYFDV
1099	HCDR1 (Combined)	GYTFTSYNMH
1100	HCDR2 (Combined)	AIYPGNGDTSYNPKFKG
1101	HCDR3 (Combined)	SYFYGSSSWYFDV
1102	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAP GQGLEWMGAIYPGNGDTSYNPKFKGRVTMTADKSTRTAYME LSSLRSEDTAVYYCARSYFYGSSSWYFDVWGQGTTVTVSS
1103	LCDR1 (Kabat)	RASSSVSSMH
1104	LCDR2 (Kabat)	ATSNLAS
1105	LCDR3 (Kabat)	QQWIFNPPT
1106	LCDR1 (Chothia)	SSSVSS
1107	LCDR2 (Chothia)	ATS
1108	LCDR3 (Chothia)	WIFNPP

1109	LCDR1 (IMGT)	SSVSS
1110	LCDR2 (IMGT)	ATS
1111	LCDR3 (IMGT)	QQWIFNPPT
1112	LCDR1 (Combined)	RASSSVSSMH
1113	LCDR2 (Combined)	ATSNLAS
1114	LCDR3 (Combined)	QQWIFNPPT
1115	VL	DIQLTQSPSFLSASVGDRVTITCRASSSVSSMHWYQQKPGKAP KPLIFATSNLASGVPSRFSGSGSGTEYTLTISSLQPEDFATYYCQ QWIFNPPTFGGGTKVEIK
1116	scFv (VH-linker-VL)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAP GQGLEWMGAIYPGNGDTSYNPKFKGRVTMTADKSTRTAYME LSSLRSEDTAVYYCARSYFYGSSSWYFDVWGQGTTVTVSSGG GGSGGGGSGGGGSGGGGSDIQLTQSPSFLSASVGDRVTITCRAS SSVSSMHWYQQKPGKAPKPLIFATSNLASGVPSRFSGSGSGTE YTLTISSLQPEDFATYYCQQWIFNPPTFGGGTKVEIK
1117	Full CAR	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGASVKVS CKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNP KFKGRVTMTADKSTRTAYMELSSLRSEDTAVYYCARSYFYGS SSWYFDVWGQGTTVTVSSGGGGSGGGGSGGGGSGGGGSDIQL TQSPSFLSASVGDRVTITCRASSSVSSMHWYQQKPGKAPKPLIF ATSNLASGVPSRFSGSGSGTEYTLTISSLQPEDFATYYCQQWIF NPPTFGGGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAA GGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRK KLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRS ADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGL YQGLSTATKDTYDALHMQALPPR
CD20-C5H3		
1118	HCDR1 (Kabat)	SYNMH
1119	HCDR2 (Kabat)	AIYPGNGDTSYNPKFKG
1120	HCDR3 (Kabat)	SYFYGSSSWYFDV
1121	HCDR1 (Chothia)	GYTFTSY
1122	HCDR2 (Chothia)	YPGNGD
1123	HCDR3 (Chothia)	SYFYGSSSWYFDV
1124	HCDR1 (IMGT)	GYTFTSYN
1125	HCDR2 (IMGT)	IYPGNGDT

1126	HCDR3 (IMGT)	ARSYFYGSSSWYFDV
1127	HCDR1 (Combined)	GYTFTSYNMH
1128	HCDR2 (Combined)	AIYPGNGDTSYNPKFKG
1129	HCDR3 (Combined)	SYFYGSSSWYFDV
1130	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYNMHWVRQAP GQGLEWMGAIYPGNGDTSYNPKFKGRVTITADKSTRTAYMEL SSLRSEDTAVYYCARSYFYGSSSWYFDVWGQGTTVTVSS
1131	LCDR1 (Kabat)	RASSSVSSMH
1132	LCDR2 (Kabat)	ATSNLAS
1133	LCDR3 (Kabat)	QQWIFNPPT
1134	LCDR1 (Chothia)	SSSVSS
1135	LCDR2 (Chothia)	ATS
1136	LCDR3 (Chothia)	WIFNPP
1137	LCDR1 (IMGT)	SSVSS
1138	LCDR2 (IMGT)	ATS
1139	LCDR3 (IMGT)	QQWIFNPPT
1140	LCDR1 (Combined)	RASSSVSSMH
1141	LCDR2 (Combined)	ATSNLAS
1142	LCDR3 (Combined)	QQWIFNPPT
1143	VL	EIVLTQSPATLSLSPGERATLSCRASSSVSSMHWYQQKPGQAPR PLIFATSNLASGIPARFSGSGSGTDYTLTISSLEPEDAAVYYCQQ WIFNPPTFGGGTKVEIK
1144	scFv (VH-linker-VL)	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYNMHWVRQAP GQGLEWMGAIYPGNGDTSYNPKFKGRVTITADKSTRTAYMEL SSLRSEDTAVYYCARSYFYGSSSWYFDVWGQGTTVTVSSGGG GSGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCRASS SVSSMHWYQQKPGQAPRPLIFATSNLASGIPARFSGSGSGTDYT LTISSLEPEDAAVYYCQQWIFNPPTFGGGTKVEIK
1145	Full CAR	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGSSVKVS CKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNP KFKGRVTITADKSTRTAYMELSSLRSEDTAVYYCARSYFYGSS SWYFDVWGQGTTVTVSSGGGGSGGGGSGGGGSGGGGSEIVLT QSPATLSLSPGERATLSCRASSSVSSMHWYQQKPGQAPRPLIFA TSNLASGIPARFSGSGSGTDYTLTISSLEPEDAAVYYCQQWIFNP

		PTFGGGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGG AVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKL LYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSAD APAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPR RKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQ GLSTATKDTYDALHMQALPPR
CD20-C5H4		
1146	HCDR1 (Kabat)	SYNMH
1147	HCDR2 (Kabat)	AIYPGNGDTSYNPKFKG
1148	HCDR3 (Kabat)	SYFYGSSSWYFDV
1149	HCDR1 (Chothia)	GYTFTSY
1150	HCDR2 (Chothia)	YPGNGD
1151	HCDR3 (Chothia)	SYFYGSSSWYFDV
1152	HCDR1 (IMGT)	GYTFTSYN
1153	HCDR2 (IMGT)	IYPGNGDT
1154	HCDR3 (IMGT)	ARSYFYGSSSWYFDV
1155	HCDR1 (Combined)	GYTFTSYNMH
1156	HCDR2 (Combined)	AIYPGNGDTSYNPKFKG
1157	HCDR3 (Combined)	SYFYGSSSWYFDV
1158	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYNMHWVRQAP GQGLEWMGAIYPGNGDTSYNPKFKGRVTITADKSTRTAYMEL SSLRSEDTAVYYCARSYFYGSSSWYFDVWGQGTTVTVSS
1159	LCDR1 (Kabat)	RASSSVSSMH
1160	LCDR2 (Kabat)	ATSNLAS
1161	LCDR3 (Kabat)	QQWIFNPPT
1162	LCDR1 (Chothia)	SSSVSS
1163	LCDR2 (Chothia)	ATS
1164	LCDR3 (Chothia)	WIFNPP
1165	LCDR1 (IMGT)	SSVSS
1166	LCDR2 (IMGT)	ATS

1167	LCDR3 (IMGT)	QQWIFNPPT
1168	LCDR1 (Combined)	RASSSVSSMH
1169	LCDR2 (Combined)	ATSNLAS
1170	LCDR3 (Combined)	QQWIFNPPT
1171	VL	DIQLTQSPSFLSASVGDRVTITCRASSSVSSMHWYQQKPGKAP KPLIFATSNLASGVPSRFSGSGSGTEYTLTISSLQPEDFATYYCQ QWIFNPPTFGGGTKVEIK
1172	scFv (VH-linker-VL)	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYNMHWVRQAP GQGLEWMGAIYPGNGDTSYNPKFKGRVTITADKSTRTAYMEL SSLRSEDTAVYYCARSYFYGSSSWYFDVWGQGTTVTVSSGGG GSGGGGSGGGGSGGGGSDIQLTQSPSFLSASVGDRVTITCRASS SVSSMHWYQQKPGKAPKPLIFATSNLASGVPSRFSGSGSGTEY TLTISSLQPEDFATYYCQQWIFNPPTFGGGTKVEIK
1173	Full CAR	MALPVTALLLPLALLLHAARPQVQLVQSGAEVKKPGSSVKVS CKASGYTFTSYNMHWVRQAPGQGLEWMGAIYPGNGDTSYNP KFKGRVTITADKSTRTAYMELSSLRSEDTAVYYCARSYFYGSS SWYFDVWGQGTTVTVSSGGGGSGGGGSGGGGSGGGGSDIQL TQSPSFLSASVGDRVTITCRASSSVSSMHWYQQKPGKAPKPLIF ATSNLASGVPSRFSGSGSGTEYTLTISSLQPEDFATYYCQQWIF NPPTFGGGTKVEIKTTTPAPRPPTPAPTIASQPLSLRPEACRPAA GGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRK KLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRS ADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGK PRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGL YQGLSTATKDTYDALHMQALPPR
CD20-C3		
1174	VH	QVQLQQPGAELVKPGASVKMSCKASGYTFTNYNLHWVKQTP GQGLEWIGAIYPGNYDTSYNQKFKGKATLTADKSSSTAYMLL SSLTSEDSAVYFCARVDFGHSRYWYFDVWGAGTTVTVSS
1175	VL	QIVLSQSPAILSASPGEKVTMTCRATSSVSSMNWYQQKPGSFPR PWIHATSNLASGVPARFSGSGSGTSYSLTISRVEAEDAATYYCQ QWTFNPPTFGAGAKLELK
CD20-C5		
1176	VH	QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTP GQGLEWIGAIYPGNGDTSYNPKFKGKATLTADKSSRTAYIHLS SLTSEDSVVYYCARSYFYGSSSWYFDVWGAGTTVTVSS
1177	VL	QIILSQSPAILSASPGEKVTLTCRASSSVSSMHWYQQKPGSSPKP WIFATSNLASGVPARFTGSGSGTSYSLTISRVEAEDAATYYCQQ WIFNPPTFGGGTSLEIK
CD20-C2		
1178	VH	QVHLQQSGAELAKPGASVKMSCKASGYTFTNYWMHWVKQR PGQGLEWIGFITPTTGYPEYNQKFKDKATLTADKSSSTAYMQL SSLTSEDSAVYYCARRKVGKGVYYALDYWGQGTSVTVSS
1179	VL	DILMTQSPASLSASVGETVTITCRASGNIHNYLAWYQQKQGNS PQLLVYNTKTLADGVPSRFSGSGSGTQYSLKINSLQTEDFGTYY CQHFWSSPWTFGGGTKLEIK

CARs that bind to CD22 are known in the art. For example, those disclosed in WO2018/067992 or WO2016/164731. Any known CD22 CAR, for example, the CD22 antigen binding domain of any known CD22 CAR, in the art can be used in accordance with the present disclosure.

Exemplary CD22-binding sequences or CD22 CAR sequences are disclosed in, for example, Tables 6A, 6B, 7A, 7B, 7C, 8A, 8B, 9A, 9B, 10A, and 10B of WO2016164731 and Tables 6-10 of WO2018067992. In some embodiments, the CD22 CAR sequences comprise a CDR, variable region, scFv or full-length sequence of a CD22 CAR disclosed in WO2018067992 or WO2016164731.

In embodiments, the CAR comprises an antigen binding domain that binds to CD22 (CD22 CAR). In some embodiments, the antigen binding domain targets human CD22. In some embodiments, the antigen binding domain includes a single chain Fv sequence as described herein.

The sequences of human CD22 CAR are provided below. In some embodiments, a human CD22 CAR is CAR22-65.

Human CD22 CAR scFv sequence
EVQLQQSGPGLVKPSQTLSLTCAISGDSMLSNSDTWNWIRQSPSRGLEWLGRTYHRSTW
YDDYASSVRGRVSINVDTSKNQYSLQLNAVTPEDTGVYYCARVRLQDGNSWSDAFDV
WGQGTMVTVSSGGGGSGGGGSGGGGSQSALTQPASASGSPGQSVTISCTGTSSDVGGY
NYVSWYQQHPGKAPKLMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCS
SYTSSSTLYVFGTGTQLTVL (SEQ ID NO: 753)

Human CD22 CAR heavy chain variable region
EVQLQQSGPGLVKPSQTLSLTCAISGDSMLSNSDTWNWIRQSPSRGLEWLGRTYHRSTW
YDDYASSVRGRVSINVDTSKNQYSLQLNAVTPEDTGVYYCARVRLQDGNSWSDAFDV
WGQGTMVTVSS (SEQ ID NO: 754)

Human CD22 CAR light chain variable region
QSALTQPASASGSPGQSVTISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYDVSNRPSG
VSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTLYVFGTGTQLTVL (SEQ ID NO
755)

In some embodiments, CD22 CARs comprise a sequence, for example, a CDR, VH, VL, scFv, or full-CAR sequence, disclosed in Tables 15-16 and Table 24 below, or a sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identity thereto.

Table 15. Heavy Chain Variable Domain CDRs of CD22 CAR (CAR22-65)

Candidate	HCDR1	SEQ ID NO:	HCDR2	SEQ ID NO:	HCDR3	SEQ ID NO:
CAR22-65 Combined	GDSMLSNS DTWN	744	RTYHRST WYDDYAS SVRG	746	VRLQDGN SWSDAFD V	748
CAR22-65 Kabat	SNSDTWN	745	RTYHRST WYDDYAS SVRG	747	VRLQDGN SWSDAFD V	749
CD22-65 Chothia	GDSMLSNS D	1180	YHRSTWY	1181	VRLQDGN SWSDAFD V	1182
CD22-65 IMGT	GDSMLSNS DT	1183	TYHRSTW YD	1184	ARVRLQD GNSWSDA FDV	1185

Table 16. Light Chain Variable Domain CDRs of CD22 CAR (CAR22-65). The LC CDR sequences in this table have the same sequence under the Kabat or combined definitions.

Candidate	LCDR1	SEQ ID NO:	LCDR2	SEQ ID NO:	LCDR3	SEQ ID NO:
CAR22-65 Combined	TGTSSDVG GYNYVS	750	DVSNRPS	751	SSYTSSSTL YV	752
CD22-65 Kabat	TGTSSDVG GYNYVS	1186	DVSNRPS	1189	SSYTSSSTL YV	1192
CD22-65 Chothia	TSSDVGGY NY	1187	DVS	1190	YTSSSTLY	1193
CD22-65 IMGT	SSDVGGY NY	1188	DVS	1191	SSYTSSSTL YV	1194

Table 24. Amino acid sequences of exemplary anti-CD22 molecules

SEQ ID NO:	Region	Sequence
CD22-65s		
1195	scFv (VH-linker-VL) (linker shown by italics and underline)	EVQLQQSGPGLVKPSQTLSLTCAISGDSMLSNSDTWNWIRQSP SRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSL QLNAVTPEDTGVYYCARVRLQDGNSWSDAFDVWGQGTMVT VSS*GGGGS*QSALTQPASASGSPGQSVTISCTGTSSDVGGYNYV SWYQQHPGKAPKLMIYDVSNRPSGVSNRFSGSKSGNTASLTIS GLQAEDEADYYCSSYTSSSTLYVFGTGTQLTVL
CD22-65ss		

1196	scFv (VH - VL) (no linker between VH-VL)	EVQLQQSGPGLVKPSQTLSLTCAISGDSMLSNSDTWNWIRQSP SRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSL QLNAVTPEDTGVYYCARVRLQDGNSWSDAFDVWGQGTMVT VSSQSALTQPASASGSPGQSVTISCTGTSSDVGGYNYVSWYQ QHPGKAPKLMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQA EDEADYYCSSYTSSSTLYVFGTGTQLTVL
CD22-65sKD		
1197	VH	EVQLQQSGPGLVKPSQTLSLTCAISGDSMLSNSDTWNWIRKSP SRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSL QLNAVTPEDTGVYYCARVRLQDGNSWSDAFDVWGQGTMVT VSS
1198	VL	QSALTQPASASGSPGQSVTISCTGTSSDVGGYNYVSWYQDHP GKAPKLMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDE ADYYCSSYTSSSTLYVFGTGTQLTVL
1199	scFv (VH-linker-VL)	EVQLQQSGPGLVKPSQTLSLTCAISGDSMLSNSDTWNWIRKSP SRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSL QLNAVTPEDTGVYYCARVRLQDGNSWSDAFDVWGQGTMVT VSSGGGGSQSALTQPASASGSPGQSVTISCTGTSSDVGGYNYV SWYQDHPGKAPKLMIYDVSNRPSGVSNRFSGSKSGNTASLTIS GLQAEDEADYYCSSYTSSSTLYVFGTGTQLTVL
CD22-64		
1200	HC CDR1 (Kabat)	SNSDTWN
1201	HC CDR2 (Kabat)	RTYHRSTWYDDYASSVRG
1202	HC CDR3 (Kabat)	VRLQDGNSWSDAFDV
1203	HC CDR1 (Chothia)	GDSVLSNSD
1204	HC CDR2 (Chothia)	YHRSTWY
1205	HC CDR3 (Chothia)	VRLQDGNSWSDAFDV
1206	HC CDR1 (IMGT)	GDSVLSNSDT
1207	HC CDR2 (IMGT)	TYHRSTWYD
1208	HC CDR3 (IMGT)	ARVRLQDGNSWSDAFDV
1209	HC CDR1 (Combined)	GDSVLSNSDTWN
1210	HC CDR2 (Combined)	RTYHRSTWYDDYASSVRG
1211	HC CDR3 (Combined)	VRLQDGNSWSDAFDV
1212	VH	EVQLQQSGPGLVKPSQTLPLTCAISGDSVLSNSDTWNWIRQSP SRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSL QLNAVTPEDTGVYYCARVRLQDGNSWSDAFDVWGQGTMVT VSS

1213	LC CDR1 (Kabat)	TGTSSDVGGYNYVS
1214	LC CDR2 (Kabat)	DVSNRPS
1215	LC CDR3 (Kabat)	SSYTSSSTLYV
1216	LC CDR1 (Chothia)	TSSDVGGYNY
1217	LC CDR2 (Chothia)	DVS
1218	LC CDR3 (Chothia)	YTSSSTLY
1219	LC CDR1 (IMGT)	SSDVGGYNY
1220	LC CDR2 (IMGT)	DVS
1221	LC CDR3 (IMGT)	SSYTSSSTLYV
1222	LC CDR1 (Combined)	TGTSSDVGGYNYVS
1223	LC CDR2 (Combined)	DVSNRPS
1224	LC CDR3 (Combined)	SSYTSSSTLYV
1225	VL	QSALTQPASASGSPGQSVTISCTGTSSDVGGYNYVSWYQQHP GKAPKLMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDE ADYYCSSYTSSSTLYVFGTGTQLTVL
1226	scFv (VH-linker-VL)	EVQLQQSGPGLVKPSQTLPLTCAISGDSVLSNSDTWNWIRQSP SRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSL QLNAVTPEDTGVYYCARVRLQDGNSWSDAFDVWGQGTMVT VSSGGGGSGGGGSGGGGPQSALTQPASASGSPGQSVTISCTGT SSDVGGYNYVSWYQQHPGKAPKLMIYDVSNRPSGVSNRFSG SKSGNTASLTISGLQAEDEADYYCSSYTSSSTLYVFGTGTQLT VL
CD22-57		
1227	HC CDR1 (Kabat)	NNNAAWN
1228	HC CDR2 (Kabat)	RTYHRSTWYNDYVGSVKS
1229	HC CDR3 (Kabat)	ETDYGDYGAFDI
1230	HC CDR1 (Chothia)	GDSVSNNNA
1231	HC CDR2 (Chothia)	YHRSTWY
1232	HC CDR3 (Chothia)	ETDYGDYGAFDI
1233	HC CDR1 (IMGT)	GDSVSNNNAA

1234	HC CDR2 (IMGT)	TYHRSTWYN
1235	HC CDR3 (IMGT)	ARETDYGDYGAFDI
1236	HC CDR1 (Combined)	GDSVSNNNAAWN
1237	HC CDR2 (Combined)	RTYHRSTWYNDYVGSVKS
1238	HC CDR3 (Combined)	ETDYGDYGAFDI
1239	VH	EVQLQQSGPGLVKPSQTLSLTCAISGDSVSNNNAAWNWIRQS PSRGLEWLGRTYHRSTWYNDYVGSVKSRITINPDTSKNQFSL QLNSVTPEDTAVYYCARETDYGDYGAFDIWGQGTTVTVSS
1240	LC CDR1 (Kabat)	TGSRNDIGAYESVS
1241	LC CDR2 (Kabat)	GVNNRPS
1242	LC CDR3 (Kabat)	SSHTTTSTLYV
1243	LC CDR1 (Chothia)	SRNDIGAYES
1244	LC CDR2 (Chothia)	GVN
1245	LC CDR3 (Chothia)	HTTTSTLY
1246	LC CDR1 (IMGT)	RNDIGAYES
1247	LC CDR2 (IMGT)	GVN
1248	LC CDR3 (IMGT)	SSHTTTSTLYV
1249	LC CDR1 (Combined)	TGSRNDIGAYESVS
1250	LC CDR2 (Combined)	GVNNRPS
1251	LC CDR3 (Combined)	SSHTTTSTLYV
1252	VL	QSALTQPASVSGSPGQSITISCTGSRNDIGAYESVSWYQQHPG NAPKLIIHGVNNRPSGVFDRFSVSQSGNTASLTISGLQAEDEAD YYCSSHTTTSTLYVFGTGTKVTVL
1253	scFv (VH-linker-VL)	EVQLQQSGPGLVKPSQTLSLTCAISGDSVSNNNAAWNWIRQS PSRGLEWLGRTYHRSTWYNDYVGSVKSRITINPDTSKNQFSL QLNSVTPEDTAVYYCARETDYGDYGAFDIWGQGTTVTVSSG GGGSGGGGSGGGGSQSALTQPASVSGSPGQSITISCTGSRNDIG AYESVSWYQQHPGNAPKLIIHGVNNRPSGVFDRFSVSQSGNT ASLTISGLQAEDEADYYCSSHTTTSTLYVFGTGTKVTVL
CD22-58		
1254	HC CDR1 (Kabat)	SNSAAWN

1255	HC CDR2 (Kabat)	RTFYRSKWYNDYAVSVKG
1256	HC CDR3 (Kabat)	GDYYYGLDV
1257	HC CDR1 (Chothia)	GDSVSSNSA
1258	HC CDR2 (Chothia)	FYRSKWY
1259	HC CDR3 (Chothia)	GDYYYGLDV
1260	HC CDR1 (IMGT)	GDSVSSNSAA
1261	HC CDR2 (IMGT)	TFYRSKWYN
1262	HC CDR3 (IMGT)	AGGDYYYGLDV
1263	HC CDR1 (Combined)	GDSVSSNSAAWN
1264	HC CDR2 (Combined)	RTFYRSKWYNDYAVSVKG
1265	HC CDR3 (Combined)	GDYYYGLDV
1266	VH	EVQLQQSGPGLVNPSQTLSITCAISGDSVSSNSAAWNWIRQSP SRGLEWLGRTFYRSKWYNDYAVSVKGRITISPDTSKNQFSLQ LNSVTPEDTAVYYCAGGDYYYGLDVWGQGTTVTVSS
1267	LC CDR1 (Kabat)	TGSSSDVGGYNSVS
1268	LC CDR2 (Kabat)	EVINRPS
1269	LC CDR3 (Kabat)	SSYTSSSTYV
1270	LC CDR1 (Chothia)	SSSDVGGYNS
1271	LC CDR2 (Chothia)	EVI
1272	LC CDR3 (Chothia)	YTSSSTY
1273	LC CDR1 (IMGT)	SSDVGGYNS
1274	LC CDR2 (IMGT)	EVI
1275	LC CDR3 (IMGT)	SSYTSSSTYV
1276	LC CDR1 (Combined)	TGSSSDVGGYNSVS
1277	LC CDR2 (Combined)	EVINRPS
1278	LC CDR3 (Combined)	SSYTSSSTYV

1279	VL	QSALTQPASVSGSPGQSITISCTGSSSDVGGYNSVSWYQQHPG KAPKLMIYEVINRPSGVSHRFSGSKSGNTASLTISGLQAEDEA DYYCSSYTSSSTYVFGTGTKVTVL
1280	scFv (VH-linker-VL)	EVQLQQSGPGLVNPSQTLSITCAISGDSVSSNSAAWNWIRQSP SRGLEWLGRTFYRSKWYNDYAVSVKGRITISPDTSKNQFSLQ LNSVTPEDTAVYYCAGGDYYYGLDVWGQGTTVTVSSGGGGS GGGGSGGGGSQSALTQPASVSGSPGQSITISCTGSSSDVGGYN SVSWYQQHPGKAPKLMIYEVINRPSGVSHRFSGSKSGNTASLT ISGLQAEDEADYYCSSYTSSSTYVFGTGTKVTVL
CD22-59		
1281	HC CDR1 (Kabat)	SNSDTWN
1282	HC CDR2 (Kabat)	RTYHRSTWYDDYASSVRG
1283	HC CDR3 (Kabat)	DRLQDGNSWSDAFDV
1284	HC CDR1 (Chothia)	GDSVLSNSD
1285	HC CDR2 (Chothia)	YHRSTWY
1286	HC CDR3 (Chothia)	DRLQDGNSWSDAFDV
1287	HC CDR1 (IMGT)	GDSVLSNSDT
1288	HC CDR2 (IMGT)	TYHRSTWYD
1289	HC CDR3 (IMGT)	ARDRLQDGNSWSDAFDV
1290	HC CDR1 (Combined)	GDSVLSNSDTWN
1291	HC CDR2 (Combined)	RTYHRSTWYDDYASSVRG
1292	HC CDR3 (Combined)	DRLQDGNSWSDAFDV
1293	VH	EVQLQQSGPGLVKPSQTLSLTCAISGDSVLSNSDTWNWIRQSP SRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSL QLNAVTPEDTGVYYCARDRLQDGNSWSDAFDVWGQGTMVT VSS
1294	LC CDR1 (Kabat)	TGSSSDIGGFNYVS
1295	LC CDR2 (Kabat)	EVTNRPS
1296	LC CDR3 (Kabat)	SSYASGSPLYV
1297	LC CDR1 (Chothia)	SSSDIGGFNY
1298	LC CDR2 (Chothia)	EVT
1299	LC CDR3 (Chothia)	YASGSPLY

1300	LC CDR1 (IMGT)	SSDIGGFNY
1301	LC CDR2 (IMGT)	EVT
1302	LC CDR3 (IMGT)	SSYASGSPLYV
1303	LC CDR1 (Combined)	TGSSSDIGGFNYVS
1304	LC CDR2 (Combined)	EVTNRPS
1305	LC CDR3 (Combined)	SSYASGSPLYV
1306	VL	QSALTQPASVSGSPGQSITISCTGSSSDIGGFNYVSWYQQHAGE APKLMIYEVTNRPSGVSDRFSGSKSDNTASLTISGLQAEDEAD YYCSSYASGSPLYVFGTGTKVTVL
1307	scFv (VH-linker-VL)	EVQLQQSGPGLVKPSQTLSLTCAISGDSVLSNSDTWNWIRQSP SRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSL QLNAVTPEDTGVYYCARDRLQDGNSWSDAFDVWGQGTMVT VSSGGGGSGGGGSGGGGSQSALTQPASVSGSPGQSITISCTGSS SDIGGFNYVSWYQQHAGEAPKLMIYEVTNRPSGVSDRFSGSK SDNTASLTISGLQAEDEADYYCSSYASGSPLYVFGTGTKVTVL
CD22-60		
1308	HC CDR1 (Kabat)	SNSDTWN
1309	HC CDR2 (Kabat)	RTYHRSTWYDDYASSVRG
1310	HC CDR3 (Kabat)	DRLQDGNSWSDAFDV
1311	HC CDR1 (Chothia)	GDSVLSNSD
1312	HC CDR2 (Chothia)	YHRSTWY
1313	HC CDR3 (Chothia)	DRLQDGNSWSDAFDV
1314	HC CDR1 (IMGT)	GDSVLSNSDT
1315	HC CDR2 (IMGT)	TYHRSTWYD
1316	HC CDR3 (IMGT)	ARDRLQDGNSWSDAFDV
1317	HC CDR1 (Combined)	GDSVLSNSDTWN
1318	HC CDR2 (Combined)	RTYHRSTWYDDYASSVRG
1319	HC CDR3 (Combined)	DRLQDGNSWSDAFDV
1320	VH	EVQLQQSGPGLVKPSQTLSLTCAISGDSVLSNSDTWNWIRQSP SRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSL QLNAVTPEDTGVYYCARDRLQDGNSWSDAFDVWGQGTMVT VSS

1321	LC CDR1 (Kabat)	TGTSSDIGGYNYVS
1322	LC CDR2 (Kabat)	EVSNRPS
1323	LC CDR3 (Kabat)	SSYTSSSTLYV
1324	LC CDR1 (Chothia)	TSSDIGGYNY
1325	LC CDR2 (Chothia)	EVS
1326	LC CDR3 (Chothia)	YTSSSTLY
1327	LC CDR1 (IMGT)	SSDIGGYNY
1328	LC CDR2 (IMGT)	EVS
1329	LC CDR3 (IMGT)	SSYTSSSTLYV
1330	LC CDR1 (Combined)	TGTSSDIGGYNYVS
1331	LC CDR2 (Combined)	EVSNRPS
1332	LC CDR3 (Combined)	SSYTSSSTLYV
1333	VL	QSALTQPASVSGSPGQSITFSCTGTSSDIGGYNYVSWYQQHPG KAPKLMIYEVSNRPSGVSNRFSGTKSGNTASLTISGLQAEDEA DYYCSSYTSSSTLYVFGTGTKLTVL
1334	scFv (VH-linker-VL)	EVQLQQSGPGLVKPSQTLSLTCAISGDSVLSNSDTWNWIRQSP SRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSL QLNAVTPEDTGVYYCARDRLQDGNSWSDAFDVWGQGTMVT VSSGGGGSGGGGSGSGGSQSALTQPASVSGSPGQSITFSCTGT SSDIGGYNYVSWYQQHPGKAPKLMIYEVSNRPSGVSNRFSGT KSGNTASLTISGLQAEDEADYYCSSYTSSSTLYVFGTGTKLTV L
CD22-61		
1335	HC CDR1 (Kabat)	SNSDTWN
1336	HC CDR2 (Kabat)	RTYHRSTWYDDYASSVRG
1337	HC CDR3 (Kabat)	DRLQDGNSWSDAFDV
1338	HC CDR1 (Chothia)	GDSVLSNSD
1339	HC CDR2 (Chothia)	YHRSTWY
1340	HC CDR3 (Chothia)	DRLQDGNSWSDAFDV
1341	HC CDR1 (IMGT)	GDSVLSNSDT

1342	HC CDR2 (IMGT)	TYHRSTWYD
1343	HC CDR3 (IMGT)	ARDRLQDGNSWSDAFDV
1344	HC CDR1 (Combined)	GDSVLSNSDTWN
1345	HC CDR2 (Combined)	RTYHRSTWYDDYASSVRG
1346	HC CDR3 (Combined)	DRLQDGNSWSDAFDV
1347	VH	QVQLQESGPGLVKPSQTLSLTCAISGDSVLSNSDTWNWIRQSP SRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSL QLNAVTPEDTGVYYCARDRLQDGNSWSDAFDVWGQGTMVT VSS
1348	LC CDR1 (Kabat)	TGTSSDVGGYNYVS
1349	LC CDR2 (Kabat)	EVSNRPS
1350	LC CDR3 (Kabat)	SSYTSSSTLYV
1351	LC CDR1 (Chothia)	TSSDVGGYNY
1352	LC CDR2 (Chothia)	EVS
1353	LC CDR3 (Chothia)	YTSSSTLY
1354	LC CDR1 (IMGT)	SSDVGGYNY
1355	LC CDR2 (IMGT)	EVS
1356	LC CDR3 (IMGT)	SSYTSSSTLYV
1357	LC CDR1 (Combined)	TGTSSDVGGYNYVS
1358	LC CDR2 (Combined)	EVSNRPS
1359	LC CDR3 (Combined)	SSYTSSSTLYV
1360	VL	QSALTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPG KAPKLMIYEVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDEA DYYCSSYTSSSTLYVFGTGTKVTVL
1361	scFv (VH-linker-VL)	QVQLQESGPGLVKPSQTLSLTCAISGDSVLSNSDTWNWIRQSP SRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSL QLNAVTPEDTGVYYCARDRLQDGNSWSDAFDVWGQGTMVT VSSGGGGSGGGGSGSGGSQSALTQPASVSGSPGQSITISCTGTS SDVGGYNYVSWYQQHPGKAPKLMIYEVSNRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYYCSSYTSSSTLYVFGTGTKVTV L
CD22-62		

1362	HC CDR1 (Kabat)	SNSDTWN
1363	HC CDR2 (Kabat)	RTYHRSTWYDDYASSVRG
1364	HC CDR3 (Kabat)	DRLQDGNSWSDAFDV
1365	HC CDR1 (Chothia)	GDSVLSNSD
1366	HC CDR2 (Chothia)	YHRSTWY
1367	HC CDR3 (Chothia)	DRLQDGNSWSDAFDV
1368	HC CDR1 (IMGT)	GDSVLSNSDT
1369	HC CDR2 (IMGT)	TYHRSTWYD
1370	HC CDR3 (IMGT)	ARDRLQDGNSWSDAFDV
1371	HC CDR1 (Combined)	GDSVLSNSDTWN
1372	HC CDR2 (Combined)	RTYHRSTWYDDYASSVRG
1373	HC CDR3 (Combined)	DRLQDGNSWSDAFDV
1374	VH	EVQLQQSGPGLVKPSQTLSLTCAISGDSVLSNSDTWNWIRQSP SRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSL QLNAVTPEDTGVYYCARDRLQDGNSWSDAFDVWGQGTMVT VSS
1375	LC CDR1 (Kabat)	TGTSSDVGGYNYVS
1376	LC CDR2 (Kabat)	DVSNRPS
1377	LC CDR3 (Kabat)	SSYTSSSTLYV
1378	LC CDR1 (Chothia)	TSSDVGGYNY
1379	LC CDR2 (Chothia)	DVS
1380	LC CDR3 (Chothia)	YTSSSTLY
1381	LC CDR1 (IMGT)	SSDVGGYNY
1382	LC CDR2 (IMGT)	DVS
1383	LC CDR3 (IMGT)	SSYTSSSTLYV
1384	LC CDR1 (Combined)	TGTSSDVGGYNYVS
1385	LC CDR2 (Combined)	DVSNRPS

1386	LC CDR3 (Combined)	SSYTSSSTLYV
1387	VL	QSALTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPG KAPKLMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDEA DYYCSSYTSSSTLYVFGTGTKVTVL
1388	scFv (VH-linker-VL)	EVQLQQSGPGLVKPSQTLSLTCAISGDSVLSNSDTWNWIRQSP SRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSL QLNAVTPEDTGVYYCARDRLQDGNSWSDAFDVWGQGTMVT VSSGGGGSGGGGSGGGGSQSALTQPASVSGSPGQSITISCTGTS SDVGGYNYVSWYQQHPGKAPKLMIYDVSNRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYYCSSYTSSSTLYVFGTGTKVTV L
CD22-63		
1389	HC CDR1 (Kabat)	SNSDTWN
1390	HC CDR2 (Kabat)	RTYHRSTWYDDYASSVRG
1391	HC CDR3 (Kabat)	DRLQDGNSWSDAFDV
1392	HC CDR1 (Chothia)	GDSVLSNSD
1393	HC CDR2 (Chothia)	YHRSTWY
1394	HC CDR3 (Chothia)	DRLQDGNSWSDAFDV
1395	HC CDR1 (IMGT)	GDSVLSNSDT
1396	HC CDR2 (IMGT)	TYHRSTWYD
1397	HC CDR3 (IMGT)	ARDRLQDGNSWSDAFDV
1398	HC CDR1 (Combined)	GDSVLSNSDTWN
1399	HC CDR2 (Combined)	RTYHRSTWYDDYASSVRG
1400	HC CDR3 (Combined)	DRLQDGNSWSDAFDV
1401	VH	EVQLQQSGPGLVKPSQTLSLTCAISGDSVLSNSDTWNWIRQSP SRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSL QLNAVTPEDTGVYYCARDRLQDGNSWSDAFDVWGQGTMVT VSS
1402	LC CDR1 (Kabat)	TGTSSDVGGYNYVS
1403	LC CDR2 (Kabat)	EVSNRPS
1404	LC CDR3 (Kabat)	SSYTSSSTLYI
1405	LC CDR1 (Chothia)	TSSDVGGYNY

1406	LC CDR2 (Chothia)	EVS
1407	LC CDR3 (Chothia)	YTSSSTLY
1408	LC CDR1 (IMGT)	SSDVGGYNY
1409	LC CDR2 (IMGT)	EVS
1410	LC CDR3 (IMGT)	SSYTSSSTLYI
1411	LC CDR1 (Combined)	TGTSSDVGGYNYVS
1412	LC CDR2 (Combined)	EVSNRPS
1413	LC CDR3 (Combined)	SSYTSSSTLYI
1414	VL	QSALTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPG KAPKLMIYEVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDEA DYYCSSYTSSSTLYIFGTGTKVTVL
1415	scFv (VH-linker-VL)	EVQLQQSGPGLVKPSQTLSLTCAISGDSVLSNSDTWNWIRQSP SRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSL QLNAVTPEDTGVYYCARDRLQDGNSWSDAFDVWGQGTMVT VSSGGGGSGGGGSGGGGSQSALTQPASVSGSPGQSITISCTGTS SDVGGYNYVSWYQQHPGKAPKLMIYEVSNRPSGVSNRFSGS KSGNTASLTISGLQAEDEADYYCSSYTSSSTLYIFGTGTKVTVL

CARs that bind to EGFR are known in the art. For example, those disclosed in WO2014/130657, incorporated by reference herein. Any known EGFR CAR, for example, the EGFR antigen binding domain of any known EGFR CAR, in the art can be used in accordance with the present disclosure. Exemplary EGFRvIII CARs can include a CDR, a variable region, an scFv, or a full-length CAR sequence disclosed in WO2014/130657, for example, Table 2 of WO2014/130657, incorporated herein by reference.

CARs that bind to CD123 are known in the art. For example, those disclosed in WO2014/130635 or WO2016/028896. Any known CD123 CAR, for example, the CD123 antigen binding domain of any known CD123 CAR, in the art can be used in accordance with the present disclosure. For example, CAR1 to CAR8 disclosed in WO2014/130635; or CAR123-1 to CAR123-4 and hzCAR123-1 to hzCAR123-32, disclosed in WO2016/028896. The amino acid and nucleotide sequences encoding the CD123 CAR molecules and antigen binding domains (for example, including one, two, three VH CDRs; and one, two, three VL CDRs according to Kabat or Chothia), are specified in WO 2014/130635 and WO2016/028896.

CARs that bind to CLL-1 are known in the art. For example, those disclosed in US2016/0051651A1, incorporated herein by reference. Any known CLL-1 CAR, for example, the CLL-1 antigen binding domain of any known CLL-1 CAR, in the art can be used in accordance with the present disclosure.

In some embodiments, the CAR comprises a CLL-1 CAR or antigen binding domain according to Table 2 of WO2016/014535, incorporated herein by reference. The amino acid and nucleotide sequences encoding the CLL-1 CAR molecules and antigen binding domains (for example, including one, two, three VH CDRs; and one, two, three VL CDRs according to Kabat or Chothia), are specified in WO2016/014535.

CARs that bind to CD33 are known in the art. For example, those disclosed in US2016/0096892A1 and WO2016/014576, incorporated by reference herein. Any known CD33 CAR, for example, the CD33 antigen binding domain of any known CD33 CAR, in the art can be used in accordance with the present disclosure. For example, CAR33-1 to CAR33-9 disclosed in WO2016/014576.

In some embodiments, the CAR comprises a CD33 CAR or antigen binding domain according to Table 2 or 9 of WO2016/014576, incorporated herein by reference. The amino acid and nucleotide sequences encoding the CD33 CAR molecules and antigen binding domains (for example, including one, two, three VH CDRs; and one, two, three VL CDRs according to Kabat or Chothia), are specified in WO2016/014576.

CARs that bind to mesothelin are known in the art. For example, those disclosed in WO2015090230 and WO2017112741, for example, Tables 2, 3, 4, and 5 of WO2017112741, incorporated herein by reference, that bind human mesothelin. Any known mesothelin CAR, for example, the mesothelin antigen binding domain of any known mesothelin CAR, in the art can be used in accordance with the present disclosure.

CARs that bind to GFR ALPHA-4 are known in the art. For example, those disclosed in WO2016/025880. Any known GFR ALPHA-4 CAR, for example, the GFR ALPHA-4 antigen binding domain of any known GFR ALPHA-4 CAR, in the art can be used in accordance with the present disclosure. The amino acid and nucleotide sequences encoding the GFR ALPHA-4 CAR molecules and antigen binding domains (for example, including one, two, three VH CDRs; and one, two, three VL CDRs according to Kabat or Chothia), are specified in WO2016/025880.

Antigen Binding Domain Structures

In some embodiments, the antigen binding domain of the encoded CAR molecule comprises an antibody, an antibody fragment, an scFv, a Fv, a Fab, a (Fab')2, a single domain antibody (SDAB), a VH or VL domain, a camelid VHH domain or a bi-functional (e.g. bi-specific) hybrid antibody (e.g., Lanzavecchia et al., Eur. J. Immunol. 17, 105 (1987)). In some instances, scFvs can be prepared according to method known in the art (see, for example, Bird et al., (1988) Science 242:423-426 and Huston et al., (1988) Proc. Natl. Acad. Sci. USA 85:5879-5883). ScFv molecules can be produced by linking VH and VL regions together using flexible polypeptide linkers. The scFv molecules comprise a linker (e.g., a Ser-Gly linker) with an optimized length and/or amino acid composition. The linker length can greatly affect how the variable regions of a scFv fold and interact. In fact, if a short polypeptide linker is employed (e.g., between 5-10 amino acids) intrachain folding is prevented. Interchain folding is also required to bring the two variable regions together to form a functional epitope binding site. For examples of linker orientation and size see, e.g., Hollinger et al. 1993 Proc Natl Acad. Sci. U.S.A. 90:6444-6448, U.S. Patent Application Publication Nos. 2005/0100543, 2005/0175606, 2007/0014794, and PCT publication Nos. WO2006/020258 and WO2007/024715, is incorporated herein by reference.

An scFv can comprise a linker of at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30, 35, 40, 45, 50, or more amino acid residues between its VL and VH regions. The linker sequence may comprise any naturally occurring amino acid. In some embodiments, the linker sequence comprises amino acids glycine and serine. In another embodiment, the linker sequence comprises sets of glycine and serine repeats such as (Gly4Ser)n, where n is a positive integer equal to or greater than 1 (SEQ ID NO:22). In some embodiments, the linker can be (Gly4Ser)4 (SEQ ID NO:29) or (Gly4Ser)3(SEQ ID NO:30). Variation in the linker length may retain or enhance activity, giving rise to superior efficacy in activity studies.

In another aspect, the antigen binding domain is a T cell receptor ("TCR"), or a fragment thereof, for example, a single chain TCR (scTCR). Methods to make such TCRs are known in the art. See, e.g., Willemsen RA et al, Gene Therapy 7: 1369–1377 (2000); Zhang T et al, Cancer Gene Ther 11: 487–496 (2004); Aggen et al, Gene Ther. 19(4):365-74 (2012) (references are incorporated herein by its entirety). For example, scTCR can be engineered that contains the

Vα and Vβ genes from a T cell clone linked by a linker (e.g., a flexible peptide). This approach is very useful to cancer associated target that itself is intracellular, however, a fragment of such antigen (peptide) is presented on the surface of the cancer cells by MHC.
In certain embodiments, the encoded antigen binding domain has a binding affinity KD of 10^{-4} M to 10^{-8} M.

In some embodiments, the encoded CAR molecule comprises an antigen binding domain that has a binding affinity KD of 10^{-4} M to 10^{-8} M, e.g., 10^{-5} M to 10^{-7} M, e.g., 10^{-6} M or 10^{-7} M, for the target antigen. In some embodiments, the antigen binding domain has a binding affinity that is at least five-fold, 10-fold, 20-fold, 30-fold, 50-fold, 100-fold or 1,000-fold less than a reference antibody, e.g., an antibody described herein. In some embodiments, the encoded antigen binding domain has a binding affinity at least 5-fold less than a reference antibody (e.g., an antibody from which the antigen binding domain is derived). In some aspects such antibody fragments are functional in that they provide a biological response that can include, but is not limited to, activation of an immune response, inhibition of signal-transduction origination from its target antigen, inhibition of kinase activity, and the like, as will be understood by a skilled artisan.

In some aspects, the antigen binding domain of the CAR is a scFv antibody fragment that is humanized compared to the murine sequence of the scFv from which it is derived.
In some aspects, the antigen binding domain of a CAR described herein (e.g., a scFv) is encoded by a nucleic acid molecule whose sequence has been codon optimized for expression in a mammalian cell. In some aspects, entire CAR construct of the invention is encoded by a nucleic acid molecule whose entire sequence has been codon optimized for expression in a mammalian cell. Codon optimization refers to the discovery that the frequency of occurrence of synonymous codons (i.e., codons that code for the same amino acid) in coding DNA is biased in different species. Such codon degeneracy allows an identical polypeptide to be encoded by a variety of nucleotide sequences. A variety of codon optimization methods is known in the art, and include, e.g., methods disclosed in at least US Patent Numbers 5,786,464 and 6,114,148.

Specific antigen antibody pairs are known in the art. Non-limiting exemplary embodiments of antigen antibody pairs and components thereof are provided herein above in the section titled Targets and below.

CD19

In some embodiments, the antigen binding domain binds to CD19 and has the same or a similar binding specificity as the FMC63 scFv fragment described in Nicholson et al. Mol. Immun. 34 (16-17): 1157-1165 (1997). In some embodiments, the antigen binding domain binds to CD19 and includes the scFv fragment described in Nicholson et al. *Mol. Immun.* 34 (16-17): 1157-1165 (1997).

In some embodiments, the antigen binding domain (for example, a humanized antigen binding domain) binds to CD19 and comprises a sequence from Table 3 of WO2014/153270, incorporated herein by reference. WO2014/153270 also describes methods of assaying the binding and efficacy of various CAR constructs.

Humanization of murine CD19 antibody is desired for the clinical setting, where the mouse-specific residues may induce a human-anti-mouse antigen (HAMA) response in patients who receive CART19 treatment, i.e., treatment with T cells transduced with the CAR19 construct. The production, characterization, and efficacy of humanized CD19 CAR sequences is described in International Application WO2014/153270 which is herein incorporated by reference in its entirety, including Examples 1-5 (p. 115-159).

In some embodiments, the antigen binding domain comprises the parental murine scFv sequence of the CAR19 construct provided in WO2012/079000 (incorporated herein by reference). In some embodiments, the antigen binding domain binds CD19 and comprises a scFv described in WO2012/079000.

BCMA

Exemplary antigen binding domains that bind BCMA are disclosed in WO2012/0163805, WO 2017/021450, WO 2017/011804, WO 2017/025038, WO 2016/090327, WO 2016/130598, WO 2016/210293, WO 2016/090320, WO 2016/014789, WO 2016/094304, WO 2016/154055, WO 2015/166073, WO 2015/188119, WO 2015/158671, US 9,243,058, US 8,920,776, US 9,273,141, US 7,083,785, US 9,034,324, US 2007/0049735, US 2015/0284467, US 2015/0051266, US 2015/0344844, US 2016/0131655, US 2016/0297884, US 2016/0297885, US 2017/0051308, US 2017/0051252, US 2017/0051252, WO 2016/020332, WO 2016/087531, WO 2016/079177, WO 2015/172800, WO 2017/008169, US 9,340,621, US 2013/0273055, US 2016/0176973, US 2015/0368351, US 2017/0051068, US 2016/0368988, and US 2015/0232557,

herein incorporated by reference in their entirety. In some embodiments, the antigen binding domain of one or more of the BCMA antigen binding domains disclosed therein.

In some embodiments, the antigen binding domain comprises a human antibody or a human antibody fragment that binds BCMA. In some embodiments, the antigen binding domain comprises one or more (for example, all three) LC CDR1, LC CDR2, and LC CDR3 of a human anti-BCMA binding domain described herein (for example, in Tables 2-14), and/or one or more (for example, all three) HC CDR1, HC CDR2, and HC CDR3 of a human anti-BCMA binding domain described herein (for example, in Tables 2-14). In some embodiments, the human anti-BCMA binding domain comprises a human VL described herein (for example, in Tables 2, 6, and 10) and/or a human VH described herein (for example, in Tables 2, 6, and 10). In some embodiments, the anitgen binding domain is a scFv comprising a VL and a VH of an amino acid sequence of Tables 2, 6, and 10. In some embodiments, the antigen binding domain (for example, an scFv) comprises: a VL comprising an amino acid sequence having at least one, two or three modifications (for example, substitutions, for example, conservative substitutions) but not more than 30, 20 or 10 modifications (for example, substitutions, for example, conservative substitutions) of an amino acid sequence provided in Tables 2, 6, and 10, or a sequence with 95-99% identity with an amino acid sequence of Tables 2, 6, and 10; and/or a VH comprising an amino acid sequence having at least one, two or three modifications (for example, substitutions, for example, conservative substitutions) but not more than 30, 20 or 10 modifications (for example, substitutions, for example, conservative substitutions) of an amino acid sequence provided in Tables 2, 6, and 10, or a sequence with 95-99% identity to an amino acid sequence of Tables 2, 6, and 10.

In certain embodiments, the antigen binding domain described herein includes:
(1) one, two, or three light chain (LC) CDRs chosen from:

(i) a LC CDR1 of SEQ ID NO: 54, LC CDR2 of SEQ ID NO: 55 and LC CDR3 of SEQ ID NO: 56; and/or

(2) one, two, or three heavy chain (HC) CDRs from one of the following:
(i) a HC CDR1 of SEQ ID NO: 44, HC CDR2 of SEQ ID NO: 45 and HC CDR3 of SEQ ID NO: 84; (ii) a HC CDR1 of SEQ ID NO: 44, HC CDR2 of SEQ ID NO: 45 and HC CDR3 of SEQ ID NO: 46; (iii) a HC CDR1 of SEQ ID NO: 44, HC CDR2 of SEQ ID NO: 45 and HC CDR3 of

SEQ ID NO: 68; or (iv) a HC CDR1 of SEQ ID NO: 44, HC CDR2 of SEQ ID NO: 45 and HC CDR3 of SEQ ID NO: 76.

In certain embodiments, the antigen binding domain described herein includes:

(1) one, two, or three light chain (LC) CDRs from one of the following:

(i) a LC CDR1 of SEQ ID NO: 95, LC CDR2 of SEQ ID NO: 131 and LC CDR3 of SEQ ID NO: 132; (ii) a LC CDR1 of SEQ ID NO: 95, LC CDR2 of SEQ ID NO: 96 and LC CDR3 of SEQ ID NO: 97; (iii) a LC CDR1 of SEQ ID NO: 95, LC CDR2 of SEQ ID NO: 114 and LC CDR3 of SEQ ID NO: 115; or (iv) a LC CDR1 of SEQ ID NO: 95, LC CDR2 of SEQ ID NO: 114 and LC CDR3 of SEQ ID NO: 97; and/or

(2) one, two, or three heavy chain (HC) CDRs from one of the following:

(i) a HC CDR1 of SEQ ID NO: 86, HC CDR2 of SEQ ID NO: 130 and HC CDR3 of SEQ ID NO: 88; (ii) a HC CDR1 of SEQ ID NO: 86, HC CDR2 of SEQ ID NO: 87 and HC CDR3 of SEQ ID NO: 88; or (iii) a HC CDR1 of SEQ ID NO: 86, HC CDR2 of SEQ ID NO: 109 and HC CDR3 of SEQ ID NO: 88.

In certain embodiments, the antigen binding domain described herein includes:

(1) one, two, or three light chain (LC) CDRs from one of the following:

(i) a LC CDR1 of SEQ ID NO: 147, LC CDR2 of SEQ ID NO: 182 and LC CDR3 of SEQ ID NO: 183; (ii) a LC CDR1 of SEQ ID NO: 147, LC CDR2 of SEQ ID NO: 148 and LC CDR3 of SEQ ID NO: 149; or (iii) a LC CDR1 of SEQ ID NO: 147, LC CDR2 of SEQ ID NO: 170 and LC CDR3 of SEQ ID NO: 171; and/or

(2) one, two, or three heavy chain (HC) CDRs from one of the following:

(i) a HC CDR1 of SEQ ID NO: 179, HC CDR2 of SEQ ID NO: 180 and HC CDR3 of SEQ ID NO: 181; (ii) a HC CDR1 of SEQ ID NO: 137, HC CDR2 of SEQ ID NO: 138 and HC CDR3 of SEQ ID NO: 139; or (iii) a HC CDR1 of SEQ ID NO: 160, HC CDR2 of SEQ ID NO: 161 and HC CDR3 of SEQ ID NO: 162.

In some embodiments, the HC CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR2, and LC CDR3 comprise the amino acid sequences of SEQ ID NOs: 44, 45, 84, 54, 55, and 56, respectively. In some embodiments, the HC CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR2, and LC CDR3 comprise the amino acid sequences of SEQ ID NOs: 44, 45, 46, 54, 55, and 56, respectively. In some embodiments, the HC CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR2, and LC CDR3 comprise the amino acid sequences of SEQ ID NOs: 44, 45, 68, 54,

55, and 56, respectively. In some embodiments, the HC CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR2, and LC CDR3 comprise the amino acid sequences of SEQ ID NOs: 44, 45, 76, 54, 55, and 56, respectively.

In some embodiments, the HC CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR2, and LC CDR3 comprise the amino acid sequences of SEQ ID NOs: 47, 48, 84, 57, 58, and 59, respectively. In some embodiments, the HC CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR2, and LC CDR3 comprise the amino acid sequences of SEQ ID NOs: 47, 48, 46, 57, 58, and 59, respectively. In some embodiments, the HC CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR2, and LC CDR3 comprise the amino acid sequences of SEQ ID NOs: 47, 48, 68, 57, 58, and 59, respectively. In some embodiments, the HC CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR2, and LC CDR3 comprise the amino acid sequences of SEQ ID NOs: 47, 48, 76, 57, 58, and 59, respectively.

In some embodiments, the HC CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR2, and LC CDR3 comprise the amino acid sequences of SEQ ID NOs: 49, 50, 85, 60, 58, and 56, respectively. In some embodiments, the HC CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR2, and LC CDR3 comprise the amino acid sequences of SEQ ID NOs: 49, 50, 51, 60, 58, and 56, respectively. In some embodiments, the HC CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR2, and LC CDR3 comprise the amino acid sequences of SEQ ID NOs: 49, 50, 69, 60, 58, and 56, respectively. In some embodiments, the HC CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR2, and LC CDR3 comprise the amino acid sequences of SEQ ID NOs: 49, 50, 77, 60, 58, and 56, respectively.

Other Exemplary Targets

Exemplary antigen binding domains that bind CD20 are described in WO2016/164731 and WO2018/067992, incorporated herein by reference. In some embodiments, the antigen binding domain of one or more of the CD20 antigen binding domains disclosed therein. Exemplary antigen binding domains that bind CD22 are described in WO2016/164731 and WO2018/067992, incorporated herein by reference.

In some embodiments, the antigen binding domain comprises a HC CDR1, a HC CDR2, and a HC CDR3 of any heavy chain binding domain amino acid sequences listed in **Table 15**. In embodiments, the antigen binding domain further comprises a LC CDR1, a LC CDR2, and a LC

CDR3. In embodiments, the antigen binding domain comprises a LC CDR1, a LC CDR2, and a LC CDR3 amino acid sequences listed in **Table 16.**

In some embodiments, the antigen binding domain comprises one, two or all of LC CDR1, LC CDR2, and LC CDR3 of any light chain binding domain amino acid sequences listed in **Table 16**, and one, two or all of HC CDR1, HC CDR2, and HC CDR3 of any heavy chain binding domain amino acid sequences listed in **Table 15**.

Exemplary antigen binding domains that bind EGFRvIII are described in in WO2014/130657.

Exemplary antigen binding domains that bind CD123 are described in WO 2014/130635 and WO2016/028896, incorporated herein by reference.

In some embodiments, the antigen binding domain comprises a sequence from Tables 1-2 of WO2014/130635, incorporated herein by reference.

In some embodiments, the antigen binding domain comprises a sequence from Tables 2, 6, and 9 of WO2016/028896, incorporated herein by reference.

Exemplary antigen binding domains that bind CLL-1 are disclosed in WO2016/014535, incorporated herein by reference.

In some embodiments, the antigen binding domain comprises one, two three (for example, all three) heavy chain CDRs, HC CDR1, HC CDR2 and HC CDR3, from an antibody described herein (for example, an antibody described in WO2015/142675, US-2015-0283178-A1, US-2016-0046724-A1, US2014/0322212A1, US2016/0068601A1, US2016/0051651A1, US2016/0096892A1, US2014/0322275A1, or WO2015/090230, incorporated herein by reference), and/or one, two, three (for example, all three) light chain CDRs, LC CDR1, LC CDR2 and LC CDR3, from an antibody described herein (for example, an antibody described in WO2015/142675, US-2015-0283178-A1, US-2016-0046724-A1, US2014/0322212A1, US2016/0068601A1, US2016/0051651A1, US2016/0096892A1, US2014/0322275A1, or WO2015/090230, incorporated herein by reference). In some embodiments, the antigen binding domain comprises a heavy chain variable region and/or a variable light chain region of an antibody listed above.

In embodiments, the antigen binding domain is an antigen binding domain described in WO2015/142675, US-2015-0283178-A1, US-2016-0046724-A1, US2014/0322212A1,

US2016/0068601A1, US2016/0051651A1, US2016/0096892A1, US2014/0322275A1, or WO2015/090230, incorporated herein by reference.

Exemplary target antigens that can be targeted using the CAR-expressing cells, include, but are not limited to, CD19, CD123, EGFRvIII, CD33, mesothelin, BCMA, and GFR ALPHA-4, among others, as described in, for example, WO2014/153270, WO 2014/130635, WO2016/028896, WO 2014/130657, WO2016/014576, WO 2015/090230, WO2016/014565, WO2016/014535, and WO2016/025880, each of which is herein incorporated by reference in its entirety.

In some embodiments, the antigen binding domain of any of the CARs described herein (for example, any of CD19, CD123, EGFRvIII, CD33, mesothelin, BCMA, and GFR ALPHA-4) comprises one, two three (for example, all three) heavy chain CDRs, HC CDR1, HC CDR2 and HC CDR3, from an antibody listed above, and/or one, two, three (for example, all three) light chain CDRs, LC CDR1, LC CDR2 and LC CDR3, from an antigen binding domain listed above. In some embodiments, the antigen binding domain comprises a heavy chain variable region and/or a variable light chain region of an antibody listed or described above.

In some embodiments, the antigen binding domain comprises one, two three (for example, all three) heavy chain CDRs, HC CDR1, HC CDR2 and HC CDR3, from an antibody listed above, and/or one, two, three (for example, all three) light chain CDRs, LC CDR1, LC CDR2 and LC CDR3, from an antibody listed above. In some embodiments, the antigen binding domain comprises a heavy chain variable region and/or a variable light chain region of an antibody listed or described above.

Bispecific CARs

In certain embodiments, the antigen binding domain is a bi- or multi- specific molecule (e.g., a multispecific antibody molecule). In some embodiments a multispecific antibody molecule is a bispecific antibody molecule. A bispecific antibody has specificity for no more than two antigens. A bispecific antibody molecule is characterized by a first immunoglobulin variable domain sequence which has binding specificity for a first epitope and a second immunoglobulin variable domain sequence that has binding specificity for a second epitope. In some embodiments the first and second epitopes are on the same antigen, e.g., the same protein (or subunit of a multimeric protein). In some embodiments the first and second epitopes overlap.

In some embodiments the first and second epitopes do not overlap. In some embodiments the first and second epitopes are on different antigens, e.g., different proteins (or different subunits of a multimeric protein). In some embodiments a bispecific antibody molecule comprises a heavy chain variable domain sequence and a light chain variable domain sequence which have binding specificity for a first epitope and a heavy chain variable domain sequence and a light chain variable domain sequence which have binding specificity for a second epitope. In some embodiments a bispecific antibody molecule comprises a half antibody having binding specificity for a first epitope and a half antibody having binding specificity for a second epitope. In some embodiments a bispecific antibody molecule comprises a half antibody, or fragment thereof, having binding specificity for a first epitope and a half antibody, or fragment thereof, having binding specificity for a second epitope. In some embodiments a bispecific antibody molecule comprises a scFv, or fragment thereof, have binding specificity for a first epitope and a scFv, or fragment thereof, have binding specificity for a second epitope.

In some embodiments, the antibody molecule is a multi-specific (e.g., a bispecific or a trispecific) antibody molecule. Such molecules include bispecific fusion proteins, e.g., an expression construct containing two scFvs with a hydrophilic helical peptide linker between them and a full constant region, as described in, e.g., US5637481; minibody constructs with linked VL and VH chains further connected with peptide spacers to an antibody hinge region and CH3 region, which can be dimerized to form bispecific/multivalent molecules, as described in, e.g., US5837821; String of VH domains (or VL domains in family members) connected by peptide linkages with crosslinkable groups at the C-terminus further associated with VL domains to form a series of FVs (or scFvs), as described in, e.g., US5864019; and single chain binding polypeptides with both a VH and a VL domain linked through a peptide linker are combined into multivalent structures through non-covalent or chemical crosslinking to form, e.g., homobivalent, heterobivalent, trivalent, and tetravalent structures using both scFV or diabody type format, as described in, e.g., US5869620. The contents of the above-referenced applications are incorporated herein by reference in their entireties.

Within each antibody or antibody fragment (e.g., scFv) of a bispecific antibody molecule, the VH can be upstream or downstream of the VL. In some embodiments, the upstream antibody or antibody fragment (e.g., scFv) is arranged with its VH (VH1) upstream of its VL (VL1) and the downstream antibody or antibody fragment (e.g., scFv) is arranged with its VL (VL2)

upstream of its VH (VH2), such that the overall bispecific antibody molecule has the arrangement VH1-VL1-VL2-VH2. In other embodiments, the upstream antibody or antibody fragment (e.g., scFv) is arranged with its VL (VL1) upstream of its VH (VH1) and the downstream antibody or antibody fragment (e.g., scFv) is arranged with its VH (VH2) upstream of its VL (VL2), such that the overall bispecific antibody molecule has the arrangement VL1-VH1-VH2-VL2. Optionally, a linker is disposed between the two antibodies or antibody fragments (e.g., scFvs), e.g., between VL1 and VL2 if the construct is arranged as VH1-VL1-VL2-VH2, or between VH1 and VH2 if the construct is arranged as VL1-VH1-VH2-VL2. The linker may be a linker as described herein, e.g., a (Gly4-Ser)n linker, wherein n is 1, 2, 3, 4, 5, or 6, preferably 4 (SEQ ID NO: 691). In general, the linker between the two scFvs should be long enough to avoid mispairing between the domains of the two scFvs. Optionally, a linker is disposed between the VL and VH of the first scFv. Optionally, a linker is disposed between the VL and VH of the second scFv. In constructs that have multiple linkers, any two or more of the linkers can be the same or different. Accordingly, in some embodiments, a bispecific CAR comprises VLs, VHs, and optionally one or more linkers in an arrangement as described herein.

Transmembrane domains

With respect to the transmembrane domain, in various embodiments, a chimeric molecule as described herein (e.g., a CAR) can be designed to comprise a transmembrane domain that is attached to the extracellular domain of the chimeric molecule. A transmembrane domain can include one or more additional amino acids adjacent to the transmembrane region, e.g., one or more amino acid associated with the extracellular region of the protein from which the transmembrane was derived (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 up to 15 amino acids of the extracellular region) and/or one or more additional amino acids associated with the intracellular region of the protein from which the transmembrane protein is derived (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 up to 15 amino acids of the intracellular region). In some aspects, the transmembrane domain is one that is associated with one of the other domains of the chimeric protein (e.g., CAR) e.g., in some embodiments, the transmembrane domain may be from the same protein that the signaling domain, costimulatory domain or the hinge domain is derived from. In another aspect, the transmembrane domain is not derived from the same protein that any other domain of the chimeric protein (e.g., CAR) is derived from. In some instances, the transmembrane domain

can be selected or modified by amino acid substitution to avoid binding of such domains to the transmembrane domains of the same or different surface membrane proteins, e.g., to minimize interactions with other members of the receptor complex. In some aspects, the transmembrane domain is capable of homodimerization with another CAR on the cell surface of a CAR-expressing cell. In a different aspect, the amino acid sequence of the transmembrane domain may be modified or substituted so as to minimize interactions with the binding domains of the native binding partner present in the same CAR-expressing cell.

The transmembrane domain may be derived either from a natural or from a recombinant source. Where the source is natural, the domain may be derived from any membrane-bound or transmembrane protein. In some aspects the transmembrane domain is capable of signaling to the intracellular domain(s) whenever the CAR has bound to a target. A transmembrane domain of particular use in this invention may include at least the transmembrane region(s) of e.g., the alpha, beta or zeta chain of the T-cell receptor, CD28, CD27, CD3 epsilon, CD45, CD4, CD5, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, CD154. In some embodiments, a transmembrane domain may include at least the transmembrane region(s) of, e.g., KIRDS2, OX40, CD2, CD27, LFA-1 (CD11a, CD18), ICOS (CD278), 4-1BB (CD137), GITR, CD40, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD160, CD19, IL2R beta, IL2R gamma, IL7R α, ITGA1, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, TNFR2, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, PAG/Cbp, NKG2D, or NKG2C.

In some instances, the transmembrane domain can be attached to the extracellular region of the CAR, e.g., the antigen binding domain of the CAR, via a hinge, e.g., a hinge from a human protein. For example, in some embodiments, the hinge can be a human Ig (immunoglobulin) hinge (e.g., an IgG4 hinge, an IgD hinge), a GS linker (e.g., a GS linker described herein), a KIR2DS2 hinge or a CD8a hinge. In some embodiments, the hinge or spacer comprises (e.g., consists of) the amino acid sequence of SEQ ID NO:4. In some aspects, the transmembrane domain comprises (e.g., consists of) a transmembrane domain of SEQ ID NO: 12.

In some embodiments, the encoded transmembrane domain comprises an amino acid sequence of a CD8 transmembrane domain having at least one, two or three modifications but not more than 20, 10 or 5 modifications of an amino acid sequence of SEQ ID NO: 12, or a sequence with 95-99% identity to an amino acid sequence of SEQ ID NO: 12. In some embodiments, the encoded transmembrane domain comprises the sequence of SEQ ID NO: 12.

In other embodiments, the nucleic acid molecule encoding the CAR comprises a nucleotide sequence of a CD8 transmembrane domain, e.g., comprising the sequence of SEQ ID NO: 13, or a sequence with 95-99% identity thereof.

In some embodiments, the encoded antigen binding domain is connected to the transmembrane domain by a hinge region. In some embodiments, the encoded hinge region comprises the amino acid sequence of a CD8 hinge, e.g., SEQ ID NO: 4; or the amino acid sequence of an IgG4 hinge, e.g., SEQ ID NO: 6, or a sequence with 95-99% identity to SEQ ID NO:4 or 6. In other embodiments, the nucleic acid sequence encoding the hinge region comprises a sequence of SEQ ID NO: 5 or SEQ ID NO: 7, corresponding to a CD8 hinge or an IgG4 hinge, respectively, or a sequence with 95-99% identity to SEQ ID NO:5 or 7.

In some aspects, the hinge or spacer comprises an IgG4 hinge. For example, in some embodiments, the hinge or spacer comprises a hinge of the amino acid sequence ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWY VDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTIS KAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGKM (SEQ ID NO:6). In some embodiments, the hinge or spacer comprises a hinge encoded by a nucleotide sequence of GAGAGCAAGTACGGCCCTCCCTGCCCCCCTTGCCCTGCCCCCGAGTTCCTGGGCGGA CCCAGCGTGTTCCTGTTCCCCCCCAAGCCCAAGGACACCCTGATGATCAGCCGGACC CCCGAGGTGACCTGTGTGGTGGTGGACGTGTCCCAGGAGGACCCCGAGGTCCAGTT CAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCAAGCCCCGGGAG GAGCAGTTCAATAGCACCTACCGGGTGGTGTCCGTGCTGACCGTGCTGCACCAGGA CTGGCTGAACGGCAAGGAATACAAGTGTAAGGTGTCCAACAAGGGCCTGCCCAGCA GCATCGAGAAAACCATCAGCAAGGCCAAGGGCCAGCCTCGGGAGCCCCAGGTGTAC ACCCTGCCCCCTAGCCAAGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCT

GGTGAAGGGCTTCTACCCCAGCGACATCGCCGTGGAGTGGGAGAGCAACGGCCAGC
CCGAGAACAACTACAAGACCACCCCCCCTGTGCTGGACAGCGACGGCAGCTTCTTC
CTGTACAGCCGGCTGACCGTGGACAAGAGCCGGTGGCAGGAGGGCAACGTCTTTAG
CTGCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCAGAAGAGCCTGAGCC
TGTCCCTGGGCAAGATG (SEQ ID NO:7).

In some aspects, the hinge or spacer comprises an IgD hinge. For example, in some embodiments, the hinge or spacer comprises a hinge of the amino acid sequence RWPESPKAQASSVPTAQPQAEGSLAKATTAPATTRNTGRGGEEKKKEKEKEEQEERETK TPECPSHTQPLGVYLLTPAVQDLWLRDKATFTCFVVGSDLKDAHLTWEVAGKVPTGGV EEGLLERHSNGSQSQHSRLTLPRSLWNAGTSVTCTLNHPSLPPQRLMALREPAAQAPVK LSLNLLASSDPPEAASWLLCEVSGFSPPNILLMWLEDQREVNTSGFAPARPPPQPGSTTF WAWSVLRVPAPPSPQPATYTCVVSHEDSRTLLNASRSLEVSYVTDH (SEQ ID NO:8). In some embodiments, the hinge or spacer comprises a hinge encoded by a nucleotide sequence of AGGTGGCCCGAAAGTCCCAAGGCCCAGGCATCTAGTGTTCCTACTGCACAGCCCCA GGCAGAAGGCAGCCTAGCCAAAGCTACTACTGCACCTGCCACTACGCGCAATACTG GCCGTGGCGGGGAGGAGAAGAAAAAGGAGAAAGAGAAAGAAGAACAGGAAGAGA GGGAGACCAAGACCCCTGAATGTCCATCCCATACCCAGCCGCTGGGCGTCTATCTCT TGACTCCCGCAGTACAGGACTTGTGGCTTAGAGATAAGGCCACCTTTACATGTTTCG TCGTGGGCTCTGACCTGAAGGATGCCCATTTGACTTGGGAGGTTGCCGGAAAGGTAC CCACAGGGGGGGTTGAGGAAGGGTTGCTGGAGCGCCATTCCAATGGCTCTCAGAGC CAGCACTCAAGACTCACCCTTCCGAGATCCCTGTGGAACGCCGGGACCTCTGTCACA TGTACTCTAAATCATCCTAGCCTGCCCCCACAGCGTCTGATGGCCCTTAGAGAGCCA GCCGCCCAGGCACCAGTTAAGCTTAGCCTGAATCTGCTCGCCAGTAGTGATCCCCCA GAGGCCGCCAGCTGGCTCTTATGCGAAGTGTCCGGCTTTAGCCCGCCCAACATCTTG CTCATGTGGCTGGAGGACCAGCGAGAAGTGAACACCAGCGGCTTCGCTCCAGCCCG GCCCCCACCCCAGCCGGGTTCTACCACATTCTGGGCCTGGAGTGTCTTAAGGGTCCC AGCACCACCTAGCCCCCAGCCAGCCACATACACCTGTGTTGTGTCCCATGAAGATAG CAGGACCCTGCTAAATGCTTCTAGGAGTCTGGAGGTTTCCTACGTGACTGACCATT (SEQ ID NO:9).

In some aspects, the transmembrane domain may be recombinant, in which case it will comprise predominantly hydrophobic residues such as leucine and valine. In some aspects a

triplet of phenylalanine, tryptophan and valine can be found at each end of a recombinant transmembrane domain.

Optionally, a short oligo- or polypeptide linker, between 2 and 10 amino acids in length may form the linkage between the transmembrane domain and the cytoplasmic region of the CAR. A glycine-serine doublet provides a particularly suitable linker. For example, in some aspects, the linker comprises the amino acid sequence of GGGGSGGGGS (SEQ ID NO:10). In some embodiments, the linker is encoded by a nucleotide sequence of GGTGGCGGAGGTTCTGGAGGTGGAGGTTCC (SEQ ID NO:11). In some embodiments, the linker comprises the amino acid sequence of GGGGS (SEQ ID NO: 877). In some embodiments the linker is encoded by a nucleotide sequence of SEQ ID NO: 876).

In some aspects, the hinge or spacer comprises a KIR2DS2 hinge.

Signaling domains

In embodiments of the invention having an intracellular signaling domain, such a domain can contain, e.g., one or more of a primary signaling domain and/or a costimulatory signaling domain. In some embodiments, the intracellular signaling domain comprises a sequence encoding a primary signaling domain. In some embodiments, the intracellular signaling domain comprises a costimulatory signaling domain. In some embodiments, the intracellular signaling domain comprises a primary signaling domain and a costimulatory signaling domain.

The intracellular signaling sequences within the cytoplasmic portion of the CAR of the invention may be linked to each other in a random or specified order. Optionally, a short oligo- or polypeptide linker, for example, between 2 and 10 amino acids (e.g., 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids) in length may form the linkage between intracellular signaling sequences. In some embodiments, a glycine-serine doublet can be used as a suitable linker. In some embodiments, a single amino acid, e.g., an alanine, a glycine, can be used as a suitable linker.

In some aspects, the intracellular signaling domain is designed to comprise two or more, e.g., 2, 3, 4, 5, or more, costimulatory signaling domains. In some embodiments, the two or more, e.g., 2, 3, 4, 5, or more, costimulatory signaling domains, are separated by a linker molecule, e.g., a linker molecule described herein. In some embodiments, the intracellular signaling domain comprises two costimulatory signaling domains. In some embodiments, the linker molecule is a glycine residue. In some embodiments, the linker is an alanine residue.

Primary Signaling domains

A primary signaling domain regulates primary activation of the TCR complex either in a stimulatory way, or in an inhibitory way. Primary intracellular signaling domains that act in a stimulatory manner may contain signaling motifs which are known as immunoreceptor tyrosine-based activation motifs or ITAMs. In CARs such domains are used for the same purpose. Examples of ITAM containing primary intracellular signaling domains that are of particular use in the invention include those of CD3 zeta, common FcR gamma (FCER1G), Fc gamma RIIa, FcR beta (Fc Epsilon R1b), CD3 gamma, CD3 delta, CD3 epsilon, CD79a, CD79b, DAP10, and DAP12. In some embodiments, a CAR of the invention comprises an intracellular signaling domain, e.g., a primary signaling domain of CD3-zeta.

In some embodiments, the encoded primary signaling domain comprises a functional signaling domain of CD3 zeta. The encoded CD3 zeta primary signaling domain can comprise an amino acid sequence having at least one, two or three modifications but not more than 20, 10 or 5 modifications of an amino acid sequence of SEQ ID NO: 18 or SEQ ID NO: 20, or a sequence with 95-99% identity to an amino acid sequence of SEQ ID NO:18 or SEQ ID NO: 20. In some embodiments, the encoded primary signaling domain comprises a sequence of SEQ ID NO:18 or SEQ ID NO: 20. In other embodiments, the nucleic acid sequence encoding the primary signaling domain comprises a sequence of SEQ ID NO:19 or SEQ ID NO: 21, or a sequence with 95-99% identity thereof.

Costimulatory Signaling Domains

In some embodiments, the encoded intracellular signaling domain comprises a costimulatory signaling domain. For example, the intracellular signaling domain can comprise a primary signaling domain and a costimulatory signaling domain. In some embodiments, the encoded costimulatory signaling domain comprises a functional signaling domain of a protein chosen from one or more of CD27, CD28, 4-1BB (CD137), OX40, CD30, CD40, PD-1, ICOS, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, B7-H3, a ligand that specifically binds with CD83, CDS, ICAM-1, GITR, BAFFR, HVEM (LIGHTR), SLAMF7, NKp80 (KLRF1), CD160, CD19, CD4, CD8alpha, CD8beta, IL2R beta, IL2R gamma, IL7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f,

ITGAD, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, NKp44, NKp30, NKp46, and NKG2D.

In some embodiments, the encoded costimulatory signaling domain comprises an amino acid sequence having at least one, two or three modifications but not more than 20, 10 or 5 modifications of an amino acid sequence of SEQ ID NO:14 or SEQ ID NO: 16, or a sequence with 95-99% identity to an amino acid sequence of SEQ ID NO:14 or SEQ ID NO: 16. In some embodiments, the encoded costimulatory signaling domain comprises a sequence of SEQ ID NO: 14 or SEQ ID NO: 16. In other embodiments, the nucleic acid sequence encoding the costimulatory signaling domain comprises a sequence of SEQ ID NO:15 or SEQ ID NO: 17, or a sequence with 95-99% identity thereof.

In other embodiments, the encoded intracellular domain comprises the sequence of SEQ ID NO: 14 or SEQ ID NO: 16, and the sequence of SEQ ID NO: 18 or SEQ ID NO: 20, wherein the sequences comprising the intracellular signaling domain are expressed in the same frame and as a single polypeptide chain.

In some embodiments, the nucleic acid sequence encoding the intracellular signaling domain comprises a sequence of SEQ ID NO:15 or SEQ ID NO: 17, or a sequence with 95-99% identity thereof, and a sequence of SEQ ID NO:19 or SEQ ID NO:21, or a sequence with 95-99% identity thereof.

In some embodiments, the nucleic acid molecule further encodes a leader sequence. In some embodiments, the leader sequence comprises the sequence of SEQ ID NO: 2.
In some aspects, the intracellular signaling domain is designed to comprise the signaling domain of CD3-zeta and the signaling domain of CD28. In some aspects, the intracellular signaling domain is designed to comprise the signaling domain of CD3-zeta and the signaling domain of 4-1BB. In some aspects, the signaling domain of 4-1BB is a signaling domain of SEQ ID NO: 14. In some aspects, the signaling domain of CD3-zeta is a signaling domain of SEQ ID NO: 18.

In some aspects, the intracellular signaling domain is designed to comprise the signaling domain of CD3-zeta and the signaling domain of CD27. In some aspects, the signaling domain

of CD27 comprises an amino acid sequence of QRRKYRSNKGESPVEPAEPCRYSCPREEEGSTIPIQEDYRKPEPACSP (SEQ ID NO:16). In some aspects, the signaling domain of CD27 is encoded by a nucleic acid sequence of AGGAGTAAGAGGAGCAGGCTCCTGCACAGTGACTACATGAACATGACTCCCCGCCG CCCCGGGCCCACCCGCAAGCATTACCAGCCCTATGCCCCACCACGCGACTTCGCAGC CTATCGCTCC (SEQ ID NO:17).

Inhibitory domains

In some embodiments, the vector comprises a nucleic acid sequence that encodes a CAR, e.g., a CAR described herein, and a nucleic acid sequence that encodes an inhibitory molecule comprising: an inhKIR cytoplasmic domain; a transmembrane domain, e.g., a KIR transmembrane domain; and an inhibitor cytoplasmic domain, e.g., an ITIM domain, e.g., an inhKIR ITIM domain. In some embodiments the inhibitory molecule is a naturally occurring inhKIR, or a sequence sharing at least 50, 60, 70, 80, 85, 90, 95, or 99% homology with, or that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, or 20 residues from, a naturally occurring inhKIR.

In some embodiments, the nucleic acid sequence that encodes an inhibitory molecule comprises: a SLAM family cytoplasmic domain; a transmembrane domain, e.g., a SLAM family transmembrane domain; and an inhibitor cytoplasmic domain, e.g., a SLAM family domain, e.g., an SLAM family ITIM domain. In some embodiments the inhibitory molecule is a naturally occurring SLAM family member, or a sequence sharing at least 50, 60, 70, 80, 85, 90, 95, or 99% homology with, or that differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, or 20 residues from, a naturally occurring SLAM family member.

In some embodiments, the vector is an *in vitro* transcribed vector, e.g., a vector that transcribes RNA of a nucleic acid molecule described herein. In some embodiments, the nucleic acid sequence in the vector further comprises a poly(A) tail, e.g., a poly A tail. In some embodiments, the nucleic acid sequence in the vector further comprises a 3'UTR, e.g., a 3' UTR described herein, e.g., comprising at least one repeat of a 3'UTR derived from human beta-globulin. In some embodiments, the nucleic acid sequence in the vector further comprises promoter, e.g., a T2A promoter.

Promoters

In some embodiments, the vector further comprises a promoter. In some embodiments, the promoter is chosen from an EF-1 promoter, a CMV IE gene promoter, an EF-1α promoter, an ubiquitin C promoter, or a phosphoglycerate kinase (PGK) promoter. In some embodiments, the promoter is an EF-1 promoter. In some embodiments, the EF-1 promoter comprises a sequence of SEQ ID NO: 1.

In some aspects of the present invention, immune effector cells, e.g., T cells, can be obtained from a unit of blood collected from a subject using any number of techniques known to the skilled artisan, such as Ficoll™ separation. In some aspects, cells from the circulating blood of an individual are obtained by apheresis. The apheresis product typically contains lymphocytes, including T cells, monocytes, granulocytes, B cells, other nucleated white blood cells, red blood cells, and platelets. In some aspects, the cells collected by apheresis may be washed to remove the plasma fraction and, optionally, to suspend the cells in a buffer or medium for subsequent processing steps. In some embodiments, the cells are washed with phosphate buffered saline (PBS). In an alternative embodiment, the wash solution lacks calcium and may lack magnesium or may lack many if not all divalent cations.

Table 17: Sequences of various components of CAR (aa – amino acids, na – nucleic acids that encodes the corresponding protein)

SEQ ID NO	description	Sequence
1	EF-1 promoter	CGTGAGGCTCCGGTGCCCGTCAGTGGGCAGAGCGCACATCG CCCACAGTCCCCGAGAAGTTGGGGGGAGGGGTCGGCAATTG AACCGGTGCCTAGAGAAGGTGGCGCGGGGTAAACTGGGAAA GTGATGTCGTGTACTGGCTCCGCCTTTTTCCCGAGGGTGGGG GAGAACCGTATATAAGTGCAGTAGTCGCCGTGAACGTTCTTT TTCGCAACGGGTTTGCCGCCAGAACACAGGTAAGTGCCGTGT GTGGTTCCCGCGGGCCTGGCCTCTTTACGGGTTATGGCCCTT GCGTGCCTTGAATTACTTCCACCTGGCTGCAGTACGTGATTC TTGATCCCGAGCTTCGGGTTGGAAGTGGGTGGGAGAGTTCG AGGCCTTGCGCTTAAGGAGCCCCTTCGCCTCGTGCTTGAGTT GAGGCCTGGCCTGGGCGCTGGGGCCGCCGCGTGCGAATCTG GTGGCACCTTCGCGCCTGTCTCGCTGCTTTCGATAAGTCTCTA GCCATTTAAAATTTTTGATGACCTGCTGCGACGCTTTTTTTCT GGCAAGATAGTCTTGTAAATGCGGGCCAAGATCTGCACACT GGTATTTCGGTTTTTGGGGCCGCGGGCGGCGACGGGGCCCGT GCGTCCCAGCGCACATGTTCGGCGAGGCGGGGCCTGCGAGC

		GCGGCCACCGAGAATCGGACGGGGGTAGTCTCAAGCTGGCC GGCCTGCTCTGGTGCCTGGCCTCGCGCCGCCGTGTATCGCCC CGCCCTGGGCGGCAAGGCTGGCCCGGTCGGCACCAGTTGCG TGAGCGGAAAGATGGCCGCTTCCCGGCCCTGCTGCAGGGAG CTCAAAATGGAGGACGCGGCGCTCGGGAGAGCGGGCGGGTG AGTCACCCACACAAAGGAAAAGGGCCTTTCCGTCCTCAGCC GTCGCTTCATGTGACTCCACGGAGTACCGGGCGCCGTCCAGG CACCTCGATTAGTTCTCGAGCTTTTGGAGTACGTCGTCTTTAG GTTGGGGGGAGGGGTTTTATGCGATGGAGTTTCCCCACACTG AGTGGGTGGAGACTGAAGTTAGGCCAGCTTGGCACTTGATG TAATTCTCCTTGGAATTTGCCCTTTTTGAGTTTGGATCTTGGT TCATTCTCAAGCCTCAGACAGTGGTTCAAAGTTTTTTTCTTCC ATTTCAGGTGTCGTGA
2	Leader (aa)	MALPVTALLLPLALLLHAARP
3	Leader (na)	ATGGCCCTGCCTGTGACAGCCCTGCTGCTGCCTCTGGCTCTG CTGCTGCATGCCGCTAGACCC
4	CD 8 hinge (aa)	TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD
5	CD8 hinge (na)	ACCACGACGCCAGCGCCGCGACCACCAACACCGGCGCCCAC CATCGCGTCGCAGCCCCTGTCCCTGCGCCCAGAGGCGTGCCG GCCAGCGGCGGGGGGCGCAGTGCACACGAGGGGGCTGGACT TCGCCTGTGAT
6	Ig4 hinge (aa)	ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQV YTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNY KTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHN HYTQKSLSLSLGKM
7	Ig4 hinge (na)	GAGAGCAAGTACGGCCCTCCCTGCCCCCCTTGCCCTGCCCCC GAGTTCCTGGGCGGACCCAGCGTGTTCCTGTTCCCCCCCAAG CCCAAGGACACCCTGATGATCAGCCGGACCCCCGAGGTGAC CTGTGTGGTGGTGGACGTGTCCCAGGAGGACCCCGAGGTCC AGTTCAACTGGTACGTGGACGGCGTGGAGGTGCACAACGCC AAGACCAAGCCCCGGGAGGAGCAGTTCAATAGCACCTACCG GGTGGTGTCCGTGCTGACCGTGCTGCACCAGGACTGGCTGAA CGGCAAGGAATACAAGTGTAAGGTGTCCAACAAGGGCCTGC CCAGCAGCATCGAGAAAACCATCAGCAAGGCCAAGGGCCAG CCTCGGGAGCCCCAGGTGTACACCCTGCCCCCTAGCCAAGA GGAGATGACCAAGAACCAGGTGTCCCTGACCTGCCTGGTGA AGGGCTTCTACCCCAGCGACATCGCCGTGGAGTGGGAGAGC AACGGCCAGCCCGAGAACAACTACAAGACCACCCCCCCTGT GCTGGACAGCGACGGCAGCTTCTTCCTGTACAGCCGGCTGAC CGTGGACAAGAGCCGGTGGCAGGAGGGCAACGTCTTTAGCT GCTCCGTGATGCACGAGGCCCTGCACAACCACTACACCCAG AAGAGCCTGAGCCTGTCCCTGGGCAAGATG

8	IgD hinge (aa)	RWPESPKAQASSVPTAQPQAEGSLAKATTAPATTRNTGRGGEE KKKEKEKEEQEERETKTPECPSHTQPLGVYLLTPAVQDLWLRD KATFTCFVVGSDLKDAHLTWEVAGKVPTGGVEEGLLERHSNG SQSQHSRLTLPRSLWNAGTSVTCTLNHPSLPPQRLMALREPAA QAPVKLSLNLLASSDPPEAASWLLCEVSGFSPPNILLMWLEDQR EVNTSGFAPARPPPQPGSTTFWAWSVLRVPAPPSPQPATYTCVV SHEDSRTLLNASRSLEVSYVTDH
9	IgD hinge (na)	AGGTGGCCCGAAAGTCCCAAGGCCCAGGCATCTAGTGTTCCT ACTGCACAGCCCCAGGCAGAAGGCAGCCTAGCCAAAGCTAC TACTGCACCTGCCACTACGCGCAATACTGGCCGTGGCGGGG AGGAGAAGAAAAAGGAGAAAGAGAAAGAAGAACAGGAAG AGAGGGAGACCAAGACCCCTGAATGTCCATCCCATACCCAG CCGCTGGGCGTCTATCTCTTGACTCCCGCAGTACAGGACTTG TGGCTTAGAGATAAGGCCACCTTTACATGTTTCGTCGTGGGC TCTGACCTGAAGGATGCCCATTTGACTTGGGAGGTTGCCGGA AAGGTACCCACAGGGGGGGTTGAGGAAGGGTTGCTGGAGCG CCATTCCAATGGCTCTCAGAGCCAGCACTCAAGACTCACCCT TCCGAGATCCCTGTGGAACGCCGGGACCTCTGTCACATGTAC TCTAAATCATCCTAGCCTGCCCCCACAGCGTCTGATGGCCCT TAGAGAGCCAGCCGCCCAGGCACCAGTTAAGCTTAGCCTGA ATCTGCTCGCCAGTAGTGATCCCCCAGAGGCCGCCAGCTGGC TCTTATGCGAAGTGTCCGGCTTTAGCCCGCCCAACATCTTGC TCATGTGGCTGGAGGACCAGCGAGAAGTGAACACCAGCGGC TTCGCTCCAGCCCGGCCCCCACCCCAGCCGGGTTCTACCACA TTCTGGGCCTGGAGTGTCTTAAGGGTCCCAGCACCACCTAGC CCCCAGCCAGCCACATACACCTGTGTTGTGTCCCATGAAGAT AGCAGGACCCTGCTAAATGCTTCTAGGAGTCTGGAGGTTTCC TACGTGACTGACCATT
10	GS hinge/linker (aa)	GGGGSGGGGS
11	GS hinge/linker (na)	GGTGGCGGAGGTTCTGGAGGTGGAGGTTCC
12	CD8 TM (aa)	IYIWAPLAGTCGVLLLSLVITLYC
13	CD8 TM (na)	ATCTACATCTGGGCGCCCTTGGCCGGGACTTGTGGGGTCCTT CTCCTGTCACTGGTTATCACCCTTTACTGC
14	4-1BB intracellular domain (aa)	KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL
15	4-1BB intracellular domain (na)	AAACGGGGCAGAAAGAAACTCCTGTATATATTCAAACAACC ATTTATGAGACCAGTACAAACTACTCAAGAGGAAGATGGCT GTAGCTGCCGATTTCCAGAAGAAGAAGAAGGAGGATGTGAA CTG

16	CD27 (aa)	QRRKYRSNKGESPVEPAEPCRYSCPREEEGSTIPIQEDYRKPEPA CSP
17	CD27 (na)	AGGAGTAAGAGGAGCAGGCTCCTGCACAGTGACTACATGAA CATGACTCCCCGCCGCCCCGGGCCCACCCGCAAGCATTACCA GCCCTATGCCCCACCACGCGACTTCGCAGCCTATCGCTCC
18	CD3-zeta (aa)	RVKFSRSADAPAYKQGQNQLYNELNLGRREEYDVLDKRRGRD PEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGK GHDGLYQGLSTATKDTYDALHMQALPPR
19	CD3-zeta (na)	AGAGTGAAGTTCAGCAGGAGCGCAGACGCCCCCGCGTACAA GCAGGGCCAGAACCAGCTCTATAACGAGCTCAATCTAGGAC GAAGAGAGGAGTACGATGTTTTGGACAAGAGACGTGGCCGG GACCCTGAGATGGGGGGAAAGCCGAGAAGGAAGAACCCTC AGGAAGGCCTGTACAATGAACTGCAGAAAGATAAGATGGCG GAGGCCTACAGTGAGATTGGGATGAAAGGCGAGCGCCGGAG GGGCAAGGGGCACGATGGCCTTTACCAGGGTCTCAGTACAG CCACCAAGGACACCTACGACGCCCTTCACATGCAGGCCCTG CCCCCTCGC
20	CD3-zeta (aa)	RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRD PEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGK GHDGLYQGLSTATKDTYDALHMQALPPR
21	CD3-zeta (na)	AGAGTGAAGTTCAGCAGGAGCGCAGACGCCCCCGCGTACCA GCAGGGCCAG AACCAGCTCTATAACGAGCTCAATCTAGGACGAAGAGAGGA GTACGATGTTT TGGACAAGAGACGTGGCCGGGACCCTGAGATGGGGGGAAA GCCGAGAAGGA AGAACCCTCAGGAAGGCCTGTACAATGAACTGCAGAAAGAT AAGATGGCGG AGGCCTACAGTGAGATTGGGATGAAAGGCGAGCGCCGGAGG GGCAAGGGGC ACGATGGCCTTTACCAGGGTCTCAGTACAGCCACCAAGGAC ACCTACGACGC CCTTCACATGCAGGCCCTGCCCCCTCGC
22	linker	GGGGS
23	linker	GGTGGCGGAGGTTCTGGAGGTGGAGGTTCC
24	PD-1 extracellular domain (aa)	Pgwfldspdrpwnpptfspallvvtegdnatftcsfsntsesfvlnwyrmspsnqtdklaafpedr sqpgqdcrfrvtqlpngrdfhmsvvrarrndsgtylcgaislapkaqikeslraelrvterraevpta hpspsprpagqfqtlv
25	PD-1 extracellular domain (na)	Cccggatggtttctggactctccggatcgcccgtggaatcccccaaccttctcaccggcactcttggt tgtgactgagggcgataatgcgaccttcacgtgctcgttctccaacacctccgaatcattcgtgctgaa ctggtaccgcatgagcccgtcaaaccagaccgacaagctcgccgcgtttccggaagatcggtcgca accgggacaggattgtcggttccgcgtgactcaactgccgaatggcagagacttccacatgagcgt ggtccgcgctaggcgaaacgactccgggacctacctgtgcggagccatctcgctggcgcctaagg cccaaatcaaagagagcttgagggccgaactgagagtgaccgagcgcagagctgaggtgccaact gcacatccatccccatcgcctcggcctgcggggcagtttcagaccctggtc

26	PD-1 CAR (aa) with signal	Malpvtalllplalllhaarppgwfldspdrpwnpptfspallvvtegdnatftcsfsntsesfvlnw yrmspsnqtdklaafpedrsqpgqdcrfrvtqlpngrdfhmsvvrarrndsgtylcgaislapka qikeslraelrvterraevptahpspsprpagqfqtlvtttpaprpptpaptiasqplslrpeacrpaag gavhtrgldfacdiyiwaplagtcgvlllslvitlyckrgrkkllyifkqpfmrpvqttqeedgcscrf peeeeggcelrvkfsrsadapaykqgqnqlynelnlgrreeydvldkrrgrdpemggkprrknp qeglynelqkdkmaeayseigmkgerrrgkghdglyqglstatkdtydalhmqalppr
27	PD-1 CAR (na)	Atggccctccctgtcactgccctgcttctccccctcgcactcctgctccacgccgctagaccacccg gatggtttctggactctccggatcgcccgtggaatcccccaaccttctcaccggcactcttggttgtga ctgagggcgataatgcgaccttcacgtgctcgttctccaacacctccgaatcattcgtgctgaactggt accgcatgagcccgtcaaaccagaccgacaagctcgccgcgtttccggaagatcggtcgcaaccg ggacaggattgtcggttccgcgtgactcaactgccgaatggcagagacttccacatgagcgtggtcc gcgctaggcgaaacgactccgggacctacctgtgcggagccatctcgctggcgcctaaggcccaa atcaaagagagcttgagggccgaactgagagtgaccgagcgcagagctgaggtgccaactgcac atccatccccatcgcctcggcctgcggggcagtttcagaccctggtcacgaccactccggcgccgc gcccaccgactccggccccaactatcgcgagccagcccctgtcgctgaggccggaagcatgccgc cctgccgccggaggtgctgtgcatacccggggattggacttcgcatgcgacatctacatttgggctcc tctcgccggaacttgtggcgtgctccttctgtccctggtcatcaccctgtactgcaagcggggtcgga aaaagcttctgtacattttcaagcagcccttcatgaggcccgtgcaaaccacccaggaggaggacgg ttgctcctgccggttccccgaagaggaagaaggaggttgcgagctgcgcgtgaagttctcccggag cgccgacgcccccgcctataagcagggccagaaccagctgtacaacgaactgaacctgggacgg cgggaagagtacgatgtgctggacaagcggcgcggccgggaccccgaaatgggcgggaagcct agaagaaagaaccctcaggaaggcctgtataacgagctgcagaaggacaagatggccgaggcct actccgaaattgggatgaagggagagcggcggaggggaaaggggcacgacggcctgtaccaag gactgtccaccgccaccaaggacacatacgatgccctgcacatgcaggcccttcccctcgc
28	linker	(Gly-Gly-Gly-Ser)n, where n = 1-10
29	linker	(Gly4 Ser)4
30	linker	(Gly4 Ser)3
31	linker	(Gly3Ser)
39	PD1 CAR (aa)	Pgwfldspdrpwnpptfspallvvtegdnatftcsfsntsesfvlnwyrmspsnqtdklaafpedr sqpgqdcrfrvtqlpngrdfhmsvvrarrndsgtylcgaislapkaqikeslraelrvterraevpta hpspsprpagqfqtlvtttpaprpptpaptiasqplslrpeacrpaaggavhtrgldfacdiyiwapl agtcgvlllslvitlyckrgrkkllyifkqpfmrpvqttqeedgcscrfpeeeeggcelrvkfsrsada paykqgqnqlynelnlgrreeydvldkrrgrdpemggkprrknpqeglynelqkdkmaeays eigmkgerrrgkghdglyqglstatkdtydalhmqalppr

In vitro CAR-T Manufacture

While methods contemplated herein relate to in vivo transduction of cells, the challenges of in vitro manufacture are also appreciated.

In some embodiments, cells transduced the viral vector as described herein, are expanded, e.g., by a method described herein. In some embodiments, the cells are expanded in culture for a period of several hours (e.g., about 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 18, 21 hours) to about 14 days (e.g., 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 days). In some embodiments, the

cells are expanded for a period of 4 to 9 days. In some embodiments, the cells are expanded for a period of 8 days or less, e.g., 7, 6 or 5 days. In some embodiments, the cells are expanded in culture for 5 days, and the resulting cells are more potent than the same cells expanded in culture for 9 days under the same culture conditions. Potency can be defined, e.g., by various T cell functions, e.g. proliferation, target cell killing, cytokine production, activation, migration, or combinations thereof. In some embodiments, the cells are expanded for 5 days show at least a one, two, three, or four-fold increase in cells doublings upon antigen stimulation as compared to the same cells expanded in culture for 9 days under the same culture conditions. In some embodiments, the cells are expanded in culture for 5 days, and the resulting cells exhibit higher proinflammatory cytokine production, e.g., IFN-γ and/or GM-CSF levels, as compared to the same cells expanded in culture for 9 days under the same culture conditions. In some embodiments, the cells expanded for 5 days show at least a one, two, three, four, five, ten-fold or more increase in pg/ml of proinflammatory cytokine production, e.g., IFN-γ and/or GM-CSF levels, as compared to the same cells expanded in culture for 9 days under the same culture conditions.

Initial activation steps in the absence of calcium can lead to magnified activation. As those of ordinary skill in the art would readily appreciate a washing step may be accomplished by methods known to those in the art, such as by using a semi-automated "flow-through" centrifuge (for example, the Cobe 2991 cell processor, the Baxter CytoMate, or the Haemonetics Cell Saver 5) according to the manufacturer's instructions. After washing, the cells may be resuspended in a variety of biocompatible buffers, such as, for example, Ca-free, Mg-free PBS, PlasmaLyte A, or other saline solution with or without buffer. Alternatively, the undesirable components of the apheresis sample may be removed, and the cells directly resuspended in culture media.

It is recognized that the in vitro methods of the application can utilize culture media conditions comprising 5% or less, for example 2%, human AB serum, and employ known culture media conditions and compositions, for example those described in Smith *et al.*, "Ex vivo expansion of human T cells for adoptive immunotherapy using the novel Xeno-free CTS Immune Cell Serum Replacement" *Clinical & Translational Immunology* (2015) 4, e31; doi:10.1038/cti.2014.31.

In some aspects, T cells are isolated from peripheral blood lymphocytes by lysing the red blood cells and depleting the monocytes, for example, by centrifugation through a PERCOLL™ gradient or by counterflow centrifugal elutriation. The isolated T cells may be further used in the methods described herein.

The methods described herein can include, e.g., selection of a specific subpopulation of immune effector cells, e.g., T cells, that are a T regulatory cell-depleted population, CD25+ depleted cells, using, e.g., a negative selection technique, e.g., described herein. Preferably, the population of T regulatory depleted cells contains less than 30%, 25%, 20%, 15%, 10%, 5%, 4%, 3%, 2%, 1% of CD25+ cells.

In some embodiments, T regulatory cells, e.g., CD25+ T cells, are removed from the population using an anti-CD25 antibody, or fragment thereof, or a CD25-binding ligand, IL-2. In some embodiments, the anti-CD25 antibody, or fragment thereof, or CD25-binding ligand is conjugated to a substrate, e.g., a bead, or is otherwise coated on a substrate, e.g., a bead. In some embodiments, the anti-CD25 antibody, or fragment thereof, is conjugated to a substrate as described herein.

In some embodiments, the T regulatory cells, e.g., CD25+ T cells, are removed from the population using CD25 depletion reagent from Miltenyi™. In some embodiments, the ratio of cells to CD25 depletion reagent is 1 x 10^7 cells to 20 µL, or 1 x 10^7 cells to 15 µL, or 1 x 10^7 cells to 10 µL, or 1 x 10^7 cells to 5 µL, or 1 x 10^7 cells to 2.5 µL, or 1 x 10^7 cells to 1.25 µL. In some embodiments, e.g., for T regulatory cells, e.g., CD25+ depletion, greater than 500 million cells/ml is used. In a further aspect, a concentration of cells of 600, 700, 800, or 900 million cells/ml is used.

In some embodiments, the population of immune effector cells to be depleted includes about 6 x 10^9 CD25+ T cells. In other aspects, the population of immune effector cells to be depleted include about 1 x 10^9 to 1x 10^{10} CD25+ T cell, and any integer value in between. In some embodiments, the resulting population T regulatory depleted cells has 2 x 10^9 T regulatory cells, e.g., CD25+ cells, or less (e.g., 1 x 10^9, 5 x 10^8, 1 x 10^8, 5 x 10^7, 1 x 10^7, or less CD25+ cells).

In some embodiments, the T regulatory cells, e.g., CD25+ cells, are removed from the population using the CliniMAC system with a depletion tubing set, such as, e.g., tubing 162-01.

In some embodiments, the CliniMAC system is run on a depletion setting such as, e.g., DEPLETION2.1.

Without wishing to be bound by a particular theory, decreasing the level of negative regulators of immune cells (e.g., decreasing the number of unwanted immune cells, e.g., T_{REG} cells), in a subject prior to apheresis or during manufacturing of a CAR-expressing cell product can reduce the risk of subject relapse. For example, methods of depleting T_{REG} cells are known in the art. Methods of decreasing T_{REG} cells include, but are not limited to, cyclophosphamide, anti-GITR antibody (an anti-GITR antibody described herein), CD25-depletion, and combinations thereof.

In some embodiments, the manufacturing methods comprise reducing the number of (e.g., depleting) T_{REG} cells prior to manufacturing of the CAR-expressing cell. For example, manufacturing methods comprise contacting the sample, e.g., the apheresis sample, with an anti-GITR antibody and/or an anti-CD25 antibody (or fragment thereof, or a CD25-binding ligand), e.g., to deplete T_{REG} cells prior to manufacturing of the CAR-expressing cell (e.g., T cell, NK cell) product.

In some embodiments, a subject is pre-treated with one or more therapies that reduce T_{REG} cells prior to collection of cells for CAR-expressing cell product manufacturing, thereby reducing the risk of subject relapse to CAR-expressing cell treatment. In some embodiments, methods of decreasing T_{REG} cells include, but are not limited to, administration to the subject of one or more of cyclophosphamide, anti-GITR antibody, CD25-depletion, or a combination thereof. Administration of one or more of cyclophosphamide, anti-GITR antibody, CD25-depletion, or a combination thereof, can occur before, during or after an infusion of the CAR-expressing cell product.

In some embodiments, a subject is pre-treated with cyclophosphamide prior to collection of cells for CAR-expressing cell product manufacturing, thereby reducing the risk of subject relapse to CAR-expressing cell treatment. In some embodiments, a subject is pre-treated with an anti-GITR antibody prior to collection of cells for CAR-expressing cell product manufacturing, thereby reducing the risk of subject relapse to CAR-expressing cell treatment.

In some embodiments, the population of cells to be removed are neither the regulatory T cells or tumor cells, but cells that otherwise negatively affect the expansion and/or function of CART cells, e.g. cells expressing CD14, CD11b, CD33, CD15, or other markers expressed by

potentially immune suppressive cells. In some embodiments, such cells are envisioned to be removed concurrently with regulatory T cells and/or tumor cells, or following said depletion, or in another order.

The methods described herein can include more than one selection step, e.g., more than one depletion step. Enrichment of a T cell population by negative selection can be accomplished, e.g., with a combination of antibodies directed to surface markers unique to the negatively selected cells. One method is cell sorting and/or selection via negative magnetic immunoadherence or flow cytometry that uses a cocktail of monoclonal antibodies directed to cell surface markers present on the cells negatively selected. For example, to enrich for CD4+ cells by negative selection, a monoclonal antibody cocktail can include antibodies to CD14, CD20, CD11b, CD16, HLA-DR, and CD8.

The methods described herein can further include removing cells from the population which express a tumor antigen, e.g., a tumor antigen that does not comprise CD25, e.g., CD19, CD30, CD38, CD123, CD20, CD14 or CD11b, to thereby provide a population of T regulatory depleted, e.g., CD25+ depleted, and tumor antigen depleted cells that are suitable for expression of a CAR, e.g., a CAR described herein. In some embodiments, tumor antigen expressing cells are removed simultaneously with the T regulatory, e.g., CD25+ cells. For example, an anti-CD25 antibody, or fragment thereof, and an anti-tumor antigen antibody, or fragment thereof, can be attached to the same substrate, e.g., bead, which can be used to remove the cells or an anti-CD25 antibody, or fragment thereof, or the anti-tumor antigen antibody, or fragment thereof, can be attached to separate beads, a mixture of which can be used to remove the cells. In other embodiments, the removal of T regulatory cells, e.g., CD25+ cells, and the removal of the tumor antigen expressing cells is sequential, and can occur, e.g., in either order.

Also provided are methods that include removing cells from the population which express a check point inhibitor, e.g., a check point inhibitor described herein, e.g., one or more of PD1+ cells, LAG3+ cells, and TIM3+ cells, to thereby provide a population of T regulatory depleted, e.g., CD25+ depleted cells, and check point inhibitor depleted cells, e.g., PD1+, LAG3+ and/or TIM3+ depleted cells. Exemplary check point inhibitors include B7-H1, B7-1, CD160, P1H, 2B4, PD1, TIM3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG3, TIGIT, CTLA-4, BTLA, and LAIR1. In some embodiments, check point inhibitor expressing cells are removed simultaneously with the T regulatory, e.g., CD25+ cells. For

example, an anti-CD25 antibody, or fragment thereof, and an anti-check point inhibitor antibody, or fragment thereof, can be attached to the same bead which can be used to remove the cells, or an anti-CD25 antibody, or fragment thereof, and the anti-check point inhibitor antibody, or fragment there, can be attached to separate beads, a mixture of which can be used to remove the cells. In other embodiments, the removal of T regulatory cells, e.g., CD25+ cells, and the removal of the check point inhibitor expressing cells is sequential, and can occur, e.g., in either order.

Methods described herein can include a positive selection step. For example, T cells can isolated by incubation with anti-CD3/anti-CD28 (e.g., 3x28)-conjugated beads, such as DYNABEADS® M-450 CD3/CD28 T, for a time period sufficient for positive selection of the desired T cells. In some embodiments, the time period is about 30 minutes. In a further embodiment, the time period ranges from 30 minutes to 36 hours or longer and all integer values there between. In a further embodiment, the time period is at least 1, 2, 3, 4, 5, or 6 hours. In yet another embodiment, the time period is 10 to 24 hours, e.g., 24 hours. Longer incubation times may be used to isolate T cells in any situation where there are few T cells as compared to other cell types, such in isolating tumor infiltrating lymphocytes (TIL) from tumor tissue or from immunocompromised individuals. Further, use of longer incubation times can increase the efficiency of capture of CD8+ T cells. Thus, by simply shortening or lengthening the time T cells are allowed to bind to the CD3/CD28 beads and/or by increasing or decreasing the ratio of beads to T cells (as described further herein), subpopulations of T cells can be preferentially selected for or against at culture initiation or at other time points during the process. Additionally, by increasing or decreasing the ratio of anti-CD3 and/or anti-CD28 antibodies on the beads or other surface, subpopulations of T cells can be preferentially selected for or against at culture initiation or at other desired time points. In some embodiments, a T cell population can be selected that expresses one or more of IFN-γ, TNFα, IL-17A, IL-2, IL-3, IL-4, GM-CSF, IL-10, IL-13, granzyme B, and perforin, or other appropriate molecules, e.g., other cytokines. Methods for screening for cell expression can be determined, e.g., by the methods described in PCT Publication No.: WO 2013/126712.

For isolation of a desired population of cells by positive or negative selection, the concentration of cells and surface (e.g., particles such as beads) can be varied. In some aspects, it may be desirable to significantly decrease the volume in which beads and cells are mixed

together (e.g., increase the concentration of cells), to ensure maximum contact of cells and beads. For example, in some aspects, a concentration of 10 billion cells/ml, 9 billion/ml, 8 billion/ml, 7 billion/ml, 6 billion/ml, or 5 billion/ml is used. In some aspects, a concentration of 1 billion cells/ml is used. In yet some aspects, a concentration of cells from 75, 80, 85, 90, 95, or 100 million cells/ml is used. In further aspects, concentrations of 125 or 150 million cells/ml can be used.

Using high concentrations can result in increased cell yield, cell activation, and cell expansion. Further, use of high cell concentrations allows more efficient capture of cells that may weakly express target antigens of interest, such as CD28-negative T cells, or from samples where there are many tumor cells present (e.g., leukemic blood, tumor tissue, etc.). Such populations of cells may have therapeutic value and would be desirable to obtain. For example, using high concentration of cells allows more efficient selection of CD8+ T cells that normally have weaker CD28 expression.

In some embodiments, it may be desirable to use lower concentrations of cells. By significantly diluting the mixture of T cells and surface (e.g., particles such as beads), interactions between the particles and cells are minimized. This selects for cells that express high amounts of desired antigens to be bound to the particles. For example, CD4+ T cells express higher levels of CD28 and are more efficiently captured than CD8+ T cells in dilute concentrations. In some aspects, the concentration of cells used is 5×10^6/ml. In other aspects, the concentration used can be from about 1×10^5/ml to 1×10^6/ml, and any integer value in between.

In other aspects, the cells may be incubated on a rotator for varying lengths of time at varying speeds at either 2-10°C or at room temperature.

T cells for stimulation can also be frozen after a washing step. Wishing not to be bound by theory, the freeze and subsequent thaw step provide a more uniform product by removing granulocytes and to some extent monocytes in the cell population. After the washing step that removes plasma and platelets, the cells may be suspended in a freezing solution. While many freezing solutions and parameters are known in the art and will be useful in this context, one method involves using PBS containing 20% DMSO and 8% human serum albumin, or culture media containing 10% Dextran 40 and 5% Dextrose, 20% Human Serum Albumin and 7.5% DMSO, or 31.25% Plasmalyte-A, 31.25% Dextrose 5%, 0.45% NaCl, 10% Dextran 40 and 5%

Dextrose, 20% Human Serum Albumin, and 7.5% DMSO or other suitable cell freezing media containing for example, Hespan and PlasmaLyte A, the cells then are frozen to -80°C at a rate of 1° per minute and stored in the vapor phase of a liquid nitrogen storage tank. Other methods of controlled freezing may be used as well as uncontrolled freezing immediately at -20° C or in liquid nitrogen.

In some aspects, cryopreserved cells are thawed and washed as described herein and allowed to rest for one hour at room temperature prior to activation using the methods of the present invention.

Also contemplated in the context of the invention is the collection of blood samples or apheresis product from a subject at a time period prior to when the expanded cells as described herein might be needed. As such, the source of the cells to be expanded can be collected at any time point necessary, and desired cells, such as T cells, can be isolated and frozen for later use in immune effector cell therapy for any number of diseases or conditions that would benefit from immune effector cell therapy, such as those described herein. In some aspects a blood sample or an apheresis is taken from a generally healthy subject. In some aspects, a blood sample or an apheresis is taken from a generally healthy subject who is at risk of developing a disease, but who has not yet developed a disease, and the cells of interest are isolated and frozen for later use. In some aspects, the T cells may be expanded, frozen, and used at a later time. In some aspects, samples are collected from a patient shortly after diagnosis of a particular disease as described herein but prior to any treatments. In a further aspect, the cells are isolated from a blood sample or an apheresis from a subject prior to any number of relevant treatment modalities, including but not limited to treatment with agents such as natalizumab, efalizumab, antiviral agents, chemotherapy, radiation, immunosuppressive agents, such as cyclosporin, azathioprine, methotrexate, mycophenolate, and FK506, antibodies, or other immunoablative agents such as CAMPATH, anti-CD3 antibodies, cytoxan, fludarabine, cyclosporin, FK506, rapamycin, mycophenolic acid, steroids, FR901228, and irradiation.

In a further aspect of the present invention, T cells are obtained from a patient directly following treatment that leaves the subject with functional T cells. In this regard, it has been observed that following certain cancer treatments, in particular treatments with drugs that damage the immune system, shortly after treatment during the period when patients would normally be recovering from the treatment, the quality of T cells obtained may be optimal or

improved for their ability to expand ex vivo. Likewise, following ex vivo manipulation using the methods described herein, these cells may be in a preferred state for enhanced engraftment and in vivo expansion. Thus, it is contemplated within the context of the present invention to collect blood cells, including T cells, dendritic cells, or other cells of the hematopoietic lineage, during this recovery phase. Further, in some aspects, mobilization (for example, mobilization with GM-CSF) and conditioning regimens can be used to create a condition in a subject wherein repopulation, recirculation, regeneration, and/or expansion of particular cell types is favored, especially during a defined window of time following therapy. Illustrative cell types include T cells, B cells, dendritic cells, and other cells of the immune system.

In some embodiments, a T cell population is diaglycerol kinase (DGK)-deficient. DGK-deficient cells include cells that do not express DGK RNA or protein or have reduced or inhibited DGK activity. DGK-deficient cells can be generated by genetic approaches, e.g., administering RNA-interfering agents, e.g., siRNA, shRNA, miRNA, to reduce or prevent DGK expression. Alternatively, DGK-deficient cells can be generated by treatment with DGK inhibitors described herein.

In some embodiments, a T cell population is Ikaros-deficient. Ikaros-deficient cells include cells that do not express Ikaros RNA or protein, or have reduced or inhibited Ikaros activity, Ikaros-deficient cells can be generated by genetic approaches, e.g., administering RNA-interfering agents, e.g., siRNA, shRNA, miRNA, to reduce or prevent Ikaros expression. Alternatively, Ikaros-deficient cells can be generated by treatment with Ikaros inhibitors, e.g., lenalidomide.

In embodiments, a T cell population is DGK-deficient and Ikaros-deficient, e.g., does not express DGK and Ikaros, or has reduced or inhibited DGK and Ikaros activity. Such DGK and Ikaros-deficient cells can be generated by any of the methods described herein.

In some embodiments, the NK cells are obtained from the subject. In another embodiment, the NK cells are an NK cell line, e.g., NK-92 cell line (Conkwest).

In a particular exemplary aspect, subjects may undergo leukapheresis, wherein leukocytes are collected, enriched, or depleted ex vivo to select and/or isolate the cells of interest, e.g., T cells.

These T cell isolates may be expanded by methods described herein. Subjects in need thereof may subsequently undergo standard treatment with high dose chemotherapy followed by peripheral blood stem cell transplantation. In some aspects, following or concurrent with the

transplant, subjects receive an infusion of the expanded CAR T cells as prepared by the methods of the present invention. In an additional aspect, expanded cells are administered before or following surgery.

Additional Expressed Agents

Co-expression of an Agent that Enhances CAR Activity

In the embodiments contemplated herein, it is appreciated that additional agents may be encoded in the vectors described herein above. Accordingly, these agents are described below in relation to the CAR-expressing cell.

In another embodiment, a CAR-expressing immune effector cell described herein can further express another agent, e.g., an agent which enhances the activity of a CAR-expressing cell. For example, in some embodiments, the agent can be an agent which inhibits an inhibitory molecule. Examples of inhibitory molecules include PD-1, PD-L1, CTLA-4, TIM-3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4 and TGFR beta, e.g., as described herein. In some embodiments, the agent that inhibits an inhibitory molecule comprises a first polypeptide, e.g., an inhibitory molecule, associated with a second polypeptide that provides a positive signal to the cell, e.g., an intracellular signaling domain described herein. In some embodiments, the agent comprises a first polypeptide, e.g., of an inhibitory molecule such as PD-1, PD-L1, CTLA-4, TIM-3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, or TGFR beta, or a fragment of any of these, and a second polypeptide which is an intracellular signaling domain described herein (e.g., comprising a costimulatory domain (e.g., 41BB, CD27 or CD28, e.g., as described herein) and/or a primary signaling domain (e.g., a CD3 zeta signaling domain described herein). In some embodiments, the agent comprises a first polypeptide of PD-1 or a fragment thereof, and a second polypeptide of an intracellular signaling domain described herein (e.g., a CD28, CD27, OX40 or 4-IBB signaling domain described herein and/or a CD3 zeta signaling domain described herein).

Co-expression of a Second CAR

In some embodiments, the CAR-expressing cell described herein can further comprise a second CAR, for example, a second CAR that includes a different antigen binding domain, for

example, to the same target (for example, CD19) or a different target (for example, a target other than CD19, for example, a target described herein).

In some embodiments, the CAR-expressing cell described herein, e.g., the CAR-expressing cell manufactured using a method described herein, comprises (i) a first nucleic acid molecule encoding a first CAR that binds to BCMA and (ii) a second nucleic acid molecule encoding a second CAR that binds to CD19. In some embodiments, the first CAR comprises an anti-BCMA binding domain, a first transmembrane domain, and a first intracellular signaling domain, wherein the anti-BCMA binding domain comprises a heavy chain variable region (VH) comprising a heavy chain complementary determining region 1 (HC CDR1), a heavy chain complementary determining region 2 (HC CDR2), and a heavy chain complementary determining region 3 (HC CDR3), and a light chain variable region (VL) comprising a light chain complementary determining region 1 (LC CDR1), a light chain complementary determining region 2 (LC CDR2), and a light chain complementary determining region 3 (LC CDR3), wherein the HC CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR2, and LC CDR3 comprise the amino acid sequences of SEQ ID NOs: 86, 87, 88, 95, 96, and 97, respectively. In some embodiments, the second CAR comprises an anti-CD19 binding domain, a second transmembrane domain, and a second intracellular signaling domain, wherein the anti-CD19 binding domain comprises a VH comprising a HC CDR1, a HC CDR2, and a HC CDR3, and a VL comprising a LC CDR1, a LC CDR2, and a LC CDR3, wherein the HC CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR2, and LC CDR3 comprise the amino acid sequences of SEQ ID NOs: 760, 687, 762, 763, 764, and 765, respectively. In some embodiments, (i) the VH and VL of the anti-BCMA binding domain comprise the amino acid sequences of SEQ ID NOs: 93 and 102, respectively. In some embodiments, the VH and VL of the anti-CD19 binding domain comprise the amino acid sequences of SEQ ID NOs: 250A and 251A, respectively. In some embodiments, the anti-BCMA binding domain comprises the amino acid sequence of SEQ ID NO: 105. In some embodiments, the anti-CD19 binding domain comprises the amino acid sequence of SEQ ID NO: 758. In some embodiments, the first CAR comprises the amino acid sequence of SEQ ID NO: 107. In some embodiments, the second CAR comprise the amino acid sequence of SEQ ID NO: 225.

In some embodiments, the CAR-expressing cell described herein, e.g., the CAR-expressing cell manufactured using a method described herein, comprises (i) a first nucleic acid

molecule encoding a first CAR that binds to CD22 and (ii) a second nucleic acid molecule encoding a second CAR that binds to CD19. In some embodiments, the CD22 CAR comprises a CD22 antigen binding domain, and a first transmembrane domain; a first co-stimulatory signaling domain; and/or a first primary signaling domain. In some embodiments, the CD19 CAR comprises a CD19 antigen binding domain, and a second transmembrane domain; a second co-stimulatory signaling domain; and/or a second primary signaling domain.

In some embodiments, the CD22 antigen binding domain comprises one or more (e.g., all three) light chain complementarity determining region 1 (LC CDR1), light chain complementarity determining region 2 (LC CDR2), and light chain complementarity determining region 3 (LC CDR3) of a CD22 binding domain described herein, e.g., in Tables 15, 16, 30, 31, or 32; and/or one or more (e.g., all three) heavy chain complementarity determining region 1 (HC CDR1), heavy chain complementarity determining region 2 (HC CDR2), and heavy chain complementarity determining region 3 (HC CDR3) of a CD22 binding domain described herein, e.g., in Tables 15, 16, 30, 31 or 32. In an embodiment, the CD22 antigen binding domain comprises a LC CDR1, LC CDR2 and LC CDR3 of a CD22 binding domain described herein, e.g., in Table 15, 16, 30, 31 or 32; and/or a HC CDR1, HC CDR2 and HC CDR3 of a CD22 binding domain described herein, e.g., in Tables 15, 16, 30, 31 or 32. In some embodiments, the CD19 antigen binding domain comprises: one or more (e.g., all three) LC CDR1, LC CDR2, and LC CDR3 of a CD19 binding domain described herein, e.g., in Tables 1, 30, 31, or 32; and/or one or more (e.g., all three) HC CDR1, HC CDR2, and HC CDR3 of a CD19 binding domain described herein, e.g., in Tables 1, 30, 31, and 32. In some embodiments, the CD19 antigen binding domain comprises a LC CDR1, LC CDR2 and LC CDR3 of a CD19 binding domain described herein, e.g., in Tables 1, 30, 31, and 32; and/or a HC CDR1, HC CDR2 and HC CDR3 of a CD19 binding domain described herein, e.g., in Tables 1, 30, 31, and 32.

In some embodiment, the CD22 antigen binding domain (e.g., an scFv) comprises a light chain variable (VL) region of a CD22 binding domain described herein, e.g., in Tables 30 or 32; and/or a heavy chain variable (VH) region of a CD22 binding domain described herein, e.g., in Tables 30 or 32. In some embodiments, the CD22 antigen binding domain comprises a VL region comprising an amino acid sequence having at least one, two or three modifications (e.g., substitutions) but not more than 30, 20 or 10 modifications (e.g., substitutions) of a CD22 VL region sequence provided in Table 30 or 32. In some embodiments, the CD22 antigen binding

domain comprises a VL region comprising an amino acid sequence provided in Table 30 or 32, or a sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity to any of the aforesaid sequences. In some embodiments, the CD22 antigen binding domain comprises a VH region comprising an amino acid sequence having at least one, two or three modifications (e.g., substitutions) but not more than 30, 20 or 10 modifications (e.g., substitutions) of a CD22 VH region sequence provided in Table 30 or 32. In some embodiments, the CD22 antigen binding domain comprises a VH region comprising the amino acid sequence of a CD22 VH region sequence provided in Table 30 or 32, or a sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity to any of the aforesaid sequences. In some embodiments, the CD19 antigen binding domain (e.g., an scFv) comprises a VL region of a CD19 binding domain described herein, e.g., in Tables 1, 30, or 32; and/or a VH region of a CD19 binding domain described herein, e.g., in Tables 1, 30, or 32. In some embodiments, the CD19 antigen binding domain comprises a VL region comprising an amino acid sequence having at least one, two or three modifications (e.g., substitutions) but not more than 30, 20 or 10 modifications (e.g., substitutions) of a CD19 VL region sequence provided in Tables 1, 30, or 32. In some embodiments, the CD19 antigen binding domain comprises a VL region comprising the amino acid sequence of a CD19 VL region sequence provided in Tables 1, 30, or 32, or a sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity to any of the aforesaid sequences. In some embodiments, the CD19 antigen binding domain comprises a VH region comprising an amino acid sequence having at least one, two or three modifications (e.g., substitutions) but not more than 30, 20 or 10 modifications (e.g., substitutions) of a CD19 VH region sequence provided in Tables 1, 30, or 32. In some embodiments, the CD19 antigen binding domain comprises a VH region comprising the amino acid sequence of a CD19 VH region sequence provided in Tables 1, 30, or 32, or a sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity to any of the aforesaid sequences.

In some embodiments, the CD22 antigen binding comprises an scFv comprising an amino acid sequence having at least one, two or three modifications (e.g., substitutions) but not more than 30, 20 or 10 modifications (e.g., substitutions) of a CD22 scFv sequence provided in Table 30 or 32. In some embodiments, the CD22 antigen binding comprises an scFv comprising an amino acid sequence of a CD22 scFv sequence provided in Table 30 or 32, or a sequence

having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity to any of the aforesaid sequences. In some embodiments, the CD19 antigen binding domain comprises an scFv comprising an amino acid sequence having at least one, two or three modifications (e.g., substitutions) but not more than 30, 20 or 10 modifications (e.g., substitutions) of a CD19 scFv sequence provided in Tables 1, 30, or 32. In some embodiments, the CD19 antigen binding domain comprises an scFv comprising the amino acid sequence of a CD19 scFv sequence provided in Tables 1, 30, or 32, or a sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity to any of the aforesaid sequences.

In some embodiments, the CD22 CAR molecule and/or the CD19 CAR molecule comprises an additional component, e.g., a signal peptide, a hinge, a transmembrane domain, a co-stimulatory signaling domain and/or a first primary signaling domain, a P2A site, and/or a linker, comprising an amino acid sequence provided in Table 33, or a sequence having at least about 70%, 75%, 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity to any of the aforesaid sequences; or is encoded by a nucleotide sequence provided in Table 33, or a sequence having at least about 70%, 75%, 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity to any of the aforesaid sequences.

Exemplary nucleotide and amino acid sequences of a CAR molecule, e.g., a dual CAR molecule comprising (i) a first CAR that binds to CD22 and (ii) a second CAR that binds to CD19 disclosed herein, is provided in Table 30.

Table 30: Dual and tandem CD19-CD22 CAR sequences

Identifier	SEQ ID NO	Sequence
Tandem CD19-CD22 CARs		
CG#c171	813	atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgctcggcccg aaattgtgatgacccagtcacccgccactcttagcctttcacccggtgagcgcgcaaccctgtc ttgcagagcctcccaagacatctcaaaataccttaattggtatcaacagaagcccggacaggc tcctcgccttctgatctaccacaccagccggctccattctggaatccctgccaggttcagcggt agcggatctgggaccgactacaccctcactatcagctcactgcagccagaggacttcgctgtc tatttctgtcagcaagggaacaccctgccctacacctttggacagggcaccaagctcgagatt aaaggtggaggtggcagcggaggaggtgggtccggcggtggaggaagccaggtccaact ccaagaaagcggaccgggtcttgtgaagccatcagaaactctttcactgacttgtactgtgagc ggagtgtctctccccgattacggggtgtcttggatcagacagccaccggggaagggtctgga atggattggagtgatttggggctctgagactacttactaccaatcatccctcaagtcacgcgtca ccatctcaaaggacaactctaagaatcaggtgtcactgaaactgtcatctgtgaccgcagccg acaccgccgtgtactattgcgctaagcattactattatggcgggagctacgcaatggattactg gggacagggtactctggtcaccgtgtccagcttggcagaagccgccgcgaaagaagtgcag

		cttcaacaatcaggaccaggactcgtcaaaccatcacagaccctctccctcacatgtgccatct ccggggactccatgttgagcaattccgacacttggaattggattagacaaagcccgtcccggg gtctggaatggttgggacgcacctaccaccggtctacttggtacgacgactacgcgtcatccg tgcggggaagagtgtccatcaacgtggacacctccaagaaccagtacagcctgcagcttaat gccgtgactcctgaggatacgggcgtctactactgcgcccgcgtccgcctgcaagacgggga acagctggagcgatgcattcgatgtctggggccagggaactatggtcaccgtgtcgtctggg ggcggtggatcgggtggcgggggttcgggggggcggcggctctcagtccgctcttacccaac cggcctcagcctcggggagccccggccagagcgtgaccatttcctgcaccggcacttcatcc gacgtgggcggctacaactacgtgtcctggtaccaacagcacccgggaaaggcccccaag ctcatgatctacgacgtgtccaacaggccctcgggagtgtccaaccggttctcgggttcgaaa tcgggaaacacagccagcctgaccatcagcggactgcaggctgaagatgaagccgactact actgctcctcctacacctcgtcatccacgctctacgtgttcggcactggaactcagctgactgtg ctgaccactaccccagcaccgaggccacccaccccggctcctaccatcgcctcccagcctct gtccctgcgtccggaggcatgtagacccgcagctggtggggccgtgcatacccggggtctt gacttcgcctgcgatatctacatttgggcccctctggctggtacttgcggggtcctgctgctttca ctcgtgatcactctttactgtaagcgcggtcggaagaagctgctgtacatctttaagcaacccctt catgaggcctgtgcagactactcaagaggaggacggctgttcatgccggttcccagaggag gaggaaggcggctgcgaactgcgcgtgaaattcagccgcagcgcagatgctccagcctac cagcaggggcagaaccagctctacaacgaactcaatcttggtcggagagaggagtacgacg tgctggacaagcggagaggacgggacccagaaatgggcgggaagccgcgcagaaagaa tccccaagagggcctgtacaacgagctccaaaaggataagatggcagaagcctatagcgag attggtatgaaaggggaacgcagaagaggcaaaggccacgacggactgtaccagggactc agcaccgccaccaaggacacctatgacgctcttcacatgcaggccctgccgcctcgg
	814	MALPVTALLLPLALLLHAARPEIVMTQSPATLSLSPGERAT LSCRASQDISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPAR FSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYTFGQGT KLEIKGGGGSGGGGSGGGGSQVQLQESGPGLVKPSETLSLT CTVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYQSS LKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCAKHYYYG GSYAMDYWGQGTLVTVSSLAEAAAKEVQLQQSGPGLVKP SQTLSLTCAISGDSMLSNSDTWNWIRQSPSRGLEWLGRTY HRSTWYDDYASSVRGRVSINVDTSKNQYSLQLNAVTPEDT GVYYCARVRLQDGNSWSDAFDVWGQGTMVTVSSGGGGS GGGGSGGGGSQSALTQPASASGSPGQSVTISCTGTSSDVGG YNYVSWYQQHPGKAPKLMIYDVSNRPSGVSNRFSGSKSG NTASLTISGLQAEDEADYYCSSYTSSSTLYVFGTGTQLTVL TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDF ACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPF MRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAY QQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRK NPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQ GLSTATKDTYDALHMQALPPR
CG#c182	815	atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgctcggcccg aagtgcagcttcaacaatcaggaccaggactcgtcaaaccatcacagaccctctccctcacat gtgccatctccggggactccatgttgagcaattccgacacttggaattggattagacaaagccc gtcccggggtctggaatggttgggacgcacctaccaccggtctacttggtacgacgactacg

		cgtcatccgtgcggggaagagtgtccatcaacgtggacacctccaagaaccagtacagcctg cagcttaatgccgtgactcctgaggatacgggcgtctactactgcgcccgcgtccgcctgcaa gacgggaacagctggagcgatgcattcgatgtctggggccagggaactatggtcaccgtgtc gtctgggggcggtggatcgggtggcgggggttcgggggggcggcggctctcagtccgctctt acccaaccggcctcagcctcggggagccccggccagagcgtgaccatttcctgcaccggc acttcatccgacgtgggcggctacaactacgtgtcctggtaccaacagcacccgggaaaggc ccccaagctcatgatctacgacgtgtccaacaggccctcgggagtgtccaaccggttctcgg gttcgaaatcgggaaacacagccagcctgaccatcagcggactgcaggctgaagatgaagc cgactactactgctcctcctacacctcgtcatccacgctctacgtgttcggcactggaactcagc tgactgtgctgggaggggggagggagtgaaattgtgatgacccagtcacccgccactcttagc ctttcacccggtgagcgcgcaaccctgtcttgcagagcctcccaagacatctcaaaatacctta attggtatcaacagaagcccggacaggctcctcgccttctgatctaccacaccagccggctcc attctggaatccctgccaggttcagcggtagcggatctgggaccgactacaccctcactatca gctcactgcagccagaggacttcgctgtctatttctgtcagcaagggaacaccctgccctaca cctttggacagggcaccaagctcgagattaaaggtggaggtggcagcggaggaggtgggt ccggcggtggaggaagccaggtccaactccaagaaagcggaccgggtcttgtgaagccat cagaaactctttcactgacttgtactgtgagcggagtgtctctccccgattacggggtgtcttgg atcagacagccaccggggaagggtctggaatggattggagtgatttggggctctgagactac ttactaccaatcatccctcaagtcacgcgtcaccatctcaaaggacaactctaagaatcaggtg tcactgaaactgtcatctgtgaccgcagccgacaccgccgtgtactattgcgctaagcattact attatggcgggagctacgcaatggattactggggacagggtactctggtcaccgtgtccagca ccactaccccagcaccgaggccacccaccccggctcctaccatcgcctcccagcctctgtcc ctgcgtccggaggcatgtagacccgcagctggtggggccgtgcatacccggggtcttgactt cgcctgcgatatctacatttgggcccctctggctggtacttgcggggtcctgctgctttcactcgt gatcactctttactgtaagcgcggtcggaagaagctgctgtacatctttaagcaacccttcatga ggcctgtgcagactactcaagaggaggacggctgttcatgccggttcccagaggaggagga aggcggctgcgaactgcgcgtgaaattcagccgcagcgcagatgctccagcctaccagcag gggcagaaccagctctacaacgaactcaatcttggtcggagagaggagtacgacgtgctgg acaagcggagaggacgggacccagaaatgggcgggaagccgcgcagaaagaatcccca agagggcctgtacaacgagctccaaaaggataagatggcagaagcctatagcgagattggt atgaaaggggaacgcagaagaggcaaaggccacgacggactgtaccagggactcagcac cgccaccaaggacacctatgacgctcttcacatgcaggccctgccgcctcgg
	816	MALPVTALLLPLALLLHAARPEVQLQQSGPGLVKPSQTLSL TCAISGDSMLSNSDTWNWIRQSPSRGLEWLGRTYHRSTWY DDYASSVRGRVSINVDTSKNQYSLQLNAVTPEDTGVYYCA RVRLQDGNSWSDAFDVWGQGTMVTVSSGGGGSGGGGSG GGGSQSALTQPASASGSPGQSVTISCTGTSSDVGGYNYVS WYQQHPGKAPKLMIYDVSNRPSGVSNRFSGSKSGNTASLT ISGLQAEDEADYYCSSYTSSSTLYVFGTGTQLTVLGGGGSE IVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPGQ APRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFAV YFCQQGNTLPYTFGQGTKLEIKGGGGSGGGGSGGGGSQVQ LQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKG LEWIGVIWGSETTYYQSSLKSRVTISKDNSKNQVSLKLSSV TAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTVSSTTT PAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFAC

		DIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLYIFKQPFM RPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQQ GQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNP QEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGL STATKDTYDALHMQALPPR
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	818	MALPVTALLLPLALLLHAARPQSALTQPASASGSPGQSVTI SCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYDVSNRPSG VSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTLY VFGTGTQLTVLGGGGSEVQLQQSGPGLVKPSQTLSLTCAIS GDSMLSNSDTWNWIRQSPSRGLEWLGRTYHRSTWYDDYA

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Full length CD19-CD22 Dual CAR amino acid	824	MALPVTALLLPLALLLHAARPEVQLQQSGPGLVKPSQTLSL TCAISGDSMLSNSDTWNWIRQSPSRGLEWLGRTYHRSTWY DDYASSVRGRVSINVDTSKNQYSLQLNAVTPEDTGVYYCA RVRLQDGNSWSDAFDVWGQGTMVTVSSGGGGSQSALTQP ASASGSPGQSVTISCTGTSSDVGGYNYVSWYQQHPGKAPK LMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDEADY YCSSYTSSSTLYVFGTGTQLTVLTTTPAPRPPTPAPTIASQPL SLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL LSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRF

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CD22 CAR (with P2A site)	825	MALPVTALLLPLALLLHAARPEVQLQQSGPGLVKPSQTLSL TCAISGDSMLSNSDTWNWIRQSPSRGLEWLGRTYHRSTWY DDYASSVRGRVSINVDTSKNQYSLQLNAVTPEDTGVYYCA RVRLQDGNSWSDAFDVWGQGTMVTVSSGGGGSQSALTQP ASASGSPGQSVTISCTGTSSDVGGYNYVSWYQQHPGKAPK LMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDEADY YCSSYTSSSTLYVFGTGTQLTVLTTTPAPRPPTPAPTIASQPL SLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL LSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRF PEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRRE EYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMA EAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQ ALPPRGSGATNFSLLKQAGDVEENPG
CD19 CAR	826	PMALPVTALLLPLALLLHAARPEIVMTQSPATLSLSPGERA TLSCRASQDISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPA RFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYTFGQG TKLEIKGGGGSGGGGSGGGGSQVQLQESGPGLVKPSETLSL TCTVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYQS SLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCAKHYYY GGSYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPLSL RPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLS LVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPE EEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEY DVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEA YSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQAL PPR
CG#c203		
Full length CD19-CD22	827	atggccttaccagtgaccgccttgctcctgccgctggccttgctgctccacgccgccaggccg gaaattgtgatgacccagtcacccgccactcttagcctttcacccggtgagcgcgcaaccctg tcttgcagagcctcccaagacatctcaaaataccttaattggtatcaacagaagcccggacag

Dual CAR nucleic acid		gctcctcgccttctgatctaccacaccagccggctccattctggaatccctgccaggttcagcg gtagcggatctgggaccgactacaccctcactatcagctcactgcagccagaggacttcgct gtctatttctgtcagcaagggaacaccctgccctacacctttggacagggcaccaagctcgag attaaaggtggaggtggcagcggaggaggtgggtccggcggtggaggaagccaggtcca actccaagaaagcggaccgggtcttgtgaagccatcagaaactctttcactgacttgtactgtg agcggagtgtctctccccgattacggggtgtcttggatcagacagccaccggggaagggtct ggaatggattggagtgatttggggctctgagactacttactaccaatcatccctcaagtcacgc gtcaccatctcaaaggacaactctaagaatcaggtgtcactgaaactgtcatctgtgaccgcag ccgacaccgccgtgtactattgcgctaagcattactattatggcgggagctacgcaatggatta ctggggacagggtactctggtcaccgtgtccagcaccacgacgccagcgccgcgaccacc aacaccggcgcccaccatcgcgtcgcagcccctgtccctgcgcccagaggcgtgccggcc agcggcgggggggcgcagtgcacacgaggggggctggacttcgcctgtgatatctacatctgg gcgcccttggccgggacttgtggggtccttctcctgtcactggttatcacccctttactgcaaacg gggcagaaagaaactcctgtatatattcaaacaaccatttatgagaccagtacaaactactcaa gaggaagatggctgtagctgccgatttccagaagaagaagaaggaggatgtgaactgagag tgaagttcagcaggagcgcagacgcccccgcgtaccagcagggccagaaccagctctata acgagctcaatctaggacgaagagaggagtacgatgttttggacaagagacgtggccggga ccctgagatgggggggaaagccgagaaggaagaaccctcaggaaggcctgtacaatgaact gcagaaagataagatggcggaggcctacagtgagattgggatgaaaggcgagcgccgga ggggcaaggggcacgatggcctttaccagggtctcagtacagccaccaaggacacctacga cgcccttcacatgcaggccctgcccccctcgcggaagcggagctactaacttcagcctgctga agcaggctggagacgtggaggagaaccctggacctatggccctccctgtcaccgccctgct gcttccgctggctcttctgctccacgccgctcggcccgaagtgcagctgcagcagtcagggc ctggcctggtcaagccgtcgcagaccctctccctgacatgcgccattagcggggactccatg ctgagcaactcggacacctggaactggattcggcagtccccttcccggggactcgagtggct cggacgcacctaccatcggagcacttggtacgacgactacgcctcctccgtgagaggtcgc gtgtcgatcaacgtggatacctcgaagaaccagtatagcttgcaactgaacgccgtgacccct gaggataccggagtgtactattgtgcgagagtcaggctgcaagacggaaactcctggtccga cgcatttgatgtctggggacagggtactatggtcacggtgtcatctggaggcggaggatcgca aagcgccctgactcagccggcttcggctagcggttcaccggggcagtccgtgactatctcct gcaccgggacttcctccgacgtgggaggctacaattacgtgtcctggtaccagcaacacccc ggcaaagccccaaagctgatgatctacgacgtcagcaacagacccagcggagtgtccaacc ggttcagcggctccaagtccggcaacaccgcctccctgaccatcagcgggcttcaggccga agatgaggcggattactactgctcctcgtacacctcaagctcaactctgtacgtgttcggcacc ggtactcagctcaccgtgctgaccactaccccagcaccgaggccacccaccccggctccta ccatcgcctcccagcctctgtccctgcgtccggaggcatgtagacccgcagctggtggggcc gtgcatacccggggtcttgacttcgcctgcgatatctacatttgggcccctctggctggtacttg cggggtcctgctgctttcactcgtgatcactctttactgtaagcgcggtcggaagaagctgctgt acatctttaagcaacccttcatgaggcctgtgcagactactcaagaggaggacggctgttcatg ccggttcccagaggaggaggaaggcggctgcgaactgcgcgtgaaattcagccgcagcgc agatgctccagcctaccagcaggggcagaaccagctctacaacgaactcaatcttggtcgga gagaggagtacgacgtgctggacaagcggagaggacgggacccagaaatgggcgggaa gccgcgcagaaagaatccccaagagggcctgtacaacgagctccaaaaggataagatggc agaagcctatagcgagattggtatgaaaggggaacgcagaagaggcaaaggccacgacg gactgtaccagggactcagcaccgccaccaaggacacctatgacgctcttcacatgcaggcc ctgccgcctcgg

Full length CD19-CD22 Dual CAR amino acid	828	MALPVTALLLPLALLLHAARPEIVMTQSPATLSLSPGERAT LSCRASQDISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPAR FSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYTFGQGT KLEIKGGGGSGGGGSGGGGSQVQLQESGPGLVKPSETLSLT CTVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYQSS LKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCAKHYYYG GSYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPLSLR PEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSL VITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEE EEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEY DVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEA YSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQAL PPRGSGATNFSLLKQAGDVEENPGPMALPVTALLLPLALLL HAARPEVQLQQSGPGLVKPSQTLSLTCAISGDSMLSNSDT WNWIRQSPSRGLEWLGRTYHRSTWYDDYASSVRGRVSIN VDTSKNQYSLQLNAVTPEDTGVYYCARVRLQDGNSWSDA FDVWGQGTMVTVSSGGGGSQSALTQPASASGSPGQSVTIS CTGTSSDVGGYNYVSWYQQHPGKAPKLMIYDVSNRPSGV SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTLYVF GTGTQLTVLTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGG AVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRK KLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKF SRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDP EMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRR GKGHDGLYQGLSTATKDTYDALHMQALPPR
CD19 CAR (with P2A site)	829	MALPVTALLLPLALLLHAARPEIVMTQSPATLSLSPGERAT LSCRASQDISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPAR FSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYTFGQGT KLEIKGGGGSGGGGSGGGGSQVQLQESGPGLVKPSETLSLT CTVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYQSS LKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCAKHYYYG GSYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPLSLR PEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSL VITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEE EEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEY DVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEA YSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQAL PPRGSGATNFSLLKQAGDVEENPG
CD22 CAR	830	PMALPVTALLLPLALLLHAARPEVQLQQSGPGLVKPSQTLS LTCAISGDSMLSNSDTWNWIRQSPSRGLEWLGRTYHRSTW YDDYASSVRGRVSINVDTSKNQYSLQLNAVTPEDTGVYYC ARVRLQDGNSWSDAFDVWGQGTMVTVSSGGGGSQSALT QPASASGSPGQSVTISCTGTSSDVGGYNYVSWYQQHPGKA PKLMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDEA DYYCSSYTSSSTLYVFGTGTQLTVLTTTPAPRPPTPAPTIAS QPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCG

		VLLLSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCS CRFPEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLG RREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDK MAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALH MQALPPR
CG#c230		
Full length CD19-CD22 Dual CAR nucleic acid	831	atggcacttcccgtcaccgccctgctgctcccactcgccctccttctgcacgccgcccgcccc gaagtgcagctgcagcagtcaggaccgggcctggtcaaaccttcgcagactctgtccctgac ttgcgctataagcggggactccatgctgagcaattcggacacttggaactggattcgccaaag ccccagccggggtctggaatggctgggaaggacctaccatcgctctacttggtacgacgact acgccagctccgtgcgaggacgcgtgtccatcaacgtggacacctccaagaaccagtactc gcttcaactcaacgcagtgacccctgaagataccggagtctactattgcgcccgcgtgcggct ccaggacgggaactcctggtcggacgctttcgatgtctggggacagggcactatggtcaccg tcagctccggcggcggcggtagccaatcggcgctgacacagccggcttccgcctcgggatc gcctggacagtcggtgaccatctcgtgcactggaacctcctccgacgtgggcggctacaatta tgtgtcatggtaccagcagcacccgggaaaggcccctaagctgatgatctacgacgtgtcca atagacctagcggggtgtcaaacagattctccggatccaaatccggaaacactgcctccctga ccatttccggactgcaggccgaggacgaagccgattactactgctcctcttacacctcctcatc caccctctacgtgtttgggactgggacccagctgaccgtcctcactaccaccccggccccgc ggcccccctacaccggcaccgactattgccagccagcctctctcgctgcggccggaggcctg ccgcccagccgccggcggagccgtgcacacccgcggtctggacttcgcgtgcgatatctac atctgggctccgctggccgggacttgtggcgtgctgctgctgtctctggtcatcacactgtact gcaagcgcggaagaaagaagctgctctacatcttcaagcaacccttcatgcggcctgtgcag accacccaggaagaggatggctgctcctgccggttcccggaggaagaagagggcggatgc gaactgcgcgtgaagttcagccgaagcgccgacgccccggcctaccagcagggccagaa ccaactgtacaacgaactcaacctgggtcggagagaagagtacgacgtgctggacaaaaga cgcggcagggaccccgagatgggcggaaagcctcgccgcaagaacccgcaggagggcc tctacaacgagctgcagaaggacaagatggccgaagcctactcagagatcggcatgaaggg ggagcggaggcgcgggaagggccacgacggtttgtaccaaggactttccactgcgaccaa ggacacctacgatgccctccatatgcaagccctgccgccccggggttccggagctaccaact tctcgctgttgaagcaggccggagatgtcgaggaaaacccgggacctatggccctgccagt gaccgcgctcctgctgcccctggctctgctgcttcacgcggcccggcctgagattgtgatgac tcagagcccggcgaccctgtccctgtccccggggagagagcaaccctgtcgtgccgggc ctcccaagacatctcaaagtacctcaattggtatcagcagaagccaggacaggctccacggtt gctgatctaccacacttcgagactgcactcaggaatccccgcgcggttttccggttccggctcc gggaccgactacaccctgaccatcagctcgctccagcctgaggatttcgcagtgtacttctgtc agcaaggaaacacccttccatacaccttcggacagggtaccaagctggaaatcaagggagg aggaggatctgggggcggtggttccggaggcggtggaagccaagtgcagctccaggaaa gcggacccgggctggtcaagccgagcgaaaccctctcactgacttgtactgtgtccggagtg tccctgcctgactatggagtgtcctggatccgacagccccccggaaagggtctggagtggatt ggggtcatctggggctccgaaactacctactaccagagcagcctcaagagccgggtcaccat ttcaaaggataactccaagaatcaagtgtccctgaagctgtcctcagtgacagccgcagacac cgccgtgtactactgcgccaagcactactactacggaggctcctacgcaatggactactggg gacaaggcactttggtcactgtgtcaagcaccaccaccctgcgcctcggcctcctaccccg gctcccactatcgcgagccagccgctgagcctgcggcctgaggcttgccgaccggccgctg gcggcgccgtgcatactcggggcctcgactttgcctgtgacatctacatctgggcccccctgg

		ccggaacgtgcggagtgctgctgctgtcgctggtcattaccctgtattgcaaacgcggaagga agaagctgttgtacattttcaagcagcccttcatgcgcccggtgcaaactactcaggaggaag atggctgttcctgtcggttccccgaagaggaagaaggcggctgcgagttgagggtcaagttct cccggtccgccgatgctcccgcctaccaacaggggcagaaccagctttataacgaactgaac ctgggcaggagggaggaatatgatgtgttggataagcgccggggccgggacccagaaatg gggggaaagcccagaagaaagaaccctcaagagggactttacaacgaattgcagaaagac aaaatggccgaggcctactccgagattgggatgaagggcgaaagacggagaggaaaggg gcacgacgggctctaccagggactcagcaccgccaccaaagatacctacgacgccctgcat atgcaggcgctgccgccgcgc
Full length CD19-CD22 Dual CAR amino acid	824	MALPVTALLLPLALLLHAARPEVQLQQSGPGLVKPSQTLSL TCAISGDSMLSNSDTWNWIRQSPSRGLEWLGRTYHRSTWY DDYASSVRGRVSINVDTSKNQYSLQLNAVTPEDTGVYYCA RVRLQDGNSWSDAFDVWGQGTMVTVSSGGGGSQSALTQP ASASGSPGQSVTISCTGTSSDVGGYNYVSWYQQHPGKAPK LMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDEADY YCSSYTSSSTLYVFGTGTQLTVLTTTPAPRPPTPAPTIASQPL SLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL LSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRF PEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRRE EYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMA EAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQ ALPPRGSGATNFSLLKQAGDVEENPGPMALPVTALLLPLAL LLHAARPEIVMTQSPATLSLSPGERATLSCRASQDISKYLN WYQQKPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTIS SLQPEDFAVYFCQQGNTLPYTFGQGTKLEIKGGGGSGGGG SGGGGSQVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVS WIRQPPGKGLEWIGVIWGSETTYYQSSLKSRVTISKDNSKN QVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGT LVTVSSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVH TRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLL YIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRS ADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEM GGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGK GHDGLYQGLSTATKDTYDALHMQALPPR
CD22 CAR (with P2A site)	825	MALPVTALLLPLALLLHAARPEVQLQQSGPGLVKPSQTLSL TCAISGDSMLSNSDTWNWIRQSPSRGLEWLGRTYHRSTWY DDYASSVRGRVSINVDTSKNQYSLQLNAVTPEDTGVYYCA RVRLQDGNSWSDAFDVWGQGTMVTVSSGGGGSQSALTQP ASASGSPGQSVTISCTGTSSDVGGYNYVSWYQQHPGKAPK LMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAEDEADY YCSSYTSSSTLYVFGTGTQLTVLTTTPAPRPPTPAPTIASQPL SLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL LSLVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRF PEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRRE EYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMA

		EAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQ ALPPRGSGATNFSLLKQAGDVEENPG
CD19 CAR	826	PMALPVTALLLPLALLLHAARPEIVMTQSPATLSLSPGERA TLSCRASQDISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPA RFSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYTFGQG TKLEIKGGGGSGGGGSGGGGSQVQLQESGPGLVKPSETLSL TCTVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYQS SLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCAKHYYY GGSYAMDYWGQGTLVTVSSTTTPAPRPPTPAPTIASQPLSL RPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLS LVITLYCKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPE EEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEY DVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEA YSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQAL PPR

CD22 and CD19 CDRs of a dual CAR of the disclosure (e.g., a dual CAR molecule comprising (i) a first CAR that binds to CD22 and (ii) a second CAR that binds to CD19) are provided in Table 31.

Table 31: CD22 and CD19 CDR sequences

Identifier	SEQ ID NO	Sequence
CD22 CDRs		
HCDR1 (Kabat)	745	SNSDTWN
HCDR2 (Kabat)	746	RTYHRSTWYDDYASSVRG
HCDR3 (Kabat)	748	VRLQDGNSWSDAFDV
HCDR1 (Chothia)	832	GDSMLSNSD
HCDR2 (Chothia)	833	YHRSTWY
HCDR3 (Chothia)	748	VRLQDGNSWSDAFDV
HCDR1 (IMGT)	834	GDSMLSNSDT
HCDR2 (IMGT)	835	TYHRSTWYD
HCDR3 (IMGT)	836	ARVRLQDGNSWSDAFDV
LCDR1 (Kabat)	95	TGTSSDVGGYNYVS

LCDR2 (Kabat)	96	DVSNRPS
LCDR3 (Kabat)	97	SSYTSSSTLYV
LCDR1 (Chothia)	98	TSSDVGGYNY
LCDR2 (Chothia)	99	DVS
LCDR3 (Chothia)	100	YTSSSTLY
LCDR1 (IMGT)	101	SSDVGGYNY
LCDR2 (IMGT)	99	DVS
LCDR3 (IMGT)	97	SSYTSSSTLYV
CD19 CDRs		
HCDR1 (Kabat)	837	GVSLPDYGVS
HCDR2 (Kabat)	838	VIWGSETTYYSSSLKS
	687	VIWGSETTYYQSSLKS
	839	VIWGSETTYYNSSLKS
HCDR3 (Kabat)	762	HYYYGGSYAMDY
LCDR1	763	RASQDISKYLN
LCDR2	764	HTSRLHS
LCDR3	300	QQGNTLPYT

Table 32 provides nucleotide and amino acid sequence for CD19 and CD22 binding domains of a dual CAR or a tandem CAR disclosed herein, e.g., a dual CAR or a tandem CAR comprising (i) a first CAR that binds to CD22 and (ii) a second CAR that binds to CD19.

Table 32: CD19 and CD22 binding domains

Identifier	SEQ ID NO	Sequence
scFv CAR19 in c201, c203 and tandem CARs c171, c182, c188	840	gaaattgtgatgacccagtcacccgccactcttagcctttcacccggtgagcgcgcaaccctgt cttgcagagcctcccaagacatctcaaaataccttaattggtatcaacagaagcccggacaggc tcctcgccttctgatctaccacaccagccggctccattctggaatccctgccaggttcagcggta gcggatctgggaccgactacaccctcactatcagctcactgcagccagaggacttcgctgtcta tttctgtcagcaagggaacaccctgccctacacctttggacagggcaccaagctcgagattaaa ggtggaggtggcagcggaggaggtgggtccggcggtggaggaagccaggtccaactccaa gaaagcggaccgggtcttgtgaagccatcagaaactctttcactgacttgtactgtgagcggag tgtctctccccgattacggggtgtcttggatcagacagccaccggggaagggtctggaatggat

		tggagtgatttggggctctgagactacttactaccaatcatccctcaagtcacgcgtcaccatctc aaaggacaactctaagaatcaggtgtcactgaaactgtcatctgtgaccgcagccgacaccgc cgtgtactattgcgctaagcattactattatggcgggagctacgcaatggattactggggacagg gtactctggtcaccgtgtccagc
	758	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPG QAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFA VYFCQQGNTLPYTFGQGTKLEIKGGGGSGGGGSGGGGSQV QLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKG LEWIGVIWGSETTYYQSSLKSRVTISKDNSKNQVSLKLSSVT AADTAVYYCAKHYYYGGSYAMDYWGQGTLVTVSS
scFv CAR19 in c224	841	gagattgtcatgactcagtccccggccacactctccctgtcacccggagaaagagcaaccctg agctgcagggcgtcccaggacatctcgaagtacctgaactggtaccagcagaagcctggaca agcaccccgcctcctgatctaccacacctcgcggctgcattcgggaatccccgccagattctca gggagcggatcaggaaccgactacaccctgactatctcgagcctgcaaccagaggatttcgc cgtgtacttctgccagcaaggaaacaccctgccctacacctttggacagggaaccaagctcga gattaaggggggtggtggatcgggaggggtggatcaggaggaggcggctcacaagtcca gctgcaagaatccggtccgggacttgtgaagccgtccgaaaccctgtcactgacttgcactgtg tccggggtgtcattgcccgactacggcgtgagctggattcggcagccccctggaaagggattg gaatggatcggcgtgatctggggttcggaaactacctactatcagtcctcactgaagtcccgcg tgaccatcagcaaggataattccaaaaaccaagtgtctctgaagctctccagcgtcactgccgc cgatactgccgtgtactactgcgccaagcactactattacggcggttcgtacgccatggactact ggggccaagggacactcgtgaccgtgtcatcc
	758	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPG QAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFA VYFCQQGNTLPYTFGQGTKLEIKGGGGSGGGGSGGGGSQV QLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKG LEWIGVIWGSETTYYQSSLKSRVTISKDNSKNQVSLKLSSVT AADTAVYYCAKHYYYGGSYAMDYWGQGTLVTVSS
scFv CAR19 in c227	842	caagtccagctgcaagaatccggtccgggacttgtgaagccgtccgaaaccctgtcactgactt gcactgtgtccggggtgtcattgcccgactacggcgtgagctggattcggcagccccctggaa agggattggaatggatcggcgtgatctggggttcggaaactacctactatcagtcctcactgaa gtcccgcgtgaccatcagcaaggataattccaaaaaccaagtgtctctgaagctctccagcgtc actgccgccgatactgccgtgtactactgcgccaagcactactattacggcggttcgtacgccat ggactactggggacaaggcactcttgtgactgtgtcaagcggcggtggagggagcggtggg ggcggttcaggaggaggcggatcagagatcgtgatgacccaatccccagccaccctgtccct cagccctggagaaagagccaccctgagctgccgggcctcccaggatatcagcaagtacttga actggtaccaacaaaagccggggcaggcgccccggctcctgatctaccacacctcgcgcctc cactcaggtatccccgccagattctcagggagcggctccggtactgactacaccctgactatttc ctcactgcagccagaggactttgccgtgtacttctgccagcagggaaacactctgccgtacacc ttcgggcagggaacgaagcttgaaattaag
	843	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPG KGLEWIGVIWGSETTYYQSSLKSRVTISKDNSKNQVSLKLSS VTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTVSSGG GGSGGGGSGGGGSEIVMTQSPATLSLSPGERATLSCRASQDI

		SKYLNWYQQKPGQAPRLLIYHTSRLHSGIPARFSGSGSGTD YTLTISSLQPEDFAVYFCQQGNTLPYTFGQGTKLEIK
scFv CAR19 in c230	844	gagattgtgatgactcagagcccggcgaccctgtccctgtcccccggggagagagcaaccct gtcgtgccgggcctcccaagacatctcaaagtacctcaattggtatcagcagaagccaggaca ggctccacggttgctgatctaccacacttcgagactgcactcaggaatccccgcgcggttttcc ggttccggctccgggaccgactacaccctgaccatcagctcgctccagcctgaggatttcgca gtgtacttctgtcagcaaggaaacacccttccatacaccttcggacagggtaccaagctggaaa tcaagggaggaggaggatctgggggcggtggttccggaggcggtggaagccaagtgcagc tccaggaaagcggacccgggctggtcaagccgagcgaaaccctctcactgacttgtactgtgt ccggagtgtccctgcctgactatggagtgtcctggatccgacagccccccggaaagggtctgg agtggattggggtcatctggggctccgaaactacctactaccagagcagcctcaagagccgg gtcaccatttcaaaggataactccaagaatcaagtgtccctgaagctgtcctcagtgacagccg cagacaccgccgtgtactactgcgccaagcactactactacggaggctcctacgcaatggact actggggacaaggcactttggtcactgtgtcaagc
	758	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPG QAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFA VYFCQQGNTLPYTFGQGTKLEIKGGGGSGGGGSGGGGSQV QLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKG LEWIGVIWGSETTYYQSSLKSRVTISKDNSKNQVSLKLSSVT AADTAVYYCAKHYYYGGSYAMDYWGQGTLVTVSS
ScFVCAR22 in c201 and c203	845	gaagtgcagctgcagcagtcagggcctggcctggtcaagccgtcgcagaccctctccctgac atgcgccattagcggggactccatgctgagcaactcggacacctggaactggattcggcagtc cccttcccggggactcgagtggctcggacgcacctaccatcggagcacttggtacgacgacta cgcctcctccgtgagaggtcgcgtgtcgatcaacgtggatacctcgaagaaccagtatagcttg caactgaacgccgtgacccctgaggataccggagtgtactattgtgcgagagtcaggctgcaa gacggaaactcctggtccgacgcatttgatgtctggggacagggtactatggtcacggtgtcat ctggaggcggaggatcgcaaagcgccctgactcagccggcttcggctagcggttcaccggg gcagtccgtgactatctcctgcaccgggacttcctccgacgtgggaggctacaattacgtgtcct ggtaccagcaacaccccggcaaagccccaaagctgatgatctacgacgtcagcaacagacc cagcggagtgtccaaccggttcagcggctccaagtccggcaacaccgcctccctgaccatca gcgggcttcaggccgaagatgaggcggattactactgctcctcgtacacctcaagctcaactct gtacgtgttcggcaccggtactcagctcaccgtgctg
	846	EVQLQQSGPGLVKPSQTLSLTCAISGDSMLSNSDTWNWIRQ SPSRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQ YSLQLNAVTPEDTGVYYCARVRLQDGNSWSDAFDVWGQG TMVTVSSGGGGSQSALTQPASASGSPGQSVTISCTGTSSDVG GYNYVSWYQQHPGKAPKLMIYDVSNRPSGVSNRFSGSKSG NTASLTISGLQAEDEADYYCSSYTSSSTLYVFGTGTQLTVL
ScFVCAR22 in 230	847	gaagtgcagctgcagcagtcaggaccgggcctggtcaaaccttcgcagactctgtccctgact tgcgctataagcggggactccatgctgagcaattcggacacttggaactggattcgccaaagc cccagccggggtctggaatggctgggaaggacctaccatcgctctacttggtacgacgactac gccagctccgtgcgaggacgcgtgtccatcaacgtggacacctccaagaaccagtactcgctt caactcaacgcagtgacccctgaagataccggagtctactattgcgcccgcgtgcggctccag gacgggaactcctggtcggacgctttcgatgtctggggacagggcactatggtcaccgtcagc tccggcggcggcggtagccaatcggcgctgacacagccggcttccgcctcgggatcgcctg gacagtcggtgaccatctcgtgcactggaacctcctccgacgtgggcggctacaattatgtgtc

		atggtaccagcagcacccgggaaaggcccctaagctgatgatctacgacgtgtccaatagacc tagcggggtgtcaaacagattctccggatccaaatccggaaacactgcctccctgaccatttcc ggactgcaggccgaggacgaagccgattactactgctcctcttacacctcctcatccaccctcta cgtgtttgggactgggacccagctgaccgtcctc
	846	EVQLQQSGPGLVKPSQTLSLTCAISGDSMLSNSDTWNWIRQ SPSRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQ YSLQLNAVTPEDTGVYYCARVRLQDGNSWSDAFDVWGQG TMVTVSSGGGGSQSALTQPASASGSPGQSVTISCTGTSSDVG GYNYVSWYQQHPGKAPKLMIYDVSNRPSGVSNRFSGSKSG NTASLTISGLQAEDEADYYCSSYTSSSTLYVFGTGTQLTVL
ScFVCAR2 2 in 171, c182	848	gaagtgcagcttcaacaatcaggaccaggactcgtcaaaccatcacagaccctctccctcacat gtgccatctccggggactccatgttgagcaattccgacacttggaattggattagacaaagccc gtcccggggtctggaatggttgggacgcacctaccaccggtctacttggtacgacgactacgc gtcatccgtgcggggaagagtgtccatcaacgtggacacctccaagaaccagtacagcctgc agcttaatgccgtgactcctgaggatacgggcgtctactactgcgcccgcgtccgcctgcaag acgggaacagctggagcgatgcattcgatgtctggggccagggaactatggtcaccgtgtcgt ctgggggcggtggatcgggtggcgggggttcgggggcggcggctctcagtccgctcttac ccaaccggcctcagcctcggggagccccggccagagcgtgaccatttcctgcaccggcactt catccgacgtgggcggctacaactacgtgtcctggtaccaacagcacccgggaaaggccccc aagctcatgatctacgacgtgtccaacaggccctcgggagtgtccaaccggttctcgggttcga aatcgggaaacacagccagcctgaccatcagcggactgcaggctgaagatgaagccgacta ctactgctcctcctacacctcgtcatccacgctctacgtgttcggcactggaactcagctgactgt gctg
	753	EVQLQQSGPGLVKPSQTLSLTCAISGDSMLSNSDTWNWIRQ SPSRGLEWLGRTYHRSTWYDDYASSVRGRVSINVDTSKNQ YSLQLNAVTPEDTGVYYCARVRLQDGNSWSDAFDVWGQG TMVTVSSGGGGSGGGGSGGGGSQSALTQPASASGSPGQSV TISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYDVSNRPSG VSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTSSSTLYV FGTGTQLTVL
ScFVCAR2 2 in c188	849	cagtccgctcttacccaaccggcctcagcctcggggagccccggccagagcgtgaccatttcc tgcaccggcacttcatccgacgtgggcggctacaactacgtgtcctggtaccaacagcacccg ggaaaggcccccaagctcatgatctacgacgtgtccaacaggccctcgggagtgtccaaccg gttctcgggttcgaaatcgggaaacacagccagcctgaccatcagcggactgcaggctgaag atgaagccgactactactgctcctcctacacctcgtcatccacgctctacgtgttcggcactgga actcagctgactgtgctgggcggaggaggctccgaagtgcagcttcaacaatcaggaccagg actcgtcaaaccatcacagaccctctccctcacatgtgccatctccggggactccatgttgagca attccgacacttggaattggattagacaaagcccgtcccggggtctggaatggttgggacgca cctaccaccggtctacttggtacgacgactacgcgtcatccgtgcggggaagagtgtccatcaa cgtggacacctccaagaaccagtacagcctgcagcttaatgccgtgactcctgaggatacggg cgtctactactgcgcccgcgtccgcctgcaagacgggaacagctggagcgatgcattcgatgt ctggggccagggaactatggtcaccgtgtcgtct
	850	QSALTQPASASGSPGQSVTISCTGTSSDVGGYNYVSWYQQH PGKAPKLMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAE DEADYYCSSYTSSSTLYVFGTGTQLTVLGGGGSEVQLQQSG PGLVKPSQTLSLTCAISGDSMLSNSDTWNWIRQSPSRGLEW

		LGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSLQLNAV TPEDTGVYYCARVRLQDGNSWSDAFDVWGQGTMVTVSS
ScFVCAR2 2 in c224	851	cagtccgctctgactcagccggcctcagcttcggggtcccctggtcaaagcgtcactatttcctg taccggaacctcatcagacgtgggcggctacaattacgtgtcctggtaccaacagcaccccgg aaaggctcctaagcttatgatctacgacgtgtccaaccggccgtcaggagtgtccaacagattct ccggctccaagagcggaaacactgccagcttgaccattagcggcttgcaggccgaggacga agccgactactactgctctagctacacatcctcgtctaccctctacgtgtttggaacggggaccc agctgactgtgctcgggggtggaggatcagaggtgcaactccagcagtccggtcctggcctc gtgaaaccgtcccaaaccctgtccctgacttgcgccatctcgggcgactccatgctgtccaattc cgacacctggaactggattagacaatcgcctagccggggactcgaatggctgggccggacct accaccggtccacgtggtatgacgactacgcaagctccgtccggggaagggtgtccattaacg tcgatacctccaagaaccagtacagccttcagctgaacgctgtgacccccgaggataccggcg tctactactgtgcaagagtgcgattgcaggatggaaactcgtggtcggacgcattcgatgtctg gggacagggaactatggtgaccgtgtcctcg
	850	QSALTQPASASGSPGQSVTISCTGTSSDVGGYNYVSWYQQH PGKAPKLMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAE DEADYYCSSYTSSSTLYVFGTGTQLTVLGGGGSEVQLQQSG PGLVKPSQTLSLTCAISGDSMLSNSDTWNWIRQSPSRGLEW LGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSLQLNAV TPEDTGVYYCARVRLQDGNSWSDAFDVWGQGTMVTVSS
ScFVCAR2 2 in c227	852	cagtccgctctgactcagccggcctcagcttcggggtcccctggtcaaagcgtcactatttcctg taccggaacctcatcagacgtgggcggctacaattacgtgtcctggtaccaacagcaccccgg aaaggctcctaagcttatgatctacgacgtgtccaaccggccgtcaggagtgtccaacagattct ccggctccaagagcggaaacactgccagcttgaccattagcggcttgcaggccgaggacga agccgactactactgctctagctacacatcctcgtctaccctctacgtgtttggaacggggaccc agctgactgtgctcgggggtggaggatcagaggtgcaactccagcagtccggtcctggcctc gtgaaaccgtcccaaaccctgtccctgacttgcgccatctcgggcgactccatgctgtccaattc cgacacctggaactggattagacaatcgcctagccggggactcgaatggctgggccggacct accaccggtccacgtggtatgacgactacgcaagctccgtccggggaagggtgtccattaacg tcgatacctccaagaaccagtacagccttcagctgaacgctgtgacccccgaggataccggcg tctactactgtgcaagagtgcgattgcaggatggaaactcgtggtcggacgcattcgatgtctg gggacagggaactatggtcactgtgtcctcc
	850	QSALTQPASASGSPGQSVTISCTGTSSDVGGYNYVSWYQQH PGKAPKLMIYDVSNRPSGVSNRFSGSKSGNTASLTISGLQAE DEADYYCSSYTSSSTLYVFGTGTQLTVLGGGGSEVQLQQSG PGLVKPSQTLSLTCAISGDSMLSNSDTWNWIRQSPSRGLEW LGRTYHRSTWYDDYASSVRGRVSINVDTSKNQYSLQLNAV TPEDTGVYYCARVRLQDGNSWSDAFDVWGQGTMVTVSS

Table 33 provides nucleotide and amino acid sequences for additional CAR components, e.g., signal peptide, linkers and P2A sites, that can be used in a CAR molecule, e.g., a dual CAR molecule described herein (for example, a dual CAR molecule comprising (i) a first CAR that binds to CD22 and (ii) a second CAR that binds to CD19).

Table 33: Additional CAR components

Identifier	SEQ ID NO	Sequence
Signal peptide for CAR22 in c201, c203, and tandem CARs c171, c182, c188	853	atggccctccctgtcaccgccctgctgcttccgctggctcttctgctccacgccgctcggcc
	2	MALPVTALLLPLALLLHAARP
Signal peptide in tandem CARs c224, c227	854	atggccctgcccgtgactgcgctcctgcttccgttggccctgctcctgcatgccgccagact
	2	MALPVTALLLPLALLLHAARP
Signal peptide CAR19 in c201 and c203	855	atggccttaccagtgaccgccttgctcctgccgctggccttgctgctccacgccgccaggccg
	2	MALPVTALLLPLALLLHAARP
Signal peptide CAR22 in c230	856	atggcacttcccgtcaccgccctgctgctcccactcgccctccttctgcacgccgcccgccc
	2	MALPVTALLLPLALLLHAARP
Signal peptide CAR19 in c230	857	atggccctgccagtgaccgcgctcctgctgcccctggctctgctgcttcacgcggcccggcct
	2	MALPVTALLLPLALLLHAARP
CD8 hinge and transmembrane CAR22 in c201 and c203, and in tandem CARs c171, c182, c188, c224, c227	858	accactaccccagcaccgaggccacccaccccggctcctaccatcgcctcccagcctctgtccctgcgtccggaggcatgtagacccgcagctggtggggccgtgcatacccggggtcttgacttcgcctgcgatatctacatttgggcccctctggctggtacttgcggggtcctgctgctttcactcgtgatcactctttactgt
	202	TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
CD8 hinge and transmembrane CAR22 In c230	859	actaccaccccggccccgcggcccccctacaccggcaccgactattgccagccagcctctctcgctgcggccggaggcctgccgcccagccgccggcggagccgtgcacacccgcggtctggacttcgcgtgcgatatctacatctgggctccgctggccgggacttgtggcgtgctgctgctgtctctggtcatcacactgtactgc
	202	TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
CD8 hinge and transmembrane CAR19 in c201 and c203	860	accacgacgccagcgccgcgaccaccaacaccggcgcccaccatcgcgtcgcagcccctgtccctgcgcccagaggcgtgccggccagcggcgggggggcgcagtgcacacgaggggggctggacttcgcctgtgatatctacatctgggcgcccttggccgggacttgtggggtccttctcctgtcactggttatcacccctttactgc
	202	TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
CD8 hinge and transmembrane CAR19 In c230	861	accaccacccctgcgcctcggcctcctaccccggctcccactatcgcgagccagccgctgagcctgcggcctgaggcttgccgaccggccgctggcggcgccgtgcatactcggggcctcgactttgcctgtgacatctacatctgggccccctggccggaacgtgcggagtgctgctgctgtcgctggtcattaccctgtattgc
	202	TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC

4-1BB CAR22 in c201 and c203, and tandem CARs c171, c182, c188, c224, c227	862	aagcgcggtcggaagaagctgctgtacatctttaagcaacccttcatgaggcctgtgcag actactcaagaggaggacggctgttcatgccggttcccagaggaggaggaaggcggct gcgaactg
	14	KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGG CEL
4-1BB CAR19 in c201 and c203	15	aaacggggcagaaagaaactcctgtatatattcaaacaaccatttatgagaccagtacaaa ctactcaagaggaagatggctgtagctgccgatttccagaagaagaagaaggaggatgt gaactg
	14	KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGG CEL
4-1BB CAR22 in c230	863	aagcgcggaagaaagaagctgctctacatcttcaagcaacccttcatgcggcctgtgcag accacccaggaagaggatggctgctcctgccggttcccggaggaagaagagggcgga tgcgaactg
	14	KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGG CEL
4-1BB CAR19 in c230	864	aaacgcggaaggaagaagctgttgtacattttcaagcagcccttcatgcgcccggtgcaa actactcaggaggaagatggctgttcctgtcggttccccgaagaggaagaaggcggctg cgagttg
	14	KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGG CEL
CD3zeta CAR22 in c201 and c203, and tandem CARs 171, c182, c188, c224, c227	865	cgcgtgaaattcagccgcagcgcagatgctccagcctaccagcaggggcagaaccagc tctacaacgaactcaatcttggtcggagagaggagtacgacgtgctggacaagcggaga ggacgggacccagaaatgggcgggaagccgcgcagaaagaatccccaagagggcct gtacaacgagctccaaaaggataagatggcagaagcctatagcgagattggtatgaaag gggaacgcagaagaggcaaaggccacgacggactgtaccagggactcagcaccgcc accaaggacacctatgacgctcttcacatgcaggccctgccgcctcgg
	20	RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKR RGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIG MKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
CD3zeta CAR19 in c201 and c203	21	agagtgaagttcagcaggagcgcagacgcccccgcgtaccagcagggccagaaccag ctctataacgagctcaatctaggacgaagagaggagtacgatgttttggacaagagacgt ggccgggaccctgagatgggggggaaagccgagaaggaagaaccctcaggaaggcct gtacaatgaactgcagaaagataagatggcggaggcctacagtgagattgggatgaaag gcgagcgccggaggggcaaggggcacgatggcctttaccagggtctcagtacagcca ccaaggacacctacgacgcccttcacatgcaggccctgcccctcgc
	20	RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKR RGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIG MKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
CD3zeta CAR22 in c230	866	cgcgtgaagttcagccgaagcgccgacgccccggcctaccagcagggccagaaccaa ctgtacaacgaactcaacctgggtcggagagaagagtacgacgtgctggacaaaagac gcggcagggaccccgagatgggcggaaagcctcgccgcaagaacccgcaggaggg cctctacaacgagctgcagaaggacaagatggccgaagcctactcagagatcggcatg aagggggagcggaggcgcgggaagggccacgacggtttgtaccaaggactttccact gcgaccaaggacacctacgatgccctccatatgcaagccctgccgccccgg

	20	RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKR RGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIG MKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
CD3zeta CAR19 in c230	867	agggtcaagttctcccggtccgccgatgctcccgcctaccaacaggggcagaaccagct ttataacgaactgaacctgggcaggagggaggaatatgatgtgttggataagcgccggg gccgggacccagaaatgggggggaaagcccagaagaaagaaccctcaagagggacttt acaacgaattgcagaaagacaaaatggccgaggcctactccgagattgggatgaaggg cgaaagacggagaggaaaggggcacgacgggctctaccagggactcagcaccgcca ccaaagatacctacgacgccctgcatatgcaggcgctgccgccgcgc
	20	RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKR RGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIG MKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
Linker between scFVs in c171	868	ttggcagaagccgccgcgaaa
	869	LAEAAAK
Linker between scFVs in c182, c188	870	ggtggaggtggcagcggaggaggtgggtccggcggtggaggaagc
	104	GGGGSGGGGSGGGGS
Linker between scFVs in c224	871	ggcggaggcgggagcggaggaggaggctctggcggaggaggaagc
	104	GGGGSGGGGSGGGGS
Linker between scFVs in c227	872	ggcggtggaggctcgggggggggcggctcaggaggaggcggctca
	104	GGGGSGGGGSGGGGS
P2A in c201, c203	873	ggaagcggagctactaacttcagcctgctgaagcaggctggagacgtggaggagaacc ctggacct
	874	GSGATNFSLLKQAGDVEENPGP
P2A in c230	875	ggttccggagctaccaacttctcgctgttgaagcaggccggagatgtcgaggaaaaccc gggacct
	874	GSGATNFSLLKQAGDVEENPGP
Gly4Ser linker	876	Ggtggaggtggcagc
	877	GGGGS

In some embodiments, the CAR-expressing immune effector cell described herein can further comprise a second CAR, e.g., a second CAR that includes a different antigen binding domain, e.g., to the same target (e.g., a target described above) or a different target. In some embodiments, the second CAR includes an antigen binding domain to a target expressed on the same cancer cell type as the target of the first CAR. In some embodiments, the CAR-expressing immune effector cell comprises a first CAR that targets a first antigen and includes an intracellular signaling domain having a costimulatory signaling domain but not a primary signaling domain, and a second CAR that targets a second, different, antigen and includes an intracellular signaling domain having a primary signaling domain but not a costimulatory signaling domain. While not wishing to be bound by theory, placement of a costimulatory

signaling domain, e.g., 4-1BB, CD28, CD27, or OX-40, onto the first CAR, and the primary signaling domain, e.g., CD3 zeta, on the second CAR can limit the CAR activity to cells where both targets are expressed. In some embodiments, the CAR expressing immune effector cell comprises a first CAR that includes an antigen binding domain that targets, e.g., a target described above, a transmembrane domain and a costimulatory domain and a second CAR that targets an antigen other than antigen targeted by the first CAR (e.g., an antigen expressed on the same cancer cell type as the first target) and includes an antigen binding domain, a transmembrane domain and a primary signaling domain. In another embodiment, the CAR expressing immune effector cell comprises a first CAR that includes an antigen binding domain that targets, e.g., a target described above, a transmembrane domain and a primary signaling domain and a second CAR that targets an antigen other than antigen targeted by the first CAR (e.g., an antigen expressed on the same cancer cell type as the first target) and includes an antigen binding domain to the antigen, a transmembrane domain and a costimulatory signaling domain.

In some embodiments, the CAR-expressing immune effector cell comprises a CAR described herein, e.g., a CAR to a target described above, and an inhibitory CAR. In some embodiments, the inhibitory CAR comprises an antigen binding domain that binds an antigen found on normal cells but not cancer cells, e.g., normal cells that also express the target. In some embodiments, the inhibitory CAR comprises the antigen binding domain, a transmembrane domain and an intracellular domain of an inhibitory molecule. For example, the intracellular domain of the inhibitory CAR can be an intracellular domain of PD1, PD-L1, CTLA-4, TIM-3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, or TGFR beta.

In some embodiments, an immune effector cell (e.g., T cell, NK cell) comprises a first CAR comprising an antigen binding domain that binds to a tumor antigen as described herein, and a second CAR comprising a PD1 extracellular domain or a fragment thereof.

In some embodiments, the cell further comprises an inhibitory molecule as described above.

In some embodiments, the second CAR in the cell is an inhibitory CAR, wherein the inhibitory CAR comprises an antigen binding domain, a transmembrane domain, and an intracellular domain of an inhibitory molecule. The inhibitory molecule can be chosen from one

or more of: PD1, PD-L1, CTLA-4, TIM-3, LAG-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, TGFR beta, CEACAM-1, CEACAM-3, and CEACAM-5. In some embodiments, the second CAR molecule comprises the extracellular domain of PD1 or a fragment thereof.

In embodiments, the second CAR molecule in the cell further comprises an intracellular signaling domain comprising a primary signaling domain and/or an intracellular signaling domain.

In other embodiments, the intracellular signaling domain in the cell comprises a primary signaling domain comprising the functional domain of CD3 zeta and a costimulatory signaling domain comprising the functional domain of 4-1BB.

In some embodiments, the antigen binding domain of the first CAR molecule comprises a scFv and the antigen binding domain of the second CAR molecule does not comprise a scFv. For example, the antigen binding domain of the first CAR molecule comprises a scFv and the antigen binding domain of the second CAR molecule comprises a camelid VHH domain.

Conformation of CARs

In the embodiments contemplated herein, it is appreciated that the conformation of one or more CARs could be modulated by the vectors described herein above. Accordingly, these conformations are described below in relation to the CAR-expressing cell.

Split CAR

In some embodiments, the CAR-expressing cell uses a split CAR. The split CAR approach is described in more detail in publications WO2014/055442 and WO2014/055657. Briefly, a split CAR system comprises a cell expressing a first CAR having a first antigen binding domain and a costimulatory domain (e.g., 41BB), and the cell also expresses a second CAR having a second antigen binding domain and an intracellular signaling domain (e.g., CD3 zeta). When the cell encounters the first antigen, the costimulatory domain is activated, and the cell proliferates. When the cell encounters the second antigen, the intracellular signaling domain is activated and cell-killing activity begins. Thus, the CAR-expressing cell is only fully activated in the presence of both antigens.

Multiple CAR

In some aspects, the CAR-expressing cell described herein can further comprise a second CAR, e.g., a second CAR that includes a different antigen binding domain, e.g., to the same target or a different target (e.g., a target other than a cancer associated antigen described herein or a different cancer associated antigen described herein). In some embodiments, the second CAR includes an antigen binding domain to a target expressed the same cancer cell type as the cancer associated antigen. In some embodiments, the CAR-expressing cell comprises a first CAR that targets a first antigen and includes an intracellular signaling domain having a costimulatory signaling domain but not a primary signaling domain, and a second CAR that targets a second, different, antigen and includes an intracellular signaling domain having a primary signaling domain but not a costimulatory signaling domain. While not wishing to be bound by theory, placement of a costimulatory signaling domain, e.g., 4-1BB, CD28, CD27 or OX-40, onto the first CAR, and the primary signaling domain, e.g.,CD3 zeta, on the second CAR can limit the CAR activity to cells where both targets are expressed. In some embodiments, the CAR expressing cell comprises a first cancer associated antigen CAR that includes an antigen binding domain that binds a target antigen described herein, a transmembrane domain and a costimulatory domain and a second CAR that targets a different target antigen (e.g., an antigen expressed on that same cancer cell type as the first target antigen) and includes an antigen binding domain, a transmembrane domain and a primary signaling domain. In another embodiment, the CAR expressing cell comprises a first CAR that includes an antigen binding domain that binds a target antigen described herein, a transmembrane domain and a primary signaling domain and a second CAR that targets an antigen other than the first target antigen (e.g., an antigen expressed on the same cancer cell type as the first target antigen) and includes an antigen binding domain to the antigen, a transmembrane domain and a costimulatory signaling domain.

In some embodiments, the claimed invention comprises a first and second CAR, wherein the antigen binding domain of one of said first CAR said second CAR does not comprise a variable light domain and a variable heavy domain. In some embodiments, the antigen binding domain of one of said first CAR said second CAR is an scFv, and the other is not an scFv. In some embodiments, the antigen binding domain of one of said first CAR said second CAR comprises a single VH domain, e.g., a camelid, shark, or lamprey single VH domain, or a single VH domain derived from a human or mouse sequence. In some embodiments, the antigen

binding domain of one of said first CAR said second CAR comprises a nanobody. In some embodiments, the antigen binding domain of one of said first CAR said second CAR comprises a camelid VHH domain.

Once the methods described herein are performed, various assays can be used to evaluate the activity of, for e.g., the ability to expand T cells following antigen stimulation, sustain T cell expansion in the absence of re-stimulation, and anti-cancer activities in appropriate in vitro and animal models. Assays to evaluate the effects of a CAR of the present invention are known to those of skill in the art and generally described below.

Western blot analysis of CAR expression in primary T cells can be used to detect the presence of monomers and dimers. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Very briefly, T cells (1:1 mixture of $CD4^+$ and $CD8^+$ T cells) expressing the CARs are expanded *in vitro* for more than 10 days followed by lysis and SDS-PAGE under reducing conditions. CARs containing the full length TCR-ζ cytoplasmic domain and the endogenous TCR-ζ chain are detected by western blotting using an antibody to the TCR-ζ chain. The same T cell subsets are used for SDS-PAGE analysis under non-reducing conditions to permit evaluation of covalent dimer formation.

In vitro expansion of CAR^+ T cells following antigen stimulation can be measured by flow cytometry.

Sustained CAR^+ T cell expansion in the absence of re-stimulation can also be measured. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). Briefly, mean T cell volume (fl) is measured on day 8 of culture using a Coulter Multisizer III particle counter, a Nexcelom Cellometer Vision or Millipore Scepter, following stimulation with αCD3/αCD28 coated magnetic beads on day 0, and transduction with the indicated CAR on day 1.

Animal models can also be used to measure a CART activity. For example, xenograft model using human a cancer associated antigen described herein-specific CAR^+ T cells to treat a primary human pre-B ALL in immunodeficient mice can be used. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009).

Dose dependent CAR treatment response can be evaluated. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009). For example, peripheral blood is obtained 35–70 days after establishing leukemia in mice injected on day 21 with CAR T cells, an equivalent number of mock-transduced T cells, or no T cells. Mice from each group are randomly bled for

determination of peripheral blood a cancer associate antigen as described herein^{+} ALL blast counts and then killed on days 35 and 49. The remaining animals are evaluated on days 57 and 70.

Assessment of cell proliferation and cytokine production has been previously described, *e.g.*, at Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009).
Cytotoxicity can be assessed by a standard 51Cr-release assay. See, *e.g.*, Milone *et al.*, Molecular Therapy 17(8): 1453-1464 (2009

Imaging technologies can be used to evaluate specific trafficking and proliferation of CARs in tumor-bearing animal models. Such assays have been described, for example, in Barrett *et al.*, Human Gene Therapy 22:1575-1586 (2011).

Other assays, including those described in the Example section herein as well as those that are known in the art can also be used to evaluate the CARs described herein.

Anti-CD28 Antibody Molecules

In some embodiments, the anti-CD28 antibody, e.g., an anti-CD28 antibody to be used in a multispecific binding molecule described herein, comprises at least one antigen-binding region, e.g., a variable region or an antigen-binding fragment thereof, from anti-CD28 (2) as described in **Table 19.** In some embodiments, the anti-CD28 antibody molecule comprises one or two variable regions from anti-CD28 (2), as described in **Table 19**. In some embodiments, the anti-CD28 antibody comprises a heavy chain variable region (VH) comprising a heavy chain complementarity determining region 1 (HCDR1), a HCDR2, and a HCDR3, and a light chain variable region (VL) comprising a light chain complementarity determining region 1 (LCDR1), a LCDR2, and a LCDR3, wherein the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 comprise the amino acid sequences of SEQ ID NOs: 538, 539, 540, 530, 531, and 532, respectively; the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 comprise the amino acid sequences of SEQ ID NOs: 541, 539, 540, 530, 531, and 532, respectively; the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 comprise the amino acid sequences of SEQ ID NOs: 542, 543, 540, 533, 534, and 535, respectively; or the HCDR1, HCDR2, HCDR3, LCDR1,

LCDR2, and LCDR3 comprise the amino acid sequences of SEQ ID NOs: 544, 545, 546, 536, 534, and 532, respectively.

In some embodiments, the anti-CD28 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 547 or 548, or a sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity to SEQ ID NO: 547 or 548. In some embodiments, the anti-CD28 antibody comprises a VL comprising the amino acid sequence of SEQ ID NO: 537, or a sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity thereto. In some embodiments, the anti-CD28 antibody comprises a VH and a VL comprising the amino acid sequences of SEQ ID NOs: 547 and 537, respectively, or a sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity to any of the aforesaid sequences. In some embodiments, the anti-CD28 antibody comprises a VH and a VL comprising the amino acid sequences of SEQ ID NOs: 548 and 537, respectively, or a sequence having at least about 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% sequence identity to any of the aforesaid sequences.

It is understood that an anti-CD28 antibody described herein can be used in the context of a multispecific binding molecule, e.g., with an additional binding domain, e.g., an anti-CD3 binding domain described herein. It is also understood that anti-CD28 antibody described herein can be used in other contexts, e.g., as a monospecific antibody.

Cell activation agents

In some embodiments, the cell activation agent is a T cell stimulating compound, an anti-idiotype antibody to a CAR antigen binding domain, and/or a tumor antigen. In some embodiments, the T-cell stimulating compound is IL-2, IL-15, anti-CD2 mAb, anti-CD3 mAb, anti-CD28 mAb, neo-antigen peptides, peptides from shared antigens such as TRP2, gp100, tumor cell lysate, CD19, CD20, CD22, ROR1, mesothelin, CD33/IL3Ra, c-Met, PSMA, Glycolipid F77, EGFRvIII, GD-2, NY-ESO-1 TCR, and/or MAGE A3 TCR. In some embodiments, the cell activation agent comprises a CD3/TCR complex and/or an agent that stimulates a costimulatory molecule and/or growth factor receptor, optionally, wherein the cell activation agent is a multispecific binding molecule comprising an agent that stimulates a

CD3/TCR complex and an agent that stimulates a costimulatory molecule and/or growth factor receptor.

In some embodiments, the agent that stimulates a CD3/TCR complex is an agent that stimulates CD3. In some embodiments, the agent that stimulates CD3 comprises one or more of a CD3 or TCR antigen binding domain, such as but not limited to an anti-CD3 or anti-TCR antibody or an antibody fragment comprising one or more CDRs, heavy chain, and/or light chain thereof.

Anti-CD3 antibody sequences and methods of making such antibodies are known in the art. Non-limiting examples of anti-CD3 antibody sequences, along with the relevant CDR, heavy chain, and light chain sequences are provided in **Table 19**. In some embodiments, the anti-CD3 binding domain comprises a VH and a VL comprising the amino acid sequences of SEQ ID NOs: 437 and 427, respectively. In some embodiments, the anti-CD3 binding domain comprises a VH and a VL comprising the amino acid sequences of SEQ ID NOs: 456 and 445, respectively. In some embodiments, the anti-CD3 binding domain comprises a VH and a VL comprising the amino acid sequences of SEQ ID NOs: 457 and 446, respectively. In some embodiments, the anti-CD3 binding domain comprises a VH and a VL comprising the amino acid sequences of SEQ ID NOs: 475 and 467, respectively. In some embodiments, the anti-CD3 binding domain comprises a VH and a VL comprising the amino acid sequences of SEQ ID NOs: 476 and 468, respectively. In some embodiments, the anti-CD3 binding domain comprises a VH and a VL comprising the amino acid sequences of SEQ ID NOs: 494 and 484, respectively

Anti-TCR antibody sequences and methods of making such antibodies are known in the art. Non-limiting examples of anti-TCR antibody sequences, along with the relevant CDR, heavy chain, and light chain sequences are provided in **Table 19**.

In some embodiments, the agent that stimulates a costimulatory molecule and/or growth factor receptor is an agent that stimulates CD28, ICOS, CD27, CD25, 4-1BB, IL6RA, IL6RB, or CD2. In some embodiments, the agent that stimulates a costimulatory molecule and/or growth factor receptor comprises one or more of a CD28, ICOS, CD27, CD25, 4-1BB, IL6RB, and/or CD2 antigen binding domain, such as but not limited to an anti- CD28, anti-ICOS, anti-CD27, anti-CD25, anti-4-1BB, anti-IL6RA, anti-IL6RB, or anti-CD2 antibody or an antibody fragment comprising one or more CDRs, heavy chain, and/or light chain thereof.

Anti-CD28 antibody sequences and methods of making such antibodies are known in the art. Non-limiting examples of anti-CD28 antibody sequences, along with the relevant CDR, VH, VL, HC and LC sequences are provided in **Table 19**.

Anti-ICOS antibody sequences and methods of making such antibodies are known in the art. Non-limiting examples of anti-ICOS antibody sequences, along with the relevant CDR, VH, VL, and LC sequences are provided in **Table 19**.

Anti-CD27 antibody sequences and methods of making such antibodies are known in the art. Non-limiting examples of anti-CD27 antibody sequences, along with the relevant CDR, VH, and VL sequences are provided in **Table 19**.

Anti-CD25 antibody sequences and methods of making such antibodies are known in the art. Non-limiting examples of anti-CD25 antibody sequences, along with the relevant CDR, VH, VL, HC, and LC sequences are provided in **Table 19**.

Anti-4-1BB antibody sequences and methods of making such antibodies are known in the art. Non-limiting examples of anti-4-IBB antibody sequences, along with the relevant CDR, VH, and VL sequences are provided in **Table 19**.

Anti-IL6RA antibody sequences and methods of making such antibodies are known in the art. Non-limiting examples of IL6RA antibody sequences, along with the relevant CDR, VH, and VL sequences are provided in **Table 19**.

Anti-IL6RB antibody sequences and methods of making such antibodies are known in the art. Non-limiting examples of IL6RB antibody sequences, along with the relevant CDR, VH, and VL sequences are provided in **Table 19**.

Anti-CD2 antibody sequences and methods of making such antibodies are known in the art. Non-limiting examples of anti-CD2 antibody sequences, along with the relevant CDR, VH, VL, HC and LC sequences are provided in **Table 19**.

In some embodiments, an antibody molecule described herein comprises a CDR, VH, VL, HC, and/or LC disclosed in **Table 19**, or sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identity thereto.

Table 19 – Exemplary antibody, CDR, heavy chain variable region (VH), light chain variable region (VL), heavy chain (HC), and light chain (LC), sequences by target antigen

SEQ ID NO	Description	Amino acid sequence
ANTI-CD3 (1)		

SEQ ID NO: 420 (Combined)	LCDR1	SASSSVSYMN
SEQ ID NO: 421 (Combined)	LCDR2	DTSKLAS
SEQ ID NO: 422 (Combined)	LCDR3	QQWSSNPFT
SEQ ID NO: 420 (Kabat)	LCDR1	SASSSVSYMN
SEQ ID NO: 421 (Kabat)	LCDR2	DTSKLAS
SEQ ID NO: 422 (Kabat)	LCDR3	QQWSSNPFT
SEQ ID NO: 423 (Chothia)	LCDR1	SSSVSY
SEQ ID NO: 424 (Chothia)	LCDR2	DTS
SEQ ID NO: 425 (Chothia)	LCDR3	WSSNPF
SEQ ID NO: 426 (IMGT)	LCDR1	SSVSY
SEQ ID NO: 424 (IMGT)	LCDR2	DTS
SEQ ID NO: 422 (IMGT)	LCDR3	QQWSSNPFT
SEQ ID NO: 427	VL	DIQMTQSPSSLSASVGDRVTITCSASSSVSYM NWYQQTPGKAPKRWIYDTSKLASGVPSRFSG SGSGTDYTFTISSLQPEDIATYYCQQWSSNPFT FGQGTKLQIT
SEQ ID NO: 428 (Combined)	HCDR1	GYTFTRYTMH
SEQ ID NO: 429 (Combined)	HCDR2	YINPSRGYTNYNQKVKD
SEQ ID NO: 430 (Combined)	HCDR3	YYDDHYSLDY
SEQ ID NO: 431 (Kabat)	HCDR1	RYTMH
SEQ ID NO: 429 (Kabat)	HCDR2	YINPSRGYTNYNQKVKD
SEQ ID NO: 430 (Kabat)	HCDR3	YYDDHYSLDY
SEQ ID NO: 432 (Chothia)	HCDR1	GYTFTRY
SEQ ID NO: 433 (Chothia)	HCDR2	NPSRGY
SEQ ID NO: 430 (Chothia)	HCDR3	YYDDHYSLDY

SEQ ID NO: 434 (IMGT)	HCDR1	GYTFTRYT
SEQ ID NO: 435 (IMGT)	HCDR2	INPSRGYT
SEQ ID NO: 436 (IMGT)	HCDR3	ARYYDDHYSLDY
SEQ ID NO: 437	VH	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTR YTMHWVRQAPGKGLEWIGYINPSRGYTNYN QKVKDRFTISRDNSKNTAFLQMDSLRPEDTG VYFCARYYDDHYSLDYWGQGTPVTVSS
ANTI-CD3 (2)		
SEQ ID NO: 438 (Combined)	LCDR1	GSSTGAVTSGNYPN
SEQ ID NO: 439 (Combined)	LCDR2	GTKFLAP
SEQ ID NO: 440 (Combined)	LCDR3	VLWYSNRWV
SEQ ID NO: 438 (Kabat)	LCDR1	GSSTGAVTSGNYPN
SEQ ID NO: 439 (Kabat)	LCDR2	GTKFLAP
SEQ ID NO: 440 (Kabat)	LCDR3	VLWYSNRWV
SEQ ID NO: 441 (Chothia)	LCDR1	STGAVTSGNY
SEQ ID NO: 442 (Chothia)	LCDR2	GTK
SEQ ID NO: 443 (Chothia)	LCDR3	WYSNRW
SEQ ID NO: 444 (IMGT)	LCDR1	TGAVTSGNY
SEQ ID NO: 442 (IMGT)	LCDR2	GTK
SEQ ID NO: 440 (IMGT)	LCDR3	VLWYSNRWV
SEQ ID NO: 445	VL	QTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSG NYPNWVQQKPGQAPRGLIGGTKFLAPGTPAR FSGSLLGGKAALTLSGVQPEDEAEYYCVLWY SNRWVFGGGTKLTVL
SEQ ID NO: 446	VL	QTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSG NYPNWVQQKPGQAPRGLIGGTKFLAPGTPAR FSGSLLGGKAALTLSGVQPEDEAEYYCVLWY SNRWVFGCGTKLTVL
SEQ ID NO: 447 (Combined)	HCDR1	GFTFNKYAMN

SEQ ID NO: 448 (Combined)	HCDR2	RIRSKYNNYATYYADSVKD
SEQ ID NO: 449 (Combined)	HCDR3	HGNFGNSYISYWAY
SEQ ID NO: 450 (Kabat)	HCDR1	KYAMN
SEQ ID NO: 448 (Kabat)	HCDR2	RIRSKYNNYATYYADSVKD
SEQ ID NO: 449 (Kabat)	HCDR3	HGNFGNSYISYWAY
SEQ ID NO: 451 (Chothia)	HCDR1	GFTFNKY
SEQ ID NO: 452 (Chothia)	HCDR2	RSKYNNYA
SEQ ID NO: 449 (Chothia)	HCDR3	HGNFGNSYISYWAY
SEQ ID NO: 453 (IMGT)	HCDR1	GFTFNKYA
SEQ ID NO: 454 (IMGT)	HCDR2	IRSKYNNYAT
SEQ ID NO: 455 (IMGT)	HCDR3	VRHGNFGNSYISYWAY
SEQ ID NO: 456	VH	EVQLVESGGGLVQPGGSLKLSCAASGFTFNK YAMNWVRQAPGKGLEWVARIRSKYNNYAT YYADSVKDRFTISRDDSKNTAYLQMNNLKTE DTAVYYCVRHGNFGNSYISYWAYWGQGTLV TVSS
SEQ ID NO: 457	VH	EVQLVESGGGLVQPGGSLKLSCAASGFTFNK YAMNWVRQAPGKCLEWVARIRSKYNNYAT YYADSVKDRFTISRDDSKNTAYLQMNNLKTE DTAVYYCVRHGNFGNSYISYWAYWGQGTLV TVSS
ANTI-CD3 (3)		
SEQ ID NO: 458 (Combined)	LCDR1	RSSTGAVTTSNYAN
SEQ ID NO: 459 (Combined)	LCDR2	GTNKRAP
SEQ ID NO: 460 (Combined)	LCDR3	ALWYSNLWV
SEQ ID NO: 458 (Kabat)	LCDR1	RSSTGAVTTSNYAN
SEQ ID NO: 459 (Kabat)	LCDR2	GTNKRAP
SEQ ID NO: 460 (Kabat)	LCDR3	ALWYSNLWV

SEQ ID NO: 461 (Chothia)	LCDR1	STGAVTTSNY
SEQ ID NO: 462 (Chothia)	LCDR2	GTN
SEQ ID NO: 463 (Chothia)	LCDR3	WYSNLW
SEQ ID NO: 464 (IMGT)	LCDR1	TGAVTTSNY
SEQ ID NO: 465 (IMGT)	LCDR2	GGT
SEQ ID NO: 466 (IMGT)	LCDR3	ALWYSNL
SEQ ID NO: 467	VL	QAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTS NYANWVQQKPGQAPRGLIGGTNKRAPWTPA RFSGSLLGDKAALTLSGAQPEDEAEYFCALW YSNLWVFGGGTKLTVL
SEQ ID NO: 468	VL	QAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTS NYANWVQQKPGQAPRGLIGGTNKRAPWTPA RFSGSLLGDKAALTLSGAQPEDEAEYFCALW YSNLWVFGCGTKLTVL
SEQ ID NO: 469 (Combined)	HCDR1	GFTFNTYAMN
SEQ ID NO: 448 (Combined)	HCDR2	RIRSKYNNYATYYADSVKD
SEQ ID NO: 470 (Combined)	HCDR3	HGNFGNSYVSWFAY
SEQ ID NO: 471 (Kabat)	HCDR1	TYAMN
SEQ ID NO: 448 (Kabat)	HCDR2	RIRSKYNNYATYYADSVKD
SEQ ID NO: 470 (Kabat)	HCDR3	HGNFGNSYVSWFAY
SEQ ID NO: 472 (Chothia)	HCDR1	GFTFNTY
SEQ ID NO: 452 (Chothia)	HCDR2	RSKYNNYA
SEQ ID NO: 470 (Chothia)	HCDR3	HGNFGNSYVSWFAY
SEQ ID NO: 473 (IMGT)	HCDR1	GFTFNTYA
SEQ ID NO: 454 (IMGT)	HCDR2	IRSKYNNYAT
SEQ ID NO: 474 (IMGT)	HCDR3	VRHGNFGNSYVSWFAY
SEQ ID NO: 475	VH	EVQLVESGGGLVQPGGSLKLSCAASGFTFNT YAMNWVRQASGKGLEWVGRIRSKYNNYAT

		YYADSVKDRFTISRDDSKSTLYLQMNSLKTE DTAVYYCVRHGNFGNSYVSWFAYWGQGTL VTVSS
SEQ ID NO: 476	VH	EVQLVESGGGLVQPGGSLKLSCAASGFTFNT YAMNWVRQASGKCLEWVGRIRSKYNNYAT YYADSVKDRFTISRDDSKSTLYLQMNSLKTE DTAVYYCVRHGNFGNSYVSWFAYWGQGTL VTVSS
ANTI-CD3 (4)		
SEQ ID NO: 477 (Combined)	LCDR1	RSSQSLVRSEGTTYFN
SEQ ID NO: 478 (Combined)	LCDR2	RVSNRFS
SEQ ID NO: 479 (Combined)	LCDR3	LQSSHFPWT
SEQ ID NO: 477 (Kabat)	LCDR1	RSSQSLVRSEGTTYFN
SEQ ID NO: 478 (Kabat)	LCDR2	RVSNRFS
SEQ ID NO: 479 (Kabat)	LCDR3	LQSSHFPWT
SEQ ID NO: 480 (Chothia)	LCDR1	SQSLVRSEGTTY
SEQ ID NO: 481 (Chothia)	LCDR2	RVS
SEQ ID NO: 482 (Chothia)	LCDR3	SSHFPW
SEQ ID NO: 483 (IMGT)	LCDR1	QSLVRSEGTTY
SEQ ID NO: 481 (IMGT)	LCDR2	RVS
SEQ ID NO: 479 (IMGT)	LCDR3	LQSSHFPWT
SEQ ID NO: 484	VL	DILVTQTPVSLPVSLGGHVSISCRSSQSLVRSE GTTYFNWYLQKPGQSPQLLIYRVSNRFSGVP DRFSGSGSGTDFTLKISRVEPEDLGVYYCLQS SHFPWTFGGGTKLELK
SEQ ID NO: 485 (Combined)	HCDR1	GFTFSKQGMH
SEQ ID NO: 486 (Combined)	HCDR2	MIYYDSSKMYYADTVKG
SEQ ID NO: 487 (Combined)	HCDR3	FWWDLDFDH
SEQ ID NO: 488 (Kabat)	HCDR1	KQGMH

SEQ ID NO: 486 (Kabat)	HCDR2	MIYYDSSKMYYADTVKG
SEQ ID NO: 487 (Kabat)	HCDR3	FWWDLDFDH
SEQ ID NO: 489 (Chothia)	HCDR1	GFTFSKQ
SEQ ID NO: 490 (Chothia)	HCDR2	YYDSSK
SEQ ID NO: 487 (Chothia)	HCDR3	FWWDLDFDH
SEQ ID NO: 491 (IMGT)	HCDR1	GFTFSKQG
SEQ ID NO: 492 (IMGT)	HCDR2	IYYDSSKM
SEQ ID NO: 493 (IMGT)	HCDR3	ASFWWDLDFDH
SEQ ID NO: 494	VH	EVKLVESGGDLVQPGDSLTLSCVASGFTFSKQ GMHWIRQAPKKGLEWIAMIYYDSSKMYYAD TVKGRFTISRDNSKNTLYLEMNSLRSEDTAM YYCASFWWDLDFDHWGQGVMVTVSS
ANTI-TCR		
SEQ ID NO: 495 (Combined)	LCDR1	SATSSVSYMH
SEQ ID NO: 421 (Combined)	LCDR2	DTSKLAS
SEQ ID NO: 496 (Combined)	LCDR3	QQWSSNPLT
SEQ ID NO: 495 (Kabat)	LCDR1	SATSSVSYMH
SEQ ID NO: 421 (Kabat)	LCDR2	DTSKLAS
SEQ ID NO: 496 (Kabat)	LCDR3	QQWSSNPLT
SEQ ID NO: 497 (Chothia)	LCDR1	TSSVSY
SEQ ID NO: 424 (Chothia)	LCDR2	DTS
SEQ ID NO: 498 (Chothia)	LCDR3	WSSNPL
SEQ ID NO: 426 (IMGT)	LCDR1	SSVSY
SEQ ID NO: 424 (IMGT)	LCDR2	DTS
SEQ ID NO: 496 (IMGT)	LCDR3	QQWSSNPLT

SEQ ID NO: 499	VL	QIVLTQSPAIMSASPGEKVTMTCSATSSVSYM HWYQQKSGTSPKRWIYDTSKLASGVPARFSG SGSGTSYSLTISSMEAEDAATYYCQQWSSNPL TFGAGTKLELK
SEQ ID NO: 500 (Combined)	HCDR1	GYKFTSYVMH
SEQ ID NO: 501 (Combined)	HCDR2	YINPYNDVTKYNEKFKG
SEQ ID NO: 502 (Combined)	HCDR3	GSYYDYDGFVY
SEQ ID NO: 503 (Kabat)	HCDR1	SYVMH
SEQ ID NO: 501 (Kabat)	HCDR2	YINPYNDVTKYNEKFKG
SEQ ID NO: 502 (Kabat)	HCDR3	GSYYDYDGFVY
SEQ ID NO: 504 (Chothia)	HCDR1	GYKFTSY
SEQ ID NO: 505 (Chothia)	HCDR2	NPYNDV
SEQ ID NO: 502 (Chothia)	HCDR3	GSYYDYDGFVY
SEQ ID NO: 506 (IMGT)	HCDR1	GYKFTSYV
SEQ ID NO: 507 (IMGT)	HCDR2	INPYNDVT
SEQ ID NO: 508 (IMGT)	HCDR3	ARGSYYDYDGFVY
SEQ ID NO: 509	VH	EVQLQQSGPELVKPGASVKMSCKASGYKFTS YVMHWVKQKPGQGLEWIGYINPYNDVTKYN EKFKGKATLTSDKSSSTAYMELSSLTSEDSAV HYCARGSYYDYDGFVYWGQGTLVTVSA
ANTI-CD28 (1)		
SEQ ID NO: 510 (Combined)	LCDR1	HASQNIYVWLN
SEQ ID NO: 511 (Combined)	LCDR2	KASNLHT
SEQ ID NO: 512 (Combined)	LCDR3	QQGQTYPYT
SEQ ID NO: 510 (Kabat)	LCDR1	HASQNIYVWLN
SEQ ID NO: 511 (Kabat)	LCDR2	KASNLHT
SEQ ID NO: 512 (Kabat)	LCDR3	QQGQTYPYT

SEQ ID NO: 513 (Chothia)	LCDR1	SQNIYVW
SEQ ID NO: 514 (Chothia)	LCDR2	KAS
SEQ ID NO: 515 (Chothia)	LCDR3	GQTYPY
SEQ ID NO: 516 (IMGT)	LCDR1	QNIYVW
SEQ ID NO: 514 (IMGT)	LCDR2	KAS
SEQ ID NO: 512 (IMGT)	LCDR3	QQGQTYPYT
SEQ ID NO: 517	VL	DIQMTQSPSSLSASVGDRVTITCHASQNIYVW LNWYQQKPGKAPKLLIYKASNLHTGVPSRFS GSGSGTDFTLTISSLQPEDFATYYCQQGQTYP YTFGGGTKVEIK
SEQ ID NO: 518	LC	DIQMTQSPSSLSASVGDRVTITCHASQNIYVW LNWYQQKPGKAPKLLIYKASNLHTGVPSRFS GSGSGTDFTLTISSLQPEDFATYYCQQGQTYP YTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSG TASVVCLLNNFYPREAKVQWKVDNALQSGN SQESVTEQDSKDSTYSLSSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 519 (Combined)	HCDR1	GYTFTSYYIH
SEQ ID NO: 520 (Combined)	HCDR2	CIYPGNVNTNYNEKFKD
SEQ ID NO: 521 (Combined)	HCDR3	SHYGLDWNFDV
SEQ ID NO: 522 (Kabat)	HCDR1	SYYIH
SEQ ID NO: 520 (Kabat)	HCDR2	CIYPGNVNTNYNEKFKD
SEQ ID NO: 521 (Kabat)	HCDR3	SHYGLDWNFDV
SEQ ID NO: 523 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 524 (Chothia)	HCDR2	YPGNVN
SEQ ID NO: 521 (Chothia)	HCDR3	SHYGLDWNFDV
SEQ ID NO: 525 (IMGT)	HCDR1	GYTFTSYY
SEQ ID NO: 526 (IMGT)	HCDR2	IYPGNVNT

SEQ ID NO: 527 (IMGT)	HCDR3	TRSHYGLDWNFDV
SEQ ID NO: 528	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTS YYIHWVRQAPGQGLEWIGCIYPGNVNTNYNE KFKDRATLTVDTSISTAYMELSRLRSDDTAV YFCTRSHYGLDWNFDVWGQGTTVTVSS
SEQ ID NO: 529	HC	QVQLVQSGAEVKKPGASVKVSCKASGYTFTS YYIHWVRQAPGQGLEWIGCIYPGNVNTNYNE KFKDRATLTVDTSISTAYMELSRLRSDDTAV YFCTRSHYGLDWNFDVWGQGTTVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSS VVTVPSSSLGTQTYICNVNHKPSNTKVDKRV EPKSC
ANTI-CD28 (2)		
SEQ ID NO: 530 (Combined)	LCDR1	SGSSSNIVSNYVN
SEQ ID NO: 531 (Combined)	LCDR2	DNNKRPS
SEQ ID NO: 532 (Combined)	LCDR3	QSYAIGSYSVV
SEQ ID NO: 530 (Kabat)	LCDR1	SGSSSNIVSNYVN
SEQ ID NO: 531 (Kabat)	LCDR2	DNNKRPS
SEQ ID NO: 532 (Kabat)	LCDR3	QSYAIGSYSVV
SEQ ID NO: 533 (Chothia)	LCDR1	SSSNIVSNY
SEQ ID NO: 534 (Chothia)	LCDR2	DNN
SEQ ID NO: 535 (Chothia)	LCDR3	YAIGSYSV
SEQ ID NO: 536 (IMGT)	LCDR1	SSNIVSNY
SEQ ID NO: 534 (IMGT)	LCDR2	DNN
SEQ ID NO: 532 (IMGT)	LCDR3	QSYAIGSYSVV
SEQ ID NO: 537	VL	DIVLTQPPSVSGAPGQRVTISCSGSSSNIVSNY VNWYQQLPGTAPKLLIYDNNKRPSGVPDRFS GSKSGTSASLAITGLQSEDEADYYCQSYAIGS YSVVFGGGTKLTVL
SEQ ID NO: 538 (Combined)	HCDR1	GFTFSTYGMS

SEQ ID NO: 539 (Combined)	HCDR2	SIFYTGSSTYYADSVKG
SEQ ID NO: 540 (Combined)	HCDR3	IGYAGDSKYAI
SEQ ID NO: 541 (Kabat)	HCDR1	TYGMS
SEQ ID NO: 539 (Kabat)	HCDR2	SIFYTGSSTYYADSVKG
SEQ ID NO: 540 (Kabat)	HCDR3	IGYAGDSKYAI
SEQ ID NO: 542 (Chothia)	HCDR1	GFTFSTY
SEQ ID NO: 543 (Chothia)	HCDR2	FYTGSS
SEQ ID NO: 540 (Chothia)	HCDR3	IGYAGDSKYAI
SEQ ID NO: 544 (IMGT)	HCDR1	GFTFSTYG
SEQ ID NO: 545 (IMGT)	HCDR2	IFYTGSST
SEQ ID NO: 546 (IMGT)	HCDR3	ARIGYAGDSKYAI
SEQ ID NO: 547	VH	QVQLVESGGGLVQPGGSLRLSCAASGFTFST YGMSWVRQAPGKGLEWVSSIFYTGSSTYYA DSVKGRFTISRDNSKNTLYLQMNSLRAEDTA VYYCARIGYAGDSKYAIWGQGTLVTVSS
SEQ ID NO: 548	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTY GMSWVRQAPGKGLEWVSSIFYTGSSTYYADS VKGRFTISRDNSKNTLYLQMNSLRAEDTAVY YCARIGYAGDSKYAIWGQGTLVTVSS
ANTI-ICOS		
SEQ ID NO: 549 (Combined)	LCDR1	KSSQSLLSGSFNYLT
SEQ ID NO: 550 (Combined)	LCDR2	YASTRHT
SEQ ID NO: 551 (Combined)	LCDR3	HHHYNAPPT
SEQ ID NO: 549 (Kabat)	LCDR1	KSSQSLLSGSFNYLT
SEQ ID NO: 550 (Kabat)	LCDR2	YASTRHT
SEQ ID NO: 551 (Kabat)	LCDR3	HHHYNAPPT
SEQ ID NO: 552 (Chothia)	LCDR1	SQSLLSGSFNY

SEQ ID NO: 553 (Chothia)	LCDR2	YAS
SEQ ID NO: 554 (Chothia)	LCDR3	HYNAPP
SEQ ID NO: 555 (IMGT)	LCDR1	QSLLSGSFNY
SEQ ID NO: 553 (IMGT)	LCDR2	YAS
SEQ ID NO: 551 (IMGT)	LCDR3	HHHYNAPPT
SEQ ID NO: 556	VL	DIVMTQSPDSLAVSLGERATINCKSSQSLLSGS FNYLTWYQQKPGQPPKLLIFYASTRHTGVPD RFSGSGSGTDFTLTISSLQAEDVAVYYCHHHY NAPPTFGPGTKVDIK
SEQ ID NO: 557	LC	DIVMTQSPDSLAVSLGERATINCKSSQSLLSGS FNYLTWYQQKPGQPPKLLIFYASTRHTGVPD RFSGSGSGTDFTLTISSLQAEDVAVYYCHHHY NAPPTFGPGTKVDIKRTVAAPSVFIFPPSDEQL KSGTASVVCLLNNFYPREAKVQWKVDNALQ SGNSQESVTEQDSKDSTYSLSSTLTLSKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 558 (Combined)	HCDR1	GFTFSDYWMD
SEQ ID NO: 559 (Combined)	HCDR2	NIDEDGSITEYSPFVKG
SEQ ID NO: 560 (Combined)	HCDR3	WGRFGFDS
SEQ ID NO: 561 (Kabat)	HCDR1	DYWMD
SEQ ID NO: 559 (Kabat)	HCDR2	NIDEDGSITEYSPFVKG
SEQ ID NO: 560 (Kabat)	HCDR3	WGRFGFDS
SEQ ID NO: 562 (Chothia)	HCDR1	GFTFSDY
SEQ ID NO: 563 (Chothia)	HCDR2	DEDGSI
SEQ ID NO: 560 (Chothia)	HCDR3	WGRFGFDS
SEQ ID NO: 564 (IMGT)	HCDR1	GFTFSDYW
SEQ ID NO: 565 (IMGT)	HCDR2	IDEDGSIT
SEQ ID NO: 566 (IMGT)	HCDR3	TRWGRFGFDS

SEQ ID NO: 567	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSD YWMDWVRQAPGKGLVWVSNIDEDGSITEYS PFVKGRFTISRDNAKNTLYLQMNSLRAEDTA VYYCTRWGRFGFDSWGQGTLVTVSS
ANTI-CD27		
SEQ ID NO: 568 (Combined)	LCDR1	RASQGISRWLA
SEQ ID NO: 55 (Combined)	LCDR2	AASSLQS
SEQ ID NO: 569 (Combined)	LCDR3	QQYNTYPRT
SEQ ID NO: 568 (Kabat)	LCDR1	RASQGISRWLA
SEQ ID NO: 55 (Kabat)	LCDR2	AASSLQS
SEQ ID NO: 569 (Kabat)	LCDR3	QQYNTYPRT
SEQ ID NO: 570 (Chothia)	LCDR1	SQGISRW
SEQ ID NO: 58 (Chothia)	LCDR2	AAS
SEQ ID NO: 571 (Chothia)	LCDR3	YNTYPR
SEQ ID NO: 572 (IMGT)	LCDR1	QGISRW
SEQ ID NO: 58 (IMGT)	LCDR2	AAS
SEQ ID NO: 569 (IMGT)	LCDR3	QQYNTYPRT
SEQ ID NO: 573	VL	DIQMTQSPSSLSASVGDRVTITCRASQGISRW LAWYQQKPEKAPKSLIYAASSLQSGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQYNTYPR TFGQGTKVEIK
SEQ ID NO: 574 (Combined)	HCDR1	GFTFSSYDMH
SEQ ID NO: 575 (Combined)	HCDR2	VIWYDGSNKYYADSVKG
SEQ ID NO: 576 (Combined)	HCDR3	GSGNWGFFDY
SEQ ID NO: 577 (Kabat)	HCDR1	SYDMH
SEQ ID NO: 575 (Kabat)	HCDR2	VIWYDGSNKYYADSVKG
SEQ ID NO: 576 (Kabat)	HCDR3	GSGNWGFFDY

SEQ ID NO: 47 (Chothia)	HCDR1	GFTFSSY
SEQ ID NO: 578 (Chothia)	HCDR2	WYDGSN
SEQ ID NO: 576 (Chothia)	HCDR3	GSGNWGFFDY
SEQ ID NO: 579 (IMGT)	HCDR1	GFTFSSYD
SEQ ID NO: 580 (IMGT)	HCDR2	IWYDGSNK
SEQ ID NO: 581 (IMGT)	HCDR3	ARGSGNWGFFDY
SEQ ID NO: 582	VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSS YDMHWVRQAPGGLEWVAVIWYDGSNKYYA DSVKGRFTISRDNSKNTLYLQMNSLRAEDTA VYYCARGSGNWGFFDYWGQGTLVTVSS
ANTI-CD25 (1)		
SEQ ID NO: 583 (Combined)	LCDR1	SASSSRSYMQ
SEQ ID NO: 421 (Combined)	LCDR2	DTSKLAS
SEQ ID NO: 584 (Combined)	LCDR3	HQRSSYT
SEQ ID NO: 583 (Kabat)	LCDR1	SASSSRSYMQ
SEQ ID NO: 421 (Kabat)	LCDR2	DTSKLAS
SEQ ID NO: 584 (Kabat)	LCDR3	HQRSSYT
SEQ ID NO: 585 (Chothia)	LCDR1	SSSRSY
SEQ ID NO: 424 (Chothia)	LCDR2	DTS
SEQ ID NO: 586 (Chothia)	LCDR3	RSSY
SEQ ID NO: 587 (IMGT)	LCDR1	SSRSY
SEQ ID NO: 424 (IMGT)	LCDR2	DTS
SEQ ID NO: 584 (IMGT)	LCDR3	HQRSSYT
SEQ ID NO: 588	VL	QIVSTQSPAIMSASPGEKVTMTCSASSSRSYM QWYQQKPGTSPKRWIYDTSKLASGVPARFSG SGSGTSYSLTISSMEAEDAATYYCHQRSSYTF GGGTKLEIK

SEQ ID NO: 589 (Combined)	HCDR1	GYSFTRYWMH
SEQ ID NO: 590 (Combined)	HCDR2	AIYPGNSDTSYNQKFEG
SEQ ID NO: 591 (Combined)	HCDR3	DYGYYFDF
SEQ ID NO: 592 (Kabat)	HCDR1	RYWMH
SEQ ID NO: 590 (Kabat)	HCDR2	AIYPGNSDTSYNQKFEG
SEQ ID NO: 591 (Kabat)	HCDR3	DYGYYFDF
SEQ ID NO: 593 (Chothia)	HCDR1	GYSFTRY
SEQ ID NO: 594 (Chothia)	HCDR2	YPGNSD
SEQ ID NO: 591 (Chothia)	HCDR3	DYGYYFDF
SEQ ID NO: 595 (IMGT)	HCDR1	GYSFTRYW
SEQ ID NO: 596 (IMGT)	HCDR2	IYPGNSDT
SEQ ID NO: 597 (IMGT)	HCDR3	SRDYGYYFDF
SEQ ID NO: 598	VH	EVQLQQSGTVLARPGASVKMSCKASGYSFTR YWMHWIKQRPGQGLEWIGAIYPGNSDTSYN QKFEGKAKLTAVTSASTAYMELSSLTHEDSA VYYCSRDYGYYFDFWGQGTTLTVSS
ANTI-CD25 (2)		
SEQ ID NO: 599 (Combined)	LCDR1	KASQSVDYDGDSYMN
SEQ ID NO: 600 (Combined)	LCDR2	AASNLES
SEQ ID NO: 601 (Combined)	LCDR3	QQSNEDPYT
SEQ ID NO: 599 (Kabat)	LCDR1	KASQSVDYDGDSYMN
SEQ ID NO: 600 (Kabat)	LCDR2	AASNLES
SEQ ID NO: 601 (Kabat)	LCDR3	QQSNEDPYT
SEQ ID NO: 602 (Chothia)	LCDR1	SQSVDYDGDSY
SEQ ID NO: 58 (Chothia)	LCDR2	AAS

SEQ ID NO: 603 (Chothia)	LCDR3	SNEDPY
SEQ ID NO: 604 (IMGT)	LCDR1	QSVDYDGDSY
SEQ ID NO: 58 (IMGT)	LCDR2	AAS
SEQ ID NO: 601 (IMGT)	LCDR3	QQSNEDPYT
SEQ ID NO: 605	VL	DIVLTQSPLSLPVTLGQPASISCKASQSVDYDG DSYMNWYQQRPGQSPRLLIYAASNLESGVPD RFSGSGSGTDFTLKISRVEAEDVGVYYCQQSN EDPYTFGGGTKVEIK
SEQ ID NO: 606	LC	DIVLTQSPLSLPVTLGQPASISCKASQSVDYDG DSYMNWYQQRPGQSPRLLIYAASNLESGVPD RFSGSGSGTDFTLKISRVEAEDVGVYYCQQSN EDPYTFGGGTKVEIKRTVAAPSVFIFPPSDEQL KSGTASVVCLLNNFYPREAKVQWKVDNALQ SGNSQESVTEQDSKDSTYSLSSTLTLSKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 607 (Combined)	HCDR1	GYAFTNYLIE
SEQ ID NO: 608 (Combined)	HCDR2	VINPGSGGTNYNEKFKG
SEQ ID NO: 609 (Combined)	HCDR3	WRGDGYYAYFDV
SEQ ID NO: 610 (Kabat)	HCDR1	NYLIE
SEQ ID NO: 608 (Kabat)	HCDR2	VINPGSGGTNYNEKFKG
SEQ ID NO: 609 (Kabat)	HCDR3	WRGDGYYAYFDV
SEQ ID NO: 611 (Chothia)	HCDR1	GYAFTNY
SEQ ID NO: 612 (Chothia)	HCDR2	NPGSGG
SEQ ID NO: 609 (Chothia)	HCDR3	WRGDGYYAYFDV
SEQ ID NO: 613 (IMGT)	HCDR1	GYAFTNYL
SEQ ID NO: 614 (IMGT)	HCDR2	INPGSGGT
SEQ ID NO: 615 (IMGT)	HCDR3	ARWRGDGYYAYFDV
SEQ ID NO: 616	VH	EVQLVQSGAEVKKPGESLKISCKGSGYAFTN YLIEWVRQMPGKGLEWMGVINPGSGGTNYN

		EKFKGQVTISADKSISTAYLQWSSLKASDTA MYYCARWRGDGYYAYFDVWGQGTTVTVSS
SEQ ID NO: 617	HC	EVQLVQSGAEVKKPGESLKISCKGSGYAFTN YLIEWVRQMPGKGLEWMGVINPGSGGTNYN EKFKGQVTISADKSISTAYLQWSSLKASDTA MYYCARWRGDGYYAYFDVWGQGTTVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDK RVEPKSC
ANTI-4-1BB		
SEQ ID NO: 618 (Combined)	LCDR1	RASQSVSSYLA
SEQ ID NO: 619 (Combined)	LCDR2	DASNRAT
SEQ ID NO: 620 (Combined)	LCDR3	QQRSNWPPALT
SEQ ID NO: 618 (Kabat)	LCDR1	RASQSVSSYLA
SEQ ID NO: 619 (Kabat)	LCDR2	DASNRAT
SEQ ID NO: 620 (Kabat)	LCDR3	QQRSNWPPALT
SEQ ID NO: 621 (Chothia)	LCDR1	SQSVSSY
SEQ ID NO: 622 (Chothia)	LCDR2	DAS
SEQ ID NO: 623 (Chothia)	LCDR3	RSNWPPAL
SEQ ID NO: 624 (IMGT)	LCDR1	QSVSSY
SEQ ID NO: 622 (IMGT)	LCDR2	DAS
SEQ ID NO: 620 (IMGT)	LCDR3	QQRSNWPPALT
SEQ ID NO: 625	VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYL AWYQQKPGQAPRLLIYDASNRATGIPARFSG SGSGTDFTLTISSLEPEDFAVYYCQQRSNWPP ALTFCGGTKVEIK
SEQ ID NO: 626 (Combined)	HCDR1	GGSFSGYYWS
SEQ ID NO: 627 (Combined)	HCDR2	EINHGGYVTYNPSLES
SEQ ID NO: 628 (Combined)	HCDR3	DYGPGNYDWYFDL

SEQ ID NO: 629 (Kabat)	HCDR1	GYYWS
SEQ ID NO: 627 (Kabat)	HCDR2	EINHGGYVTYNPSLES
SEQ ID NO: 628 (Kabat)	HCDR3	DYGPGNYDWYFDL
SEQ ID NO: 630 (Chothia)	HCDR1	GGSFSGY
SEQ ID NO: 631 (Chothia)	HCDR2	NHGGY
SEQ ID NO: 628 (Chothia)	HCDR3	DYGPGNYDWYFDL
SEQ ID NO: 632 (IMGT)	HCDR1	GGSFSGYY
SEQ ID NO: 633 (IMGT)	HCDR2	INHGGYV
SEQ ID NO: 634 (IMGT)	HCDR3	ARDYGPGNYDWYFDL
SEQ ID NO: 635	VH	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSG YYWSWIRQSPEKGLEWIGEINHGGYVTYNPS LESRVTISVDTSKNQFSLKLSSVTAADTAVYY CARDYGPGNYDWYFDLWGRGTLVTVSS
ANTI-IL6RA		
SEQ ID NO: 636 (Combined)	LCDR1	RASQDISSYLN
SEQ ID NO: 637 (Combined)	LCDR2	YTSRLHS
SEQ ID NO: 300 (Combined)	LCDR3	QQGNTLPYT
SEQ ID NO: 636 (Kabat)	LCDR1	RASQDISSYLN
SEQ ID NO: 637 (Kabat)	LCDR2	YTSRLHS
SEQ ID NO: 300 (Kabat)	LCDR3	QQGNTLPYT
SEQ ID NO: 638 (Chothia)	LCDR1	SQDISSY
SEQ ID NO: 639 (Chothia)	LCDR2	YTS
SEQ ID NO: 640 (Chothia)	LCDR3	GNTLPY
SEQ ID NO: 641 (IMGT)	LCDR1	QDISSY
SEQ ID NO: 639 (IMGT)	LCDR2	YTS

SEQ ID NO: 300 (IMGT)	LCDR3	QQGNTLPYT
SEQ ID NO: 642	VL	DIQMTQSPSSLSASVGDRVTITCRASQDISSYL NWYQQKPGKAPKLLIYYTSRLHSGVPSRFSG SGSGTDFTFTISSLQPEDIATYYCQQGNTLPYT FGQGTKVEIK
SEQ ID NO: 643 (Combined)	HCDR1	GYSITSDHAWS
SEQ ID NO: 644 (Combined)	HCDR2	YISYSGITTYNPSLKS
SEQ ID NO: 645 (Combined)	HCDR3	SLARTTAMDY
SEQ ID NO: 646 (Kabat)	HCDR1	SDHAWS
SEQ ID NO: 644 (Kabat)	HCDR2	YISYSGITTYNPSLKS
SEQ ID NO: 645 (Kabat)	HCDR3	SLARTTAMDY
SEQ ID NO: 647 (Chothia)	HCDR1	GYSITSDH
SEQ ID NO: 648 (Chothia)	HCDR2	SYSGI
SEQ ID NO: 645 (Chothia)	HCDR3	SLARTTAMDY
SEQ ID NO: 649 (IMGT)	HCDR1	GYSITSDHA
SEQ ID NO: 650 (IMGT)	HCDR2	ISYSGIT
SEQ ID NO: 651 (IMGT)	HCDR3	ARSLARTTAMDY
SEQ ID NO: 652	VH	QVQLQESGPGLVRPSQTLSLTCTVSGYSITSD HAWSWVRQPPGRGLEWIGYISYSGITTYNPSL KSRVTMLRDTSKNQFSLRLSSVTAADTAVYY CARSLARTTAMDYWGQGSLVTVSS
ANTI-IL6RB		
SEQ ID NO: 54 (Combined)	LCDR1	RASQSISSYLN
SEQ ID NO: 55 (Combined)	LCDR2	AASSLQS
SEQ ID NO: 653 (Combined)	LCDR3	QQSYSTPPIT
SEQ ID NO: 54 (Kabat)	LCDR1	RASQSISSYLN
SEQ ID NO: 55 (Kabat)	LCDR2	AASSLQS

SEQ ID NO: 653 (Kabat)	LCDR3	QQSYSTPPIT
SEQ ID NO: 57 (Chothia)	LCDR1	SQSISSY
SEQ ID NO: 58 (Chothia)	LCDR2	AAS
SEQ ID NO: 654 (Chothia)	LCDR3	SYSTPPI
SEQ ID NO: 60 (IMGT)	LCDR1	QSISSY
SEQ ID NO: 58 (IMGT)	LCDR2	AAS
SEQ ID NO: 653 (IMGT)	LCDR3	QQSYSTPPIT
SEQ ID NO: 655	VL	DIQMTQSPSSLSASVGDRVTITCRASQSISSYL NWYQQKPGKAPKLLIYAASSLQSGVPSRFSG SGSGTDFTLTISSLQPEDFATYYCQQSYSTPPI TFGQGTRLEIK
SEQ ID NO: 656 (Combined)	HCDR1	GFTFSDYYMT
SEQ ID NO: 657 (Combined)	HCDR2	YISSSGTNKYNADSVKG
SEQ ID NO: 658 (Combined)	HCDR3	DPPWGMDV
SEQ ID NO: 659 (Kabat)	HCDR1	DYYMT
SEQ ID NO: 657 (Kabat)	HCDR2	YISSSGTNKYNADSVKG
SEQ ID NO: 658 (Kabat)	HCDR3	DPPWGMDV
SEQ ID NO: 562 (Chothia)	HCDR1	GFTFSDY
SEQ ID NO: 660 (Chothia)	HCDR2	SSSGTN
SEQ ID NO: 658 (Chothia)	HCDR3	DPPWGMDV
SEQ ID NO: 661 (IMGT)	HCDR1	GFTFSDYY
SEQ ID NO: 662 (IMGT)	HCDR2	ISSSGTNK
SEQ ID NO: 663 (IMGT)	HCDR3	VRDPPWGMDV
SEQ ID NO: 664	VH	QVQLVESGGGLVKPGGSLRLSCAASGFTFSD YYMTWIRQTPGKGLDWVSYISSSGTNKYNA DSVKGRFTISRDNAKNSLYLQMNSLRAEDTA VYYCVRDPPWGMDVWGQGTTVTVSS

ANTI-CD2 (1)		
SEQ ID NO: 665 (Combined)	LCDR1	RSSQSLLHSSGNTYLN
SEQ ID NO: 666 (Combined)	LCDR2	LVSKLES
SEQ ID NO: 667 (Combined)	LCDR3	MQFTHYPYT
SEQ ID NO: 665 (Kabat)	LCDR1	RSSQSLLHSSGNTYLN
SEQ ID NO: 666 (Kabat)	LCDR2	LVSKLES
SEQ ID NO: 667 (Kabat)	LCDR3	MQFTHYPYT
SEQ ID NO: 668 (Chothia)	LCDR1	SQSLLHSSGNTY
SEQ ID NO: 669 (Chothia)	LCDR2	LVS
SEQ ID NO: 670 (Chothia)	LCDR3	FTHYPY
SEQ ID NO: 671 (IMGT)	LCDR1	QSLLHSSGNTY
SEQ ID NO: 669 (IMGT)	LCDR2	LVS
SEQ ID NO: 667 (IMGT)	LCDR3	MQFTHYPYT
SEQ ID NO: 672	VL	DVVMTQSPPSLLVTLGQPASISCRSSQSLLHSS GNTYLNWLLQRPGQSPQPLIYLVSKLESGVPD RFSGSGSGTDFTLKISGVEAEDVGVYYCMQF THYPYTFGQGTKLEIK
SEQ ID NO: 673	LC	DVVMTQSPPSLLVTLGQPASISCRSSQSLLHSS GNTYLNWLLQRPGQSPQPLIYLVSKLESGVPD RFSGSGSGTDFTLKISGVEAEDVGVYYCMQF THYPYTFGQGTKLEIKRTVAAPSVFIFPPSDEQ LKSGTASVVCLLNNFYPREAKVQWKVDNAL QSGNSQESVTEQDSKDSTYSLSSTLTLSKADY EKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 674 (Combined)	HCDR1	GYIFTEYYMY
SEQ ID NO: 675 (Combined)	HCDR2	RIDPEDGSIDYVEKFKK
SEQ ID NO: 676 (Combined)	HCDR3	GKFNYRFAY
SEQ ID NO: 677 (Kabat)	HCDR1	EYYMY
SEQ ID NO: 675 (Kabat)	HCDR2	RIDPEDGSIDYVEKFKK

SEQ ID NO: 676 (Kabat)	HCDR3	GKFNYRFAY
SEQ ID NO: 678 (Chothia)	HCDR1	GYIFTEY
SEQ ID NO: 679 (Chothia)	HCDR2	DPEDGS
SEQ ID NO: 676 (Chothia)	HCDR3	GKFNYRFAY
SEQ ID NO: 680 (IMGT)	HCDR1	GYIFTEYY
SEQ ID NO: 681 (IMGT)	HCDR2	IDPEDGSI
SEQ ID NO: 682 (IMGT)	HCDR3	ARGKFNYRFAY
SEQ ID NO: 683	VH	QVQLVQSGAEVQRPGASVKVSCKASGYIFTE YYMYWVRQAPGQGLELVGRIDPEDGSIDYVE KFKKKVTLTADTSSSTAYMELSSLTSDDTAV YYCARGKFNYRFAYWGQGTLVTVSS
SEQ ID NO: 684	HC	QVQLVQSGAEVQRPGASVKVSCKASGYIFTE YYMYWVRQAPGQGLELVGRIDPEDGSIDYVE KFKKKVTLTADTSSSTAYMELSSLTSDDTAV YYCARGKFNYRFAYWGQGTLVTVSSASTKG PSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV TVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSSLGTQTYICNVNHKPSNTKVDKKVEP KSC

In some embodiments, the agent that stimulates a CD3/TCR complex and the agent that stimulates a costimulatory molecule and/or growth factor receptor are comprised in a multispecific binding molecule. Thus, contemplated herein are multispecific binding molecules comprising an agent that stimulates a CD3/TCR complex and an agent that stimulates a costimulatory molecule and/or growth factor receptor, such as but not limited to a multispecific binding molecule comprising a CD3 antigen binding domain and one or more of a CD28, ICOS, CD27, CD25, 4-1BB, IL6RA, IL6RB, and/or CD2 antigen binding domain. Non-limiting examples of such binding domains, as noted above, are provided above, for example in **Table 19** and the publications incorporated by reference herein.

In some embodiments, the multispecific binding molecule comprises a CD3 antigen binding domain and a CD28 or CD2 antigen binding domain. In some embodiments, the CD3 antigen binding domain is an anti-CD3 antibody, optionally the anti-CD3 (1), anti-CD3 (2), anti-CD3 (3), or anti-CD3 (4) provided in **Table 19**, or an antibody fragment comprising one or more

CDRs, VH, and/or VL thereof. In some embodiments, the CD28 antigen binding domain is an anti-CD28 antibody, optionally the anti-CD28 (1) or anti-CD28 (2) provided in **Table 19**, or an antibody fragment comprising one or more CDRs, VH heavy chain, VL, and/or light chain thereof. In some embodiments, the CD2 antigen binding domain is an anti-CD2 antibody, optionally the anti-CD2 (1) provided in **Table 19**, or an antibody fragment comprising one or more CDRs, VH, heavy chain, VL, and/or light chain thereof.

In some embodiments, the multispecific binding molecules comprise one or more heavy and/or light chains. Non-limiting exemplary heavy and light chain sequences that may be comprised in these multispecific binding molecules are provided in **Table 20** below. Non-limiting exemplary combinations thereof are suggested in **Table 20** based on the categorization of the recited heavy and/or light chains as within a Construct. This Construct organization provides examples of configurations of heavy and/or light chains but that further combinations and permutations thereof are also possible. Non-limiting examples of the format of any of these Constructs is provided in **Figure 37A-B, 48A-B, 49A-B, and 50A-B**.

In some embodiments, the multispecific binding molecule comprises one or more heavy and/or light chain sequences disclosed in **Table 20**, or a sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, or 99% identity thereto.

Table 20 – Exemplary Fc, heavy chain (HC), and light chain (LC) sequences

SEQ ID NO:	Chain	Amino acid sequence
701	Wild type Fc	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
702	Fc DANAPA	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYA STYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYP SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVD KSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
879	Human IgG1 Fc variant L234A/L235A/	apeaaggpsvflfppkpkdtlmisrtpevtcvvvdvshedpevkfnwyvdgvevhn aktkpreeqynstyrvvsvltvlhqdwlngkeykckvsnkalaapiektiskakgqpr epqvytlppsrdeltknqvsltclvkgfypsdiavewesngqpennykttppvldsdg sfflyskltvdksrwqqgnvfscsvmhealhnhytqkslslspgk

	P329A (LALAPA)	
880	Human IgG1 Fc variant L234A/L235A/ G237A (LALAGA)	apeaagapsvflfppkpkdtlmisrtpevtcvvvdvshedpevkfnwyvdgvevhn aktkpreeqynstyrvvsvltvlhqdwlngkeykckvsnkalpapiektiskakgqpr epqvytlppsrdeltknqvsltclvkgfypsdiavewesngqpennykttppvldsdg sfflyskltvdksrwqqgnvfscsvmhealhnhytqkslslspgk
881	Human IgG1 Fc variant L234A/L235A/ P329G (LALAPG)	apeaaggpsvflfppkpkdtlmisrtpevtcvvvdvshedpevkfnwyvdgvevhn aktkpreeqynstyrvvsvltvlhqdwlngkeykckvsnkalgapiektiskakgqpr epqvytlppsrdeltknqvsltclvkgfypsdiavewesngqpennykttppvldsdg sfflyskltvdksrwqqgnvfscsvmhealhnhytqkslslspgk
882	Fc LALAPG (L234A/ L235A/P329G)	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALGAPIEKT ISKAKGQPREPQVYTLPPSRREEMKNQVSLTCLVKGFYP SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVD KSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
883	Human IgG1 Fc variant D265A/P329A (DAPA)	apellggpsvflfppkpkdtlmisrtpevtcvvvavshedpevkfnwyvdgvevhna ktkpreeqynstyrvvsvltvlhqdwlngkeykckvsnkalaapiektiskakgqpre pqvytlppsrdeltknqvsltclvkgfypsdiavewesngqpennykttppvldsdgs fflyskltvdksrwqqgnvfscsvmhealhnhytqkslslspgk
884	Fc DAPA (D265A/ P329A)	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYP SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVD KSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
885	Human IgG1 Fc variant L234A/L235A/ S267K/P329A (LALASKPA)	apeaaggpsvflfppkpkdtlmisrtpevtcvvvdvkhedpevkfnwyvdgvevh naktkpreeqynstyrvvsvltvlhqdwlngkeykckvsnkalaapiektiskakgqp repqvytlppsrdeltknqvsltclvkgfypsdiavewesngqpennykttppvldsd gsfflyskltvdksrwqqgnvfscsvmhealhnhytqkslslspgk
886	Fc LALASKPA (L234A/ L235A/S267K/ P329A)	DKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKT ISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYP SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVD KSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
887	Human IgG1 Fc variant D265A/P329A /S267K (DAPASK)	apellggpsvflfppkpkdtlmisrtpevtcvvvavkhedpevkfnwyvdgvevhn aktkpreeqynstyrvvsvltvlhqdwlngkeykckvsnkalaapiektiskakgqpr epqvytlppsrdeltknqvsltclvkgfypsdiavewesngqpennykttppvldsdg sfflyskltvdksrwqqgnvfscsvmhealhnhytqkslslspgk
888	Human IgG1 Fc variant	apellgapsvflfppkpkdtlmisrtpevtcvvvavshedpevkfnwyvdgvevhna ktkpreeqynstyrvvsvltvlhqdwlngkeykckvsnkalaapiektiskakgqpre

	G237A/D265A /P329A (GADAPA)	pqvytlppsrdeltknqvsltclvkgfypsdiavewesngqpennykttppvldsdgs fflyskltvdksrwqqgnvfscsvmhealhnhytqkslslspgk
889	Human IgG1 Fc variant G237A/D265A /P329A/S267K (GADAPASK)	apellgapsvflfppkpkdtlmisrtpevtcvvvavkhedpevkfnwyvdgvevhn aktkpreeqynstyrvvsvltvlhqdwlngkeykckvsnkalaapiektiskakgqpr epqvytlppsrdeltknqvsltclvkgfypsdiavewesngqpennykttppvldsdg sfflyskltvdksrwqqgnvfscsvmhealhnhytqkslslspgk
890	Fc GADAPASK (G237A/ D265A/ P329A/S267K)	DKTHTCPPCPAPELLGAPSVFLFPPKPKDTLMISRTPEVT CVVVAVKHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKT ISKAKGQPREPQVYTLPPSRREEMKNQVSLTCLVKGFYP SDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVD KSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
891	Human IgG1 Fc variant D265A/N297A /P329A (DANAPA)	apellggpsvflfppkpkdtlmisrtpevtcvvvavshedpevkfnwyvdgvevhna ktkpreeqyastyrvvsvltvlhqdwlngkeykckvsnkalaapiektiskakgqpre pqvytlppsrdeltknqvsltclvkgfypsdiavewesngqpennykttppvldsdgs fflyskltvdksrwqqgnvfscsvmhealhnhytqkslslspgk
673	NEG2042 LC	DVVMTQSPPSLLVTLGQPASISCRSSQSLLHSSGNTYLN WLLQRPGQSPQPLIYLVSKLESGVPDRFSGSGSGTDFTLK ISGVEAEDVGVYYCMQFTHYPYTFGQGTKLEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKV YACEVTHQGLSSPVTKSFNRGEC
703	NEG2042 HC	QVQLVQSGAEVQRPGASVKVSCKASGYIFTEYYMYWV RQAPGQGLELVGRIDPEDGSIDYVEKFKKKVTLTADTSS STAYMELSSLTSDDTAVYYCARGKFNYRFAYWGQGTL VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS SLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCP APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHED PEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLT VLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPRE PQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGGGGSGGGGSGGGGS GGGGSQVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYT MHWVRQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTIS RDNSKNTAFLQMDSLRPEDTGVYFCARYYDDHYSLDY WGQGTPVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQ SPSSLSASVGDRVTITCSASSSVSYMNWYQQTPGKAPKR WIYDTSKLASGVPSRFSGSGSGTDYTFTISSLQPEDIATY YCQQWSSNPFTFGQGTKLQIT
518	NEG2043 LC	DIQMTQSPSSLSASVGDRVTITCHASQNIYVWLNWYQQ KPGKAPKLLIYKASNLHTGVPSRFSGSGSGTDFTLTISSL

		QPEDFATYYCQQGQTYPYTFGGGTKVEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ SGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYAC EVTHQGLSSPVTKSFNRGEC
704	NEG2043 HC	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYIHWVR QAPGQGLEWIGCIYPGNVNTNYNEKFKDRATLTVDTSIS TAYMELSRLRSDDTAVYFCTRSHYGLDWNFDVWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPS SSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHE DPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVL TVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGGGGSGGGGSGGGG SGGGGSQVQLVQSGGGVVQPGRSLRLSCKASGYTFTRY TMHWVRQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTI SRDNSKNTAFLQMDSLRPEDTGVYFCARYYDDHYSLDY WGQGTPVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQ SPSSLSASVGDRVTITCSASSSVSYMNWYQQTPGKAPKR WIYDTSKLASGVPSRFSGSGSGTDYTFTISSLQPEDIATY YCQQWSSNPFTFGQGTKLQIT
705	NEG2044 LC	DIVLTQPPSVSGAPGQRVTISCSGSSSNIVSNYVNWYQQL PGTAPKLLIYDNNKRPSGVPDRFSGSKSGTSASLAITGLQ SEDEADYYCQSYAIGSYSVVFGGGTKLTVLGQGTKVEIK RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKV QWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA DYEKHKVYACEVTHQGLSSPVTKSFNRGEC
706	NEG2044 HC	QVQLVESGGGLVQPGGSLRLSCAASGFTFSTYGMSWVR QAPGKGLEWVSSIFYTGSSTYYADSVKGRFTISRDNSKN TLYLQMNSLRAEDTAVYYCARIGYAGDSKYAIWGQGTL VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS SLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCP APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHED PEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLT VLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPRE PQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGGGGSGGGGSGGGGS GGGGSQVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYT MHWVRQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTIS RDNSKNTAFLQMDSLRPEDTGVYFCARYYDDHYSLDY WGQGTPVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQ SPSSLSASVGDRVTITCSASSSVSYMNWYQQTPGKAPKR

		WIYDTSKLASGVPSRFSGSGSGTDYTFTISSLQPEDIATY YCQQWSSNPFTFGQGTKLQIT
673	NEG2050 LC	DVVMTQSPPSLLVTLGQPASISCRSSQSLLHSSGNTYLN WLLQRPGQSPQPLIYLVSKLESGVPDRFSGSGSGTDFTLK ISGVEAEDVGVYYCMQFTHYPYTFGQGTKLEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKV YACEVTHQGLSSPVTKSFNRGEC
707	NEG2050 HC	QVQLVQSGAEVQRPGASVKVSCKASGYIFTEYYMYWV RQAPGQGLELVGRIDPEDGSIDYVEKFKKKVTLTADTSS STAYMELSSLTSDDTAVYYCARGKFNYRFAYWGQGTL VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS SLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCP APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHED PEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLT VLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPRE PQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGGGGSGGGGSGGGGS GGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYA MNWVRQAPGKCLEWVARIRSKYNNYATYYADSVKDRF TISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSY ISYWAYWGQGTLVTVSSGGGGSGGGGSGGGGSGGGGS QTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWV QQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTL SGVQPEDEAEYYCVLWYSNRWVFGCGTKLTVL
673	NEG2051 LC	DVVMTQSPPSLLVTLGQPASISCRSSQSLLHSSGNTYLN WLLQRPGQSPQPLIYLVSKLESGVPDRFSGSGSGTDFTLK ISGVEAEDVGVYYCMQFTHYPYTFGQGTKLEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKV YACEVTHQGLSSPVTKSFNRGEC
708	NEG2051 HC	QVQLVQSGAEVQRPGASVKVSCKASGYIFTEYYMYWV RQAPGQGLELVGRIDPEDGSIDYVEKFKKKVTLTADTSS STAYMELSSLTSDDTAVYYCARGKFNYRFAYWGQGTL VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS SLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCP APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHED PEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLT VLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPRE PQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGGGGSGGGGSGGGGS GGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNTYA

		MNWVRQASGKCLEWVGRIRSKYNNYATYYADSVKDRF TISRDDSKSTLYLQMNSLKTEDTAVYYCVRHGNFGNSY VSWFAYWGQGTLVTVSSGGGGSGGGGSGGGGSQAVVT QEPSLTVSPGGTVTLTCRSSTGAVTTSNYANWVQQKPG QAPRGLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQP EDEAEYFCALWYSNLWVFGCGTKLTVL
518	NEG2052 LC	DIQMTQSPSSLSASVGDRVTITCHASQNIYVWLNWYQQ KPGKAPKLLIYKASNLHTGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQGQTYPYTFGGGTKVEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ SGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYAC EVTHQGLSSPVTKSFNRGEC
709	NEG2052 HC	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYIHWVR QAPGQGLEWIGCIYPGNVNTNYNEKFKDRATLTVDTSIS TAYMELSRLRSDDTAVYFCTRSHYGLDWNFDVWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPS SSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHE DPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVL TVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGGGGSGGGGSGGGG SGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKY AMNWVRQAPGKCLEWVARIRSKYNNYATYYADSVKD RFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGN SYISYWAYWGQGTLVTVSSGGGGSGGGGSGGGGSGGG GSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNW VQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALT LSGVQPEDEAEYYCVLWYSNRWVFGCGTKLTVL
518	NEG2053 LC	DIQMTQSPSSLSASVGDRVTITCHASQNIYVWLNWYQQ KPGKAPKLLIYKASNLHTGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQGQTYPYTFGGGTKVEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ SGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYAC EVTHQGLSSPVTKSFNRGEC
710	NEG2053 HC	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYIHWVR QAPGQGLEWIGCIYPGNVNTNYNEKFKDRATLTVDTSIS TAYMELSRLRSDDTAVYFCTRSHYGLDWNFDVWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPS SSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVAVSHE DPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVL TVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPR

		EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGGGGSGGGGSGGGG SGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNTYA MNWVRQASGKCLEWVGRIRSKYNNYATYYADSVKDRF TISRDDSKSTLYLQMNSLKTEDTAVYYCVRHGNFGNSY VSWFAYWGQGTLVTVSSGGGGSGGGGSGGGGSQAVVT QEPSLTVSPGGTVTLTCRSSTGAVTTSNYANWVQQKPG QAPRGLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQP EDEAEYFCALWYSNLWVFGCGTKLTVL
673	Construct 1 Light Chain	DVVMTQSPPSLLVTLGQPASISCRSSQSLLHSSGNTYLN WLLQRPGQSPQPLIYLVSKLESGVPDRFSGSGSGTDFTLK ISGVEAEDVGVYYCMQFTHYPYTFGQGTKLEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKV YACEVTHQGLSSPVTKSFNRGEC
711	Construct 1 Heavy Chain	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWV RQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTISRDNSK NTAFLQMDSLRPEDTGVYFCARYYDDHYSLDYWGQGT PVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSA SVGDRVTITCSASSSVSYMNWYQQTPGKAPKRWIYDTS KLASGVPSRFSGSGSGTDYTFTISSLQPEDIATYYCQQWS SNPFTFGQGTKLQITGGGGSGGGGSGGGGSGGGGSQVQ LVQSGAEVQRPGASVKVSCKASGYIFTEYYMYWVRQAP GQGLELVGRIDPEDGSIDYVEKFKKKVTLTADTSSSTAY MELSSLTSDDTAVYYCARGKFNYRFAYWGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQ TYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVM HEALHNHYTQKSLSLSPGK
518	Construct 2 Light Chain	DIQMTQSPSSLSASVGDRVTITCHASQNIYVWLNWYQQ KPGKAPKLLIYKASNLHTGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQGQTYPYTFGGGTKVEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ SGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYAC EVTHQGLSSPVTKSFNRGEC
712	Construct 2 Heavy Chain	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWV RQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTISRDNSK NTAFLQMDSLRPEDTGVYFCARYYDDHYSLDYWGQGT PVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSA SVGDRVTITCSASSSVSYMNWYQQTPGKAPKRWIYDTS

		KLASGVPSRFSGSGSGTDYTFTISSLQPEDIATYYCQQWS SNPFTFGQGTKLQITGGGGSGGGGSGGGGSGGGGSQVQ LVQSGAEVKKPGASVKVSCKASGYTFTSYYIHWVRQAP GQGLEWIGCIYPGNVNTNYNEKFKDRATLTVDTSISTAY MELSRLRSDDTAVYFCTRSHYGLDWNFDVWGQGTTVT VSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPV TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSL GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAP ELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQ PENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNHYTQKSLSLSPGK
673	Construct 3 Light Chain	DVVMTQSPPSLLVTLGQPASISCRSSQSLLHSSGNTYLN WLLQRPGQSPQPLIYLVSKLESGVPDRFSGSGSGTDFTLK ISGVEAEDVGVYYCMQFTHYPYTFGQGTKLEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKV YACEVTHQGLSSPVTKSFNRGEC
713	Construct 3 Heavy Chain	QVQLVQSGAEVQRPGASVKVSCKASGYIFTEYYMYWV RQAPGQGLELVGRIDPEDGSIDYVEKFKKKVTLTADTSS STAYMELSSLTSDDTAVYYCARGKFNYRFAYWGQGTL VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS SLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCP APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVF SCSVMHEALHNHYTQKSLSLSPGGGGSGGGGSGGGGSG GGGSQVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTM HWVRQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTISR DNSKNTAFLQMDSLRPEDTGVYFCARYYDDHYSLDYW GQGTPVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSP SSLSASVGDRVTITCSASSSVSYMNWYQQTPGKAPKRWI YDTSKLASGVPSRFSGSGSGTDYTFTISSLQPEDIATYYC QQWSSNPFTFGQGTKLQIT
518	Construct 4 Light Chain	DIQMTQSPSSLSASVGDRVTITCHASQNIYVWLNWYQQ KPGKAPKLLIYKASNLHTGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQGQTYPYTFGGGTKVEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ SGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYAC EVTHQGLSSPVTKSFNRGEC

714	Construct 4 Heavy Chain	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYIHWVR QAPGQGLEWIGCIYPGNVNTNYNEKFKDRATLTVDTSIS TAYMELSRLRSDDTAVYFCTRSHYGLDWNFDVWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPS SSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHE DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGGGGSGGGGSGGGG SGGGGSQVQLVQSGGGVVQPGRSLRLSCKASGYTFTRY TMHWVRQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTI SRDNSKNTAFLQMDSLRPEDTGVYFCARYYDDHYSLDY WGQGTPVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQ SPSSLSASVGDRVTITCSASSSVSYMNWYQQTPGKAPKR WIYDTSKLASGVPSRFSGSGSGTDYTFTISSLQPEDIATY YCQQWSSNPFTFGQGTKLQIT
673	Construct 5 Light Chain	DVVMTQSPPSLLVTLGQPASISCRSSQSLLHSSGNTYLN WLLQRPGQSPQPLIYLVSKLESGVPDRFSGSGSGTDFTLK ISGVEAEDVGVYYCMQFTHYPYTFGQGTKLEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKV YACEVTHQGLSSPVTKSFNRGEC
715	Construct 5 Heavy Chain	QVQLVQSGAEVQRPGASVKVSCKASGYIFTEYYMYWV RQAPGQGLELVGRIDPEDGSIDYVEKFKKKVTLTADTSS STAYMELSSLTSDDTAVYYCARGKFNYRFAYWGQGTL VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS SLGTQTYICNVNHKPSNTKVDKRVEPKSCGGGGSGGGG SQVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHW VRQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTISRDNS KNTAFLQMDSLRPEDTGVYFCARYYDDHYSLDYWGQG TPVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLS ASVGDRVTITCSASSSVSYMNWYQQTPGKAPKRWIYDT SKLASGVPSRFSGSGSGTDYTFTISSLQPEDIATYYCQQW SSNPFTFGQGTKLQITGGGGSGGGGSGGGGSGGGGSDKT HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK AKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
518	Construct 6 Light Chain	DIQMTQSPSSLSASVGDRVTITCHASQNIYVWLNWYQQ KPGKAPKLLIYKASNLHTGVPSRFSGSGSGTDFTLTISSL

		QPEDFATYYCQQGQTYPYTFGGGTKVEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ SGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYAC EVTHQGLSSPVTKSFNRGEC
716	Construct 6 Heavy Chain	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYIHWVR QAPGQGLEWIGCIYPGNVNTNYNEKFKDRATLTVDTSIS TAYMELSRLRSDDTAVYFCTRSHYGLDWNFDVWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPS SSLGTQTYICNVNHKPSNTKVDKRVEPKSCGGGGSGGG GSQVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMH WVRQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTISRD NSKNTAFLQMDSLRPEDTGVYFCARYYDDHYSLDYWG QGTPVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPS SLSASVGDRVTITCSASSSVSYMNWYQQTPGKAPKRWI YDTSKLASGVPSRFSGSGSGTDYTFTISSLQPEDIATYYC QQWSSNPFTFGQGTKLQITGGGGSGGGGSGGGGSGGGG SDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
673	Construct 7 Light Chain	DVVMTQSPPSLLVTLGQPASISCRSSQSLLHSSGNTYLN WLLQRPGQSPQPLIYLVSKLESGVPDRFSGSGSGTDFTLK ISGVEAEDVGVYYCMQFTHYPYTFGQGTKLEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKV YACEVTHQGLSSPVTKSFNRGEC
717	Construct 7 Heavy Chain	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWV RQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTISRDNSK NTAFLQMDSLRPEDTGVYFCARYYDDHYSLDYWGQGT PVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSA SVGDRVTITCSASSSVSYMNWYQQTPGKAPKRWIYDTS KLASGVPSRFSGSGSGTDYTFTISSLQPEDIATYYCQQWS SNPFTFGQGTKLQITGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGGGGSGGGGSGGGGSGGGGSQVQLV QSGAEVQRPGASVKVSCKASGYIFTEYYMYWVRQAPG QGLELVGRIDPEDGSIDYVEKFKKKVTLTADTSSSTAYM ELSSLTSDDTAVYYCARGKFNYRFAYWGQGTLVTVSSA STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS

		WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQ TYICNVNHKPSNTKVDKRVEPKSC
518	Construct 8 Light Chain	DIQMTQSPSSLSASVGDRVTITCHASQNIYVWLNWYQQ KPGKAPKLLIYKASNLHTGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQGQTYPYTFGGGTKVEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ SGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYAC EVTHQGLSSPVTKSFNRGEC
718	Construct 8 Heavy Chain	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWV RQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTISRDNSK NTAFLQMDSLRPEDTGVYFCARYYDDHYSLDYWGQGT PVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSA SVGDRVTITCSASSSVSYMNWYQQTPGKAPKRWIYDTS KLASGVPSRFSGSGSGTDYTFTISSLQPEDIATYYCQQWS SNPFTFGQGTKLQITGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRE EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGGGGSGGGGSGGGGSGGGGSQVQLV QSGAEVKKPGASVKVSCKASGYTFTSYYIHWVRQAPGQ GLEWIGCIYPGNVNTNYNEKFKDRATLTVDTSISTAYME LSRLRSDDTAVYFCTRSHYGLDWNFDVWGQGTTVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQ TYICNVNHKPSNTKVDKRVEPKSC
673	Construct 9 Light Chain	DVVMTQSPPSLLVTLGQPASISCRSSQSLLHSSGNTYLN WLLQRPGQSPQPLIYLVSKLESGVPDRFSGSGSGTDFTLK ISGVEAEDVGVYYCMQFTHYPYTFGQGTKLEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKV YACEVTHQGLSSPVTKSFNRGEC
719	Construct 9 Heavy Chain 1	QVQLVQSGAEVQRPGASVKVSCKASGYIFTEYYMYWV RQAPGQGLELVGRIDPEDGSIDYVEKFKKKVTLTADTSS STAYMELSSLTSDDTAVYYCARGKFNYRFAYWGQGTL VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS SLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCP APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVCTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVF SCSVMHEALHNRFTQKSLSLSPGK

720	Construct 9 Heavy Chain 2	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWV RQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTISRDNSK NTAFLQMDSLRPEDTGVYFCARYYDDHYSLDYWGQGT PVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSA SVGDRVTITCSASSSVSYMNWYQQTPGKAPKRWIYDTS KLASGVPSRFSGSGSGTDYTFTISSLQPEDIATYYCQQWS SNPFTFGQGTKLQITGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCRE EMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGK
518	Construct 10 Light Chain	DIQMTQSPSSLSASVGDRVTITCHASQNIYVWLNWYQQ KPGKAPKLLIYKASNLHTGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQGQTYPYTFGGGTKVEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ SGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYAC EVTHQGLSSPVTKSFNRGEC
721	Construct 10 Heavy Chain 1	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYIHWVR QAPGQGLEWIGCIYPGNVNTNYNEKFKDRATLTVDTSIS TAYMELSRLRSDDTAVYFCTRSHYGLDWNFDVWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPS SSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHE DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPR EPQVCTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGN VFSCSVMHEALHNRFTQKSLSLSPGK
720	Construct 10 Heavy Chain 2	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWV RQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTISRDNSK NTAFLQMDSLRPEDTGVYFCARYYDDHYSLDYWGQGT PVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSA SVGDRVTITCSASSSVSYMNWYQQTPGKAPKRWIYDTS KLASGVPSRFSGSGSGTDYTFTISSLQPEDIATYYCQQWS SNPFTFGQGTKLQITGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCRE EMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGK
722	Construct 11 Heavy Chain 1	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN

		STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVCTLPPSREEMTKNQVSLSCAVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDK SRWQQGNVFSCSVMHEALHNRFTQKSLSLSPGK
720	Construct 11 Heavy Chain 2	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWV RQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTISRDNSK NTAFLQMDSLRPEDTGVYFCARYYDDHYSLDYWGQGT PVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSA SVGDRVTITCSASSSVSYMNWYQQTPGKAPKRWIYDTS KLASGVPSRFSGSGSGTDYTFTISSLQPEDIATYYCQQWS SNPFTFGQGTKLQITGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCRE EMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGK
673	Construct 12 Light Chain	DVVMTQSPPSLLVTLGQPASISCRSSQSLLHSSGNTYLN WLLQRPGQSPQPLIYLVSKLESGVPDRFSGSGSGTDFTLK ISGVEAEDVGVYYCMQFTHYPYTFGQGTKLEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKV YACEVTHQGLSSPVTKSFNRGEC
719	Construct 12 Heavy Chain 1	QVQLVQSGAEVQRPGASVKVSCKASGYIFTEYYMYWV RQAPGQGLELVGRIDPEDGSIDYVEKFKKKVTLTADTSS STAYMELSSLTSDDTAVYYCARGKFNYRFAYWGQGTL VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS SLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCP APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVCTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVF SCSVMHEALHNRFTQKSLSLSPGK
723	Construct 12 Heavy Chain 2	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWV RQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTISRDNSK NTAFLQMDSLRPEDTGVYFCARYYDDHYSLDYWGQGT PVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSA SVGDRVTITCSASSSVSYMNWYQQTPGKAPKRWIYDTS KLASGVPSRFSGSGSGTDYTFTISSLQPEDIATYYCQQWS SNPFTFGQGTKLQITGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCRE EMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTT

		PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGGGGGSGGGGSGGGGSEEDPCACES LVKFQAKVEGLLQALTRKLEAVSKRLAILENTVV
518	Construct 13 Light Chain	DIQMTQSPSSLSASVGDRVTITCHASQNIYVWLNWYQQ KPGKAPKLLIYKASNLHTGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQGQTYPYTFGGGTKVEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ SGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYAC EVTHQGLSSPVTKSFNRGEC
721	Construct 13 Heavy Chain 1	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYIHWVR QAPGQGLEWIGCIYPGNVNTNYNEKFKDRATLTVDTSIS TAYMELSRLRSDDTAVYFCTRSHYGLDWNFDVWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPS SSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHE DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPR EPQVCTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGN VFSCSVMHEALHNRFTQKSLSLSPGK
723	Construct 13 Heavy Chain 2	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWV RQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTISRDNSK NTAFLQMDSLRPEDTGVYFCARYYDDHYSLDYWGQGT PVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSA SVGDRVTITCSASSSVSYMNWYQQTPGKAPKRWIYDTS KLASGVPSRFSGSGSGTDYTFTISSLQPEDIATYYCQQWS SNPFTFGQGTKLQITGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCRE EMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGGGGGSGGGGSGGGGSEEDPCACES LVKFQAKVEGLLQALTRKLEAVSKRLAILENTVV
722	Construct 14 Heavy Chain 1	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVCTLPPSREEMTKNQVSLSCAVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDK SRWQQGNVFSCSVMHEALHNRFTQKSLSLSPGK
723	Construct 14 Heavy Chain 2	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWV RQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTISRDNSK NTAFLQMDSLRPEDTGVYFCARYYDDHYSLDYWGQGT PVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSA SVGDRVTITCSASSSVSYMNWYQQTPGKAPKRWIYDTS

		KLASGVPSRFSGSGSGTDYTFTISSLQPEDIATYYCQQWS SNPFTFGQGTKLQITGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCRE EMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGGGGGSGGGGSGGGGSEEDPCACES LVKFQAKVEGLLQALTRKLEAVSKRLAILENTVV
673	Construct 15 Light Chain	DVVMTQSPPSLLVTLGQPASISCRSSQSLLHSSGNTYLN WLLQRPGQSPQPLIYLVSKLESGVPDRFSGSGSGTDFTLK ISGVEAEDVGVYYCMQFTHYPYTFGQGTKLEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKV YACEVTHQGLSSPVTKSFNRGEC
719	Construct 15 Heavy Chain 1	QVQLVQSGAEVQRPGASVKVSCKASGYIFTEYYMYWV RQAPGQGLELVGRIDPEDGSIDYVEKFKKKVTLTADTSS STAYMELSSLTSDDTAVYYCARGKFNYRFAYWGQGTL VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS SLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCP APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHED PEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVCTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNG QPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGNVF SCSVMHEALHNRFTQKSLSLSPGK
724	Construct 15 Heavy Chain 2	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWV RQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTISRDNSK NTAFLQMDSLRPEDTGVYFCARYYDDHYSLDYWGQGT PVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSA SVGDRVTITCSASSSVSYMNWYQQTPGKAPKRWIYDTS KLASGVPSRFSGSGSGTDYTFTISSLQPEDIATYYCQQWS SNPFTFGQGTKLQITGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCRE EMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGGGGGSDLGPQMLRELQETNAALQD VRELLRQQVREITFLKNTVMECDACGMQQ
518	Construct 16 Light Chain	DIQMTQSPSSLSASVGDRVTITCHASQNIYVWLNWYQQ KPGKAPKLLIYKASNLHTGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQGQTYPYTFGGGTKVEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ

		SGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYAC EVTHQGLSSPVTKSFNRGEC
721	Construct 16 Heavy Chain 1	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYIHWVR QAPGQGLEWIGCIYPGNVNTNYNEKFKDRATLTVDTSIS TAYMELSRLRSDDTAVYFCTRSHYGLDWNFDVWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPS SSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHE DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPR EPQVCTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLVSKLTVDKSRWQQGN VFSCSVMHEALHNRFTQKSLSLSPGK
724	Construct 16 Heavy Chain 2	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWV RQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTISRDNSK NTAFLQMDSLRPEDTGVYFCARYYDDHYSLDYWGQGT PVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSA SVGDRVTITCSASSSVSYMNWYQQTPGKAPKRWIYDTS KLASGVPSRFSGSGSGTDYTFTISSLQPEDIATYYCQQWS SNPFTFGQGTKLQITGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCRE EMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL HNHYTQKSLSLSPGGGGGSDLGPQMLRELQETNAALQD VRELLRQQVREITFLKNTVMECDACGMQQ
722	Construct 17 Heavy Chain 1	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVCTLPPSREEMTKNQVSLSCAVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLVSKLTVDK SRWQQGNVFSCSVMHEALHNRFTQKSLSLSPGK
724	Construct 17 Heavy Chain 2	QVQLVQSGGGVVQPGRSLRLSCKASGYTFTRYTMHWV RQAPGKGLEWIGYINPSRGYTNYNQKVKDRFTISRDNSK NTAFLQMDSLRPEDTGVYFCARYYDDHYSLDYWGQGT PVTVSSGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSA SVGDRVTITCSASSSVSYMNWYQQTPGKAPKRWIYDTS KLASGVPSRFSGSGSGTDYTFTISSLQPEDIATYYCQQWS SNPFTFGQGTKLQITGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCRE EMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEAL

		HNHYTQKSLSLSPGGGGGSDLGPQMLRELQETNAALQD VRELLRQQVREITFLKNTVMECDACGMQQ
SEQ ID NO: 726	Anti-CD3 (4)/anti-CD28 (2) bispecific heavy chain	QVQLVESGGGLVQPGGSLRLSCAASGFTFSTYGMSWVR QAPGKGLEWVSSIFYTGSSTYYADSVKGRFTISRDNSKN TLYLQMNSLRAEDTAVYYCARIGYAGDSKYAIWGQGTL VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS SLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHE DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSGGG GSGGGGSEVKLVESGGDLVQPGDSLTLSCVASGFTFSKQ GMHWIRQAPKKGLEWIAMIYYDSSKMYYADTVKGRFTI SRDNSKNTLYLEMNSLRSEDTAMYYCASFWWDLDFDH WGQGVMVTVSSGGGGSGGGGSGGGGSGGGGSDILVTQ TPVSLPVSLGGHVSISCRSSQSLVRSEGTTYFNWYLQKPG QSPQLLIYRVSNRFSGVPDRFSGSGSGTDFTLKISRVEPED LGVYYCLQSSHFPWTFGGGTKLELK
SEQ ID NO: 1416	Anti-CD3 (4)/anti-CD28 (2) bispecific alternative heavy chain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYGMSWVR QAPGKGLEWVSSIFYTGSSTYYADSVKGRFTISRDNSKN TLYLQMNSLRAEDTAVYYCARIGYAGDSKYAIWGQGTL VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS SLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHE DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSGGG GSGGGGSEVKLVESGGDLVQPGDSLTLSCVASGFTFSKQ GMHWIRQAPKKGLEWIAMIYYDSSKMYYADTVKGRFTI SRDNSKNTLYLEMNSLRSEDTAMYYCASFWWDLDFDH WGQGVMVTVSSGGGGSGGGGSGGGGSGGGGSDILVTQ TPVSLPVSLGGHVSISCRSSQSLVRSEGTTYFNWYLQKPG QSPQLLIYRVSNRFSGVPDRFSGSGSGTDFTLKISRVEPED LGVYYCLQSSHFPWTFGGGTKLELK
SEQ ID NO: 728	Anti-CD3 (4)/anti-CD28 (2) bispecific light chain 1	DIVLTQPPSVSGAPGQRVTISCSGSSSNIVSNYVNWYQQL PGTAPKLLIYDNNKRPSGVPDRFSGSKSGTSASLAITGLQ SEDEADYYCQSYAIGSYSVVFGGGTKLTVLGQGTKVEIK RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKV QWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA DYEKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 730	Anti-CD3 (4)/anti-CD28 (2) bispecific light chain 2	DIVLTQPPSVSGAPGQRVTISCSGSSSNIVSNYVNWYQQL PGTAPKLLIYDNNKRPSGVPDRFSGSKSGTSASLAITGLQ SEDEADYYCQSYAIGSYSVVFGGGTKLTVLGQPKAAPSV TLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSP VKAGVETTTPSKQSNNKYAASSYLSLTPEQWKSHRSYS CQVTHEGSTVEKTVAPTECS
892	Anti-CD3 (2)/anti-CD28 (2) light chain	DIVLTQPPSVSGAPGQRVTISCSGSSSNIVSNYVNWYQQL PGTAPKLLIYDNNKRPSGVPDRFSGSKSGTSASLAITGLQ SEDEADYYCQSYAIGSYSVVFGGGTKLTVLGQGTKVEIK RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKV QWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKA DYEKHKVYACEVTHQGLSSPVTKSFNRGEC
893	Anti-CD3 (2)/anti-CD28 (2) heavy chain	QVQLVESGGGLVQPGGSLRLSCAASGFTFSTYGMSWVR QAPGKGLEWVSSIFYTGSSTYYADSVKGRFTISRDNSKN TLYLQMNSLRAEDTAVYYCARIGYAGDSKYAIWGQGTL VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS SLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHE DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSGGG GSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNK YAMNWVRQAPGKCLEWVARIRSKYNNYATYYADSVK DRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFG NSYISYWAYWGQGTLVTVSSGGGGSGGGGSGGGGSGG GGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAA LTLSGVQPEDEAEYYCVLWYSNRWVFGCGTKLTVL
SEQ ID NO: 1417	Anti-CD3 (2)/anti-CD28 (2) alternative heavy chain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYGMSWVR QAPGKGLEWVSSIFYTGSSTYYADSVKGRFTISRDNSKN TLYLQMNSLRAEDTAVYYCARIGYAGDSKYAIWGQGTL VTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPE PVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSS SLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCP APEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHE DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVL TVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPR EPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGGGGGSGGGGSGGG GSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNK YAMNWVRQAPGKCLEWVARIRSKYNNYATYYADSVK DRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFG

		NSYISYWAYWGQGTLVTVSSGGGGSGGGGSGGGGSGG GGSQTVVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPN WVQQKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAA LTLSGVQPEDEAEYYCVLWYSNRWVFGCGTKLTVL
894	Anti-CD3 (4)/anti-CD28 (1) light chain	DIQMTQSPSSLSASVGDRVTITCHASQNIYVWLNWYQQ KPGKAPKLLIYKASNLHTGVPSRFSGSGSGTDFTLTISSL QPEDFATYYCQQGQTYPYTFGGGTKVEIKRTVAAPSVFI FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ SGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYAC EVTHQGLSSPVTKSFNRGEC
895	Anti-CD3 (4)/anti-CD28 (1) heavy chain	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYIHWVR QAPGQGLEWIGCIYPGNVNTNYNEKFKDRATLTVDTSIS TAYMELSRLRSDDTAVYFCTRSHYGLDWNFDVWGQGT TVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFP EPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPS SSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPC PAPEAAGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKH EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQP REPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGGGSEVKLVESGG DLVQPGDSLTLSCVASGFTFSKQGMHWIRQAPKKGLEW IAMIYYDSSKMYYADTVKGRFTISRDNSKNTLYLEMNSL RSEDTAMYYCASFWWDLDFDHWGQGVMVTVSSGGGG SGGGGSGGGGSGGGGSDILVTQTPVSLPVSLGGHVSISC RSSQSLVRSEGTTYFNWYLQKPGQSPQLLIYRVSNRFSG VPDRFSGSGSGTDFTLKISRVEPEDLGVYYCLQSSHFPWT FGGGTKLELK

In some embodiments, the multispecific binding molecule comprises a bispecific antibody. In some embodiments, the bispecific antibody is configured in any one of the schema provided in **FIGs. 37A-37B**, **FIG. 48A-48B**, **FIG. 49A-49C** ,and **FIG. 50A-50B**. In some embodiments, the bispecific antibody is monovalent or bivalent. In some embodiments, the bispecific antibody comprises an Fc region. In some embodiments, the Fc region of the bispecific antibody is silenced.

In some embodiments, the multispecific binding molecule comprises a plurality of bispecific antibodies. In some embodiments, one or more of the plurality of bispecific antibodies is monovalent. In some embodiments, one or more of the plurality of bispecific antibodies comprises an Fc region. In some embodiments, the Fc region of the one or more of the plurality of bispecific antibodies is silenced. In some embodiments, one or more of the plurality of

bispecific antibodies are conjugated together into a multimer. In some embodiments, the multimer is configured in any one of the multispecific schema provided in **FIG. 37B** and **FIG. 48B**.

In some embodiments, a multispecific binding molecule described herein comprises an Fc region, e.g., wherein the Fc region is Fc silent. In some embodiments, the Fc region comprises a mutation at one or more of (e.g., all of) D265, N297, and P329, numbered according to the Eu numbering system. In some embodiments, the Fc region comprises the mutations D265A, N297A, and P329A (DANAPA), numbered according to the Eu numbering system.

In some embodiments, a multispecific binding molecule described herein comprises a first binding domain and a second binding domain. For instance, the first binding domain may be an anti-CD3 binding domain and the second binding domain may be a costimulatory molecule binding domain, or the first binding domain may be a costimulatory molecule binding domain and the second binding domain may be an anti-CD3 binding domain. In some embodiments, the costimulatory molecule binding domain binds to CD2, CD28, CD25, CD27, IL6Rb, ICOS, or 41BB. In some embodiments, the costimulatory molecule binding domain activates CD2, CD28, CD25, CD27, IL6Rb, ICOS, or 41BB. In some embodiments, a multispecific binding molecule described herein comprises an Fc region that is mutated to have reduced binding to Fc receptor or reduced ADCC, ADCP, or CDC activity, e.g., an Fc region comprising the mutations D265A, N297A, and P329A (DANAPA), numbered according to the Eu numbering system.

In some embodiments, the first binding domain (e.g., an scFv) is N-terminal of the VH of the second binding domain (e.g., a Fab fragment), e.g., linked via a peptide linker. In some embodiments, the multispecific binding molecule further comprises one or more of (e.g., all of) a CH1, CH2, and CH3, e.g., in order from N-terminal to C-terminal. In some embodiments, a polypeptide of the multispecific binding molecule comprises the following sequences, from N-terminal to C-terminal: VH of the first binding domain, first peptide linker (e.g., a (G4S)4 linker (SEQ ID NO: 29)), VL of first binding domain, second peptide linker (e.g., a (G4S)4 linker (SEQ ID NO: 29)), VH of the second binding domain, CH1, CH2, and CH3. In some embodiments, a polypeptide of the multispecific binding molecule comprises the following sequences: from N-terminal to C-terminal: VL of the second binding domain and CL. In some embodiments, the multispecific binding molecule comprises an Fc region that is mutated to have reduced binding to Fc receptor or reduced ADCC, ADCP, or CDC activity, e.g., an Fc region

comprising the mutations D265A, N297A, and P329A (DANAPA), numbered according to the Eu numbering system. In some embodiments, the first binding fragment comprises an anti-CD3 binding domain, e.g., an anti-CD3 scFv, e.g., comprising an anti-CD3 sequence disclosed in Table 19. In some embodiments, the second binding domain comprises a costimulatory molecule binding domain, e.g., an anti-CD2 binding domain, e.g., an anti-CD2 Fab, e.g., comprising an anti-CD2 sequence disclosed in Table 19. In some embodiments, the second binding domain comprises a costimulatory molecule binding domain, e.g., an anti-CD28 binding domain, e.g., an anti-CD28 Fab, e.g., comprising an anti-CD28 sequence disclosed in Table 19. In some embodiments, the first binding fragment comprises a costimulatory molecule binding domain, e.g., an anti-CD2 or anti-CD28 binding domain, e.g., an anti-CD2 or anti-CD28 scFv, e.g., comprising an anti-CD2 or anti-CD28 sequence disclosed in Table 19. In some embodiments, the second binding domain comprises an anti-CD3 binding domain, e.g., an anti-CD3 Fab, e.g., comprising an anti-CD3 sequence disclosed in Table 19. Examples of such multispecific binding molecules are depicted as the top left construct in **FIG. 37A**; Construct 1 or Construct 2 in **FIG. 48A**; and Construct 1 or Construct 2 in Table 20.

In some embodiments, the first binding domain (e.g., a Fab fragment) is N-terminal to a second binding domain (e.g., an scFv), e.g., wherein an Fc region is situated between the first and second binding domain. In some embodiments, the Fc region is mutated to have reduced binding to Fc receptor or reduced ADCC, ADCP, or CDC activity, e.g., an Fc region comprising the mutations D265A, N297A, and P329A (DANAPA), numbered according to the Eu numbering system. In some embodiments the Fc region is comprises the mutations L234A, L235A, S267K, and P329A (LALASKPA), numbered according to the Eu numbering system. In some embodiments, the Fc region comprises the mutations L234A, L235A, and P329G (LALAPG), numbered according to the Eu numbering system. In some embodiments, the Fc region comprises the mutations G237A, D265A, P329A, and S267K (GADAPASK), numbered according to the Eu numbering system. In some embodiments, the multispecific binding molecule further comprises one or more of (e.g., all of) a CH1, CH2, and CH3, e.g., in order from N-terminal to C-terminal. In some embodiments, a polypeptide of the multispecific binding molecule comprises the following sequences, from N-terminal to C-terminal: VH of the first binding domain, CH1, CH2, CH3, first peptide linker (e.g., a (G4S)4 linker (SEQ ID NO: 29)), VH of second binding domain, second peptide linker (e.g., a (G4S)4 linker (SEQ ID NO:

29)), and VL of the second binding domain. In some embodiments, a polypeptide of the multispecific binding molecule comprises the following sequences: from N-terminal to C-terminal: VL of the first binding domain and CL. In some embodiments, the first binding domain comprises a costimulatory molecule binding domain, e.g., an anti-CD2 binding domain, e.g., an anti-CD2 Fab, e.g., comprising an anti-CD2 sequence disclosed in Table 19. In some embodiments, the first binding domain comprises a costimulatory molecule binding domain, e.g., an anti-CD28 binding domain, e.g., an anti-CD28 Fab, e.g., comprising an anti-CD28 sequence disclosed in Table 19, e.g., anti-CD28 (1) or anti-CD28 (2). In some embodiments, the second binding domain comprises an anti-CD3 binding domain, e.g., an anti-CD3 scFv, e.g., comprising an anti-CD3 sequence disclosed in Table 19, e.g., anti-CD3 (1), anti-CD3 (2), anti-CD3 (3), or anti-CD3 (4). In some embodiments, the first binding domain comprises an anti-CD3 binding domain, e.g., an anti-CD3 Fab, e.g., comprising an anti-CD3 sequence disclosed in Table 19, e.g., anti-CD3 (1), anti-CD3 (2), anti-CD3 (3), or anti-CD3 (4). In some embodiments, the second binding domain comprises a costimulatory molecule binding domain, e.g., an anti-CD2 or anti-CD28 binding domain, e.g., an anti-CD2 or anti-CD28 scFv, e.g., comprising an anti-CD2 or anti-CD28 sequence disclosed in Table 19. Examples of such multispecific binding molecules are depicted as the second construct from the left in the top row of **FIG. 37A**; Construct 3 or Construct 4 in **FIG. 48A**; and Construct 3 or Construct 4 in Table 20.

In some embodiments, the first binding domain (e.g., a Fab fragment) is N terminal to a second binding domain (e.g., a scFv), e.g., via a peptide linker. In some embodiments, the multispecific binding molecule further comprises one or more of (e.g., all of) a CH1, CH2, and CH3, e.g., in order from N-terminal to C-terminal. In some embodiments, a polypeptide of the multispecific binding molecule comprises the following sequences, from N-terminal to C-terminal: VH of the first binding domain, CH1, first peptide linker (e.g., a (G4S)2 linker (SEQ ID NO: 767)), VH of the second binding domain, second peptide linker (e.g., a (G4S)4 linker (SEQ ID NO: 29)), VL of the second binding domain, third peptide linker (e.g., a (G4S)4 linker (SEQ ID NO: 29)), CH2, and CH3. In some embodiments, a polypeptide of the multispecific binding molecule comprises the following sequences: from N-terminal to C-terminal: VL of the first binding domain and CL. In some embodiments, the multispecific binding molecule comprises an Fc region that is mutated to have reduced binding to Fc receptor or reduced ADCC, ADCP, or CDC activity, e.g., an Fc region comprising the mutations D265A, N297A, and

P329A (DANAPA), numbered according to the Eu numbering system. In some embodiments, the first binding domain comprises a costimulatory molecule binding domain, e.g., an anti-CD2 binding domain, e.g., an anti-CD2 Fab, e.g., comprising an anti-CD2 sequence disclosed in Table 19. In some embodiments, the first binding domain comprises a costimulatory molecule binding domain, e.g., an anti-CD28 binding domain, e.g., an anti-CD28 Fab, e.g., comprising an anti-CD28 sequence disclosed in Table 19, e.g., anti-CD28 (1) or anti-CD28 (2). In some embodiments, the first binding domain comprises a costimulatory molecule binding domain, e.g., an anti-CD25 binding domain (for example, an anti-CD25 Fab), an anti-CD27 binding domain (for example, an anti-CD27 Fab), an anti-IL6Rb binding domain (for example, an anti-IL6Rb Fab), an anti-ICOS binding domain (for example, an anti-ICOS Fab), or an anti-41BB binding domain (for example, an anti-41BB Fab). In some embodiments, the second binding domain comprises an anti-CD3 binding domain, e.g., an anti-CD3 scFv, e.g., comprising an anti-CD3 sequence disclosed in Table 19, e.g., anti-CD3 (1), anti-CD3 (2), anti-CD3 (3), or anti-CD3 (4). In some embodiments, the first binding domain comprises an anti-CD3 binding domain, e.g., an anti-CD3 Fab, e.g., comprising an anti-CD3 sequence disclosed in Table 19, e.g., anti-CD3 (1), anti-CD3 (2), anti-CD3 (3), or anti-CD3 (4). In some embodiments, the second binding domain comprises a costimulatory molecule binding domain, e.g., an anti-CD2 binding domain (for example, an anti-CD2 scFv), an anti-CD28 binding domain (for example, an anti-CD28 scFv), an anti-CD25 binding domain (for example, an anti-CD25 scFv), an anti-CD27 binding domain (for example, an anti-CD27 scFv), an anti-IL6Rb binding domain (for example, an anti-IL6Rb scFv), an anti-ICOS binding domain (for example, an anti-ICOS scFv), or an anti-41BB binding domain (for example, an anti-41BB scFv). Examples of such multispecific binding molecules are depicted as the third construct from the left in the top row of **FIG. 37A**; Construct 5 or Construct 6 in **FIG. 48A**; and Construct 5 or Construct 6 in Table 20.

In some embodiments, the first binding domain (e.g., an scFv) is N-terminal to a second binding domain (e.g., a Fab fragment), e.g., wherein an Fc region is situated between the first and second binding domain. In some embodiments, the Fc region is mutated to have reduced binding to Fc receptor or reduced ADCC, ADCP, or CDC activity, e.g., an Fc region comprising the mutations D265A, N297A, and P329A (DANAPA), numbered according to the Eu numbering system. In some embodiments, the multispecific binding molecule further comprises one or more of (e.g., all of) a CH2, CH3, and CH1, e.g., in order from N-terminal to C-terminal.

In some embodiments, a polypeptide of the multispecific binding molecule comprises the following sequences, from N-terminal to C-terminal: VH of the first binding domain, first peptide linker (e.g., a (G4S)4 linker) (SEQ ID NO: 29), VL of the first binding domain, second peptide linker (e.g., a (G4S) linker (SEQ ID NO: 768)), CH2, CH3, third peptide linker (e.g., a (G4S)4 linker (SEQ ID NO: 29)), VH of the second binding domain, and CH1. In some embodiments, a polypeptide of the multispecific binding molecule comprises the following sequences: from N-terminal to C-terminal: VL of the second binding domain and CL. In some embodiments, the first binding domain comprises an anti-CD3 binding domain, e.g., an anti-CD3 scFv, e.g., comprising an anti-CD3 sequence disclosed in Table 19. In some embodiments, the second binding domain comprises a costimulatory molecule binding domain, e.g., an anti-CD2 binding domain, e.g., an anti-CD2 Fab, e.g., comprising an anti-CD2 sequence disclosed in Table 19. In some embodiments, the second binding domain comprises a costimulatory molecule binding domain, e.g., an anti-CD28 binding domain, e.g., an anti-CD28 Fab, e.g., comprising an anti-CD28 sequence disclosed in Table 19. In some embodiments, the first binding domain comprises a costimulatory molecule binding domain, e.g., an anti-CD2 or anti-CD28 binding domain, e.g., an anti-CD2 or anti-CD28 scFv, e.g., comprising an anti-CD2 or anti-CD28 sequence disclosed in Table 19. In some embodiments, the second binding domain comprises an anti-CD3 binding domain, e.g., an anti-CD3 Fab, e.g., comprising an anti-CD3 sequence disclosed in Table 19. Examples of such multispecific binding molecules are depicted as the rightmost construct in the top row of **FIG. 37A**; Construct 7 or Construct 8 in **FIG. 48A**; and Construct 7 or Construct 8 in Table 20.

In some embodiments, the first binding domain (e.g., a Fab fragment) is situated N terminal to a first Fc region. In some embodiments, the multispecific binding molecule comprises one or more of (e.g., all of) a first CH1, a first CH2, and a first CH3, e.g., in order from N-terminal to C-terminal. In some embodiments, the second binding domain (e.g., an scFv) is situated N terminal to a second Fc region, e.g., in a second polypeptide chain. In some embodiments, the multispecific binding molecule comprises, e.g., in the second polypeptide chain, one or more of (e.g., both of) a second CH2 and a second CH3, e.g., in order from N-terminal to C-terminal. In some embodiments, the multispecific binding molecule comprises a heterodimeric antibody molecule, such as for instance, wherein the first and second Fc regions comprise knob-into-hole mutations. In some embodiments, the first Fc region binds the second

Fc region more strongly than the first Fc region binds another copy of the first Fc region. In some embodiments, a first polypeptide of the multispecific binding molecule comprises the following sequences, from N-terminal to C-terminal: VH of the first binding domain, a first CH1, a first CH2, and a first CH3. In some embodiments, a second polypeptide of the multispecific binding molecule comprises the following sequences, from N-terminal to C-terminal: VH of the second binding domain, a first peptide linker (e.g., a (G4S) linker (SEQ ID NO: 768)), VL of the second binding domain, a second CH2, and a second CH3. In some embodiments, a third polypeptide of the multispecific binding molecule comprises the following sequences: from N-terminal to C-terminal: VL of the first binding domain and CL. In some embodiments, the second polypeptide of the multispecific binding molecule further comprises a homomultimerization domain, e.g., a Matrilin1 protein or the coiled-coil domain of cartilage oligomeric matrix protein (COMPcc), C-terminal to the second CH3, e.g., via a peptide linker (e.g., a (G4S)4 linker (SEQ ID NO: 29), a (G4S) linker (SEQ ID NO: 768), or a (G4S)3 linker (SEQ ID NO: 30)). In some embodiments, the multispecific binding molecule comprises two, three, four, or five copies of the first binding domain and the same number of copies of the second binding domain, e.g., as depicted in **FIG. 37B**. In some embodiments, the first binding domain comprises a costimulatory molecule binding domain, e.g., an anti-CD2 binding domain (for example, an anti-CD2 Fab). In some embodiments, the first binding domain comprises a costimulatory molecule binding domain, e.g., an anti-CD28 binding domain (for example, an anti-CD28 Fab). In some embodiments, the second binding domain comprises an anti-CD3 binding domain, e.g., an anti-CD3 scFv. Examples of such multispecific binding molecules are depicted as the leftmost construct in the bottom row of **FIG. 37A**; constructs in **FIG. 37B**, Construct 9, Construct 10, Construct 12, Construct 13, Construct 15, and Construct 16 in **FIG. 48B**; and Construct 9, Construct 10, Construct 12, Construct 13, Construct 15, and Construct 16 in Table 20.

In some embodiments, a binding molecule described herein comprises a binding domain. In some embodiments the binding domain (e.g., an scFv) is situated N terminal to an Fc region. In some embodiments, the binding molecule comprises a heterodimeric antibody molecule, such as for instance, wherein the first and second Fc regions comprise knob-into-hole mutations. In some embodiments, the first Fc region binds the second Fc region more strongly than the first Fc region binds another copy of the first Fc region. In some embodiments, the binding molecule

comprises one or more of (e.g., all of) a CH2 and a CH3, e.g., in order from N-terminal to C-terminal. In some embodiments, a second polypeptide of the binding molecule comprises the following sequences, from N-terminal to C-terminal: VH of the binding domain, first peptide linker (e.g., a (G4S)4 linker (SEQ ID NO: 29)), VL of the binding domain, second peptide linker (e.g., (G4S)4 linker (SEQ ID NO: 29) or (G4S) linker (SEQ ID NO: 768)), CH2, and CH3. In some embodiments, the second polypeptide of the binding molecule further comprises a homomultimerization domain, e.g., a Matrilin1 protein or the coiled-coil domain of cartilage oligomeric matrix protein (COMPcc), C-terminal to the second CH3, e.g., via a peptide linker (e.g., (G4S)4 linker (SEQ ID NO: 29), (GS4)3 linker (SEQ ID NO: 878), or (G4S) linker (SEQ ID NO: 768)). In some embodiments, the binding molecule comprises two, three, four, or five copies of the binding, e.g., as depicted in **FIG. 37B**. In some embodiments, the binding domain comprises an anti-CD3 binding domain, e.g., an anti-CD3 scFv. In some embodiments, a costimulatory molecule binding domain is absent. Examples of such binding molecules are depicted as the rightmost construct in the bottom row of **FIG. 37A**; Construct 11, Construct 14, and Construct 17 in **FIG. 48B**; and Construct 11, Construct 14, and Construct 17 in Table 20.

In some embodiments, the multispecific binding protein comprises an anti-CD28 binding domain, e.g., an anti-CD28 Fab, e.g., comprising an anti-CD28 (2) sequence of Table 19 (or a sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto), and an anti-CD3 scFv, e.g., comprising an anti-CD3 (4) sequence of Table 19 (or a sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto). In some embodiments, the multispecific binding protein comprises an Fc region, wherein the anti-CD28 Fab is fused to the Fc region, which is further fused to the anti-CD3 scFv. In some embodiments, the Fc region comprises L234A, L235A, S267K, and P329A mutations (LALASKPA), numbered according to the Eu numbering system. In some embodiments, the multispecific binding protein comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 726 or 1416, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 726 or 1416. In some embodiments, the multispecific binding protein comprises a light chain comprising the amino acid sequence of SEQ ID NO: 728 or 730, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 728 or 730. In some embodiments, the multispecific binding protein comprises a heavy chain comprising the amino

acid sequence of SEQ ID NO: 726 or 1416, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 726 or 1416, and a light chain comprising the amino acid sequence of SEQ ID NO: 728 or 730, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 728 or 730. In some embodiments, the multispecific binding protein comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 726, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 728, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In some embodiments, the multispecific binding protein comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 726, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 730, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In some embodiments, the multispecific binding protein comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 1416, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 728, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In some embodiments, the multispecific binding protein comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 1416, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 730, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto.

In some embodiments, the multispecific binding protein comprises an anti-CD28 binding domain, e.g., an anti-CD28 Fab, e.g., comprising an anti-CD28 (2) sequence of Table 19 (or a sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto), and an anti-CD3 scFv, e.g., comprising an anti-CD3 (2) sequence of Table 19 (or a sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto). In some embodiments, the multispecific binding protein comprises an Fc region, wherein the anti-CD28 Fab is fused to the Fc region, which is further fused to the anti-CD3 scFv. In some embodiments, the Fc region comprises L234A, L235A, S267K, and P329A

mutations (LALASKPA), numbered according to the Eu numbering system, numbered according to the Eu numbering system. In some embodiments, the multispecific binding protein comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 893 or 1417, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO: 893 or 1417. In some embodiments, the multispecific binding protein comprises a light chain comprising the amino acid sequence of SEQ ID NO: 892, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In some embodiments, the multispecific binding protein comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 893, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 892, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In some embodiments, the multispecific binding protein comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 1417, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 892, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto.

In some embodiments, the multispecific binding protein comprises an anti-CD28 binding domain, e.g., an anti-CD28 Fab, e.g., comprising an anti-CD28 (1) sequence of Table 19 (or a sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto) and an anti-CD3 scFv, e.g., comprising an anti-CD3 (4) sequence of Table 19 (or a sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto). In some embodiments, the multispecific binding protein comprises an Fc region, wherein the anti-CD28 Fab is fused to the Fc region, which is further fused to the anti-CD3 scFv. In some embodiments, the Fc region comprises L234A, L235A, S267K, and P329A mutations (LALASKPA), numbered according to the Eu numbering system. In some embodiments, the multispecific binding protein comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 895, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto. In some embodiments, the multispecific binding protein comprises a light chain comprising the amino acid sequence of SEQ ID NO: 894, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99%

identical thereto. In some embodiments, the multispecific binding protein comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 895, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 894, or an amino acid sequence at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical thereto.

It is understood that in many of the embodiments herein, a multispecific binding molecule comprises two or more polypeptide chains that are covalently linked to each other, e.g., via a disulfide bridge. However, in some embodiments, the two or more polypeptide chains of the multispecific binding molecule may be noncovalently bound to each other.

It is also understood that a Fab fragment may be present as part of a larger protein, for instance, a Fab fragment may be fused with CH2 and CH3 and thus be part of full length antibody.

The multispecific binding molecule comprising an agent that stimulates a CD3/TCR complex and an agent that stimulates a costimulatory molecule and/or growth factor receptor disclosed herein is contemplated for use as a cell activation agent disclosed herein.

Fc Variants

In some embodiments, a multispecific binding molecule described herein comprises an Fc region, e.g., as described herein. In some embodiments, the Fc region is a wild type Fc region, e.g., a wild type human Fc region. In some embodiments, the Fc region comprises a variant, e.g., an Fc region comprising an addition, substitution, or deletion of at least one amino acid residue in the Fc region which results in, e.g., reduced or ablated affinity for at least one Fc receptor. In some embodiments, the multispecific binding molecule comprises the amino acid sequence of an Fc region provided in **Table 20**, or a sequence having at least 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% sequence identity thereto.

In some embodiments, the Fc region of an antibody interacts with a number of receptors or ligands including Fc Receptors (e.g., FcγRI, FcγRIIA, FcγRIIIA), the complement protein CIq, and other molecules such as proteins A and G. These interactions promote a variety of effector functions and downstream signaling events including: antibody dependent cell-mediated cytotoxicity (ADCC), Antibody-dependent cellular phagocytosis (ADCP) and complement

dependent cytotoxicity (CDC). Non-limiting exemplary Fc regions featuring these and other silencing modifications disclosed herein are provided in **Table 20** above.

In some embodiments, a multispecific binding molecule described herein comprising a variant Fc region has reduced, e.g., ablated, affinity for an Fc receptor, e.g., an Fc receptor described herein. In some embodiments, the reduced affinity is compared to an otherwise similar antibody with a wild type Fc region.

In some embodiments, a multispecific binding molecule described herein comprising a variant Fc region has one or more of the following properties: (1) reduced effector function (e.g., reduced ADCC, ADCP and/or CDC); (2) reduced binding to one or more Fc receptors; and/or (3) reduced binding to C1q complement. In some embodiments, the reduction in any one, or all of properties (1)-(3) is compared to an otherwise similar antibody with a wildtype Fc region.

Exemplary Fc region variants are provided in **Table 34** and also disclosed in Saunders O, (2019) *Frontiers in Immunology;* vol 10, article1296, the entire contents of which is hereby incorporated by reference.

In some embodiments, a multispecific binding molecule described herein comprises any one or all, or any combination of Fc region variants, e.g., mutations, disclosed in **Table 34**. In some embodiments, the Fc region of a multispecific binding molecule described herein is silenced. In some embodiments, the Fc region of a multispecific binding protein described herein is silenced by a combination of amino acid substitutions selected from the group consisting of LALA, DAPA, DANAPA, LALADANAPS, LALAGA, LALASKPA, DAPASK, GADAPA, GADAPASK, LALAPG, and LALAPA (numbered according to the Eu numbering system).

In some embodiments, a multispecific binding molecule described herein comprises any one or all, or any combination of a mutant comprising a L234, e.g., L234A and/or L235, e.g., L234A mutation (LALA) in the IgG1 Fc amino acid sequence, numbered according to the Eu numbering system; D265, e.g., D265A and/or P329, e.g., P329A (DAPA), numbered according to the Eu numbering system; N297, e.g., N297A, numbered according to the Eu numbering system; DANAPA (D265A, N297A, and P329A), numbered according to the Eu numbering system; and/or L234, e.g. L234A, L235, e.g., L235A, D265, e.g., D265A, N297, e.g., N297A, and P331, e.g., P331S (LALADANAPS), numbered according to the Eu numbering system. In some embodiments, a multispecific binding molecule described herein comprises a human IgG1

Fc variant of a wild-type human IgG1 Fc region, wherein the Fc variant comprises any one or all of: an L234 (e.g., L234A), L235 (e.g., L235A), and/or G237 (e.g., G237A) mutation (LALAGA), numbered according to the Eu numbering system; an L234 (e.g., L234A), L235 (e.g., L235A), S267 (e.g., S267K), and/or P329 (e.g., P329A) mutation (LALASKPA), numbered according to the Eu numbering system; a D265 (e.g., D265A), P329 (e.g., P329A), and/or S267 (e.g., S267K) mutation (DAPASK), numbered according to the Eu numbering system; a G237 (e.g., G237A), D265 (e.g., D265A), and/or P329 (e.g., P329A) mutation (GADAPA), numbered according to the Eu numbering system; a G237 (e.g., G237A), D265 (e.g., D265A), P329 (e.g., P329A), and/or S267 (e.g., S267K) mutation (GADAPASK), numbered according to the Eu numbering system; a L234 (e.g., L234A), L235 (e.g., L235A), and/or P329 (e.g., P329G) mutation (LALAPG), numbered according to the Eu numbering system; or a L234 (e.g., L234A), L235 (e.g., L235A), and/or P329 (e.g., P329A) mutation (LALAPA), wherein the amino acid residues are numbered according to the Eu numbering system.

In some embodiments, the Fc region of a multispecific binding protein described herein comprises a mutation that results in reduced binding to an Fc receptor or reduced ADCC, ADCP, or CDC activity, e.g., an Fc region comprising: a D265 (e.g., D265A), N297 (e.g., N297A), and P329 (e.g., P329A) mutation (DANAPA), numbered according to the Eu numbering system; an L234 (e.g., L234A), L235 (e.g., L235A), and G237 (G237A) mutation (LALAGA), numbered according to the Eu numbering system; an L234 (L234A), L235 (e.g., L235A), S267 (e.g., S267K), and P329 (e.g., P329A) mutation (LALASKPA), numbered according to the Eu numbering system; a D265 (e.g., D265A), P329 (e.g., P329A), and S267 (e.g., S267K) mutation (DAPASK), numbered according to the Eu numbering system; a G237 (e.g., G237A), a D265 (e.g., D265A), and P329 (P329A) mutation (GADAPA), numbered according to the Eu numbering system; a G237 (e.g., G237A), D265 (e.g., D265A), P329 (e.g., P329A), and S267 (e.g., S267K) mutation (GADAPASK), numbered according to the Eu numbering system; an L234 (e.g., L234A), L235 (e.g., L235A), and P329 (e.g., P329G) mutation (LALAPG), numbered according to the Eu numbering system; or an L234 (e.g., L234A), L235 (e.g., L235A), and P329 (e.g., P329A) mutation (LALAPA), numbered according to the Eu numbering system.

It is understood that the terms “LALA,” “DAPA,” “DANAPA,” “LALADANAPS,” “LALAGA”, “LALASKPA”, “DAPASK”, “GADAPA”, “GADAPASK”, “LALAPG”, and

"LALAPA" represent shorthand terminology for the different combinations of substitutions described herein rather than contiguous amino acid sequences.

Table 34: Exemplary Fc modifications

Modification or mutation	Altered effector function
Leu235Glu	ADCC;
Leu234Ala/Leu235Ala (LALA)	ADCC; ADCP; CDC
Ser228Pro/Leu235Glu	
Leu234Ala/Leu235Ala/Pro329Gly	ADCP
Pro331Ser/Leu234Glu/Leu235Phe	CDC
Asp265Ala	ADCC, ADCP
Gly237Ala	ADCP
Glu318Ala	ADCP
Glu233Pro	
Gly236Arg/Leu328Arg	ADCC
His268Gln/Val309Leu/Ala330Ser/Pro331Ser	ADCC; ADCP; CDC
Val234Ala/Gly237Ala/Pro238Ser/ His268Ala/Val309Leu/Ala330Ser/Pro331Ser	ADCC; ADCP; CDC
Leu234Ala/L235Ala/Gly237Ala/P238Ser/ His268Ala/Ala330Ser/Pro331Ser	ADCC; CDC
Ala330Leu	CDC
Asp270Ala	CDC
Lys322Ala	CDC
Pro329Ala	CDC
Pro331Ala	CDC
Val264Ala	CDC
High mannose glycosylation	CDC
Phe241Ala	CDC
Asn297Ala or Gly or Gln	ADCC; ADCP; CDC
S228P/Phe234Ala/Leu235Ala	ADCC; CDC

Compositions of mesoporous silica particles, viral vectors, and cell activation agents

Also described herein is a composition comprising an extended release agent, e.g., a population of mesoporous silica particles, and a viral vector. Also described herein is a composition, comprising a first population of mesoporous silica particles and a viral vector. In some embodiments, the MSPs (e.g., MSRs) further comprise a plurality of functional groups adsorbed or covalently bonded onto the surfaces lining the pores and/or nanochannels or the surface. In some embodiments, the functional group is a –OH (hydroxyl), amine, carboxylic acid, phosphonate, halide, azide, alkyne, epoxide, sulfhydryl, disulfide, polyethyleneimine, hydrophobic moiety or salts thereof. In some embodiments, the functional group (i.e. –OH

(hydroxyl), amine, carboxylic acid, phosphonate, halide, azide, alkyne, epoxide, sulfhydryl, disulfide, polyethyleneimine, hydrophobic moiety, or salts thereof) may be directly attached to the surface of the MSP. In some embodiments, the functional group is covalently bonded to the MSP (e.g., MSR) surface via a C_1 to C_{20} alkyl linker. In other embodiments, the functional group is covalently bonded to the MSP surface via a polyethyleneglycol linker. In particular embodiments, the polyethylene glycol linker has the formula $(-O(CH2-CH_2-)_{1-25}$. In particular embodiments, the surface modification is a C_1 to C_{20} alkyl perhaloalkyl or a C_1 to C_{20} alkyl perfluoroalkyl.

In some embodiments, the MSPs (e.g., MSRs) are surface modified with a primary, secondary, tertiary, or quaternary amine. In particular embodiments, the mesoporous silica rods are modified with polyethyleneimine. In specific embodiments, the polyethyleneimine is branched or unbranched. In alternate embodiments, the polyethyleneimine group has an average molecular weight in the range of about 1000 to 20,000 Daltons (Da), as measured by gel permeation chromatography (GPC). In some embodiments, the polyethyleneimine group has an average molecular weight of about 1,200 to 15,000 Da, about 1,500 to 12,000 Da, about 2,000 Da, about 3,000 Da, about 4,000 Da, about 5,000 Da, about 6,000 Da, about 7,000 Da, about 8,000 Da, about 9,000 Da, or about 10,000 Da, as measured by gel permeation chromatography (GPC).

In some embodiments, the viral vector is conjugated to the mesoporous silica particles. In some embodiments, the viral vector is electrostatically or covalently conjugated to the mesoporous silica particles. In some embodiments, the electrostatic conjugation between the mesoporous silica particles and the viral vector is due to oppositely surface-charged viral vectors and mesoporous silica particles. For example, and without being bound by theory, mesoporous silica particles that are surface modified by polyethyleneimine or primary, secondary, tertiary, or quaternary ammonium groups that are positively charged can be conjugated to negatively surface-charged viral vectors. Thus, in some embodiments, the viral vector is negatively charged, and the mesoporous silica particles are positively charged. In some embodiments, the covalent conjugation between the mesoporous silica particles and the viral vector is achieved by methods known to those of skill in the art, either via linkers or without linkers. For example, and without limitation, the linkers may be polyethylene glycol, alkyl groups, polymers, polyamide linkages, etc.

In some aspects, provided herein includes pharmaceutical compositions comprising mesoporous silica particles as described herein, formulated for use in the manufacture of a population of immune effector cells, e.g., T lymphocyte cells. In some embodiments, the T lymphocyte cells are transduced with a CAR. In some embodiments, the MSPs are conjugated to a viral vector as described herein. In some embodiments, the MSPs are conjugated to a cell activation agent. IN some embodiments a cell activation agent is absorbed on the MSPs. In some embodiments, the MSPs for use in in the manufacture of a population of immune effector cells, e.g., T lymphocyte cells, may be surface modified as described herein.

In some embodiments, the composition is suitable for use as an injectable composition comprising mesoporous silica particles, a viral vector, and, optionally, a cell activation agent, wherein the viral vector comprises an expression vector comprising a recombinant polynucleotide comprising an expression control sequence operatively linked to a nucleotide sequence to be expressed. In some embodiments, the viral vector is conjugated to the mesoporous silica particles as described herein. In some embodiments, the cell activation agent is absorbed on or conjugated to the mesoporous silica particles as described herein. Adsorption to the MSP (e.g., MSR) surface is as commonly understood as a molecule adhering to the surface.

Without wishing to be bound by theory, in some embodiments, an MSP-virus composition, e.g., a composition comprising an MSP and a viral vector, e.g., a viral vector encoding a CAR, limits viral vector drainage to the draining lymph node, decreasing potential off-site transduction, compared to an otherwise similar composition lacking an MSP.

In compositions of mesoporous silica particles described herein, the MSPs (e.g., MSRs) may be present in a concentration of 0.01 to 1000 μg/ml. In alternative embodiments, the concentration of MSPs or MSRs in the compositions described herein may be 0.1 to 500 μg/ml, 0.5 to 100 μg/ml, 1 to 90 μg/ml, 1 to 80 μg/ml, 1 to 70 μg/ml, 1 to 60 μg/ml, 1 to 50 μg/ml, or 1 to 40 μg/ml.

In particular embodiments, the MSPs (e.g., MSRs) may be present in a concentration of about 1 μg/ml, 10
μg/ml, 20 μg/ml, 30 μg/ml, 40 μg/ml, 50 μg/ml, 60 μg/ml, 70 μg/ml, 80 μg/ml, 90
μg/ml, 100 μg/ml, 110 μg/ml, 120 μg/ml, 130 μg/ml, 140 μg/ml, or 150 μg/ml.

In general, compositions described herein may be administered in therapeutically effective amounts as described above via any of the usual and acceptable modes known in the art, either singly or in combination with one or more therapeutic agents.

Injectable compositions may be aqueous isotonic suspensions. The compositions may be sterilized and/or contain adjuvants, such as preserving, stabilizing, wetting or emulsifying agents, solution promoters, salts for regulating the osmotic pressure and/or buffers. In addition, they may also contain other therapeutically effective substances.

Pharmaceutical compositions of the present invention may be administered in a manner appropriate to the disease to be treated (or prevented). The quantity and frequency of administration will be determined by such factors as the condition of the patient, and the type and severity of the patient's disease, although appropriate dosages may be determined by clinical trials.

In some embodiments, the pharmaceutical composition is substantially free of, e.g., there are no detectable levels of a contaminant, e.g., selected from the group consisting of endotoxin, mycoplasma, replication competent lentivirus (RCL), p24, VSV-G nucleic acid, HIV gag, residual anti-CD3/anti-CD28 coated beads, mouse antibodies, pooled human serum, bovine serum albumin, bovine serum, culture media components, vector packaging cell or plasmid components, a bacterium and a fungus. In some embodiments, the bacterium is at least one selected from the group consisting of *Alcaligenes faecalis*, *Candida albicans*, *Escherichia coli*, *Haemophilus influenza*, *Neisseria meningitides*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Streptococcus pneumonia*, and *Streptococcus pyogenes* group A.

The pharmaceutical composition (or formulation) for application may be packaged in a variety of ways depending upon the method used for administering the compositions described herein. Generally, an article for distribution includes a container having deposited therein the pharmaceutical formulation in an appropriate form. Suitable containers are well-known to those skilled in the art and include materials such as bottles (plastic and glass), sachets, ampoules, plastic bags, metal cylinders, and the like. The container may also include a tamper-proof assemblage to prevent indiscreet access to the contents of the package. In addition, the container has deposited thereon a label that describes the contents of the container. The label may also include appropriate warnings.

In some embodiments, the compositions described herein further include a cell activation agent. In some embodiments, cell activation agent is a T cell stimulating compound, an anti-idiotype antibody to a CAR antigen binding domain, and/or tumor antigen. In some embodiments, the cell activation agent is conjugated to or adsorbed on the first population of mesoporous silica particles. In additional or alternative embodiments, the T cell stimulating compound or tumor antigen is conjugated to or adsorbed on to a second population of mesoporous silica particles. In further embodiments, the T-cell stimulating compound or tumor antigen is IL-2, IL-15, GM-CSF, anti-CD2 mAb, anti-CD3 mAb, anti-CD28 mAb, neo-antigen peptides, peptides from shared antigens such as TRP2, gp100, tumor cell lysate, CD19, CD20, CD22, ROR1, mesothelin, CD33/IL3Ra, c-Met, PSMA, Glycolipid F77, EGFRvIII, GD-2, NY-ESO-1 TCR, and/or MAGE A3 TCR. In some embodiments, the cell activation agent comprises a CD3/TCR complex and/or an agent that stimulates a costimulatory molecule and/or growth factor receptor, optionally, wherein the cell activation agent is a multispecific binding molecule comprising an agent that stimulates a CD3/TCR complex and an agent that stimulates a costimulatory molecule and/or growth factor receptor

In embodiments where the cell activation agent is conjugated to the second population of mesoporous silica particles, the T cell stimulating compound or tumor antigen may be conjugated to a lipid bilayer on the surface of the second population of mesoporous silica particles. Methods of making lipid bilayers on the mesoporous silica particles are known. See e.g., International Appl. Publ. No. WO 2018/013797. Briefly, liposomes containing predefined amounts of a label such as biotin are used to coat the MSPs. The labels may then be used to affix to the T-cell stimulating compound using a complementary label, e.g., streptavidin. Lipids used to make liposomes are known to those of skill in the art and include, without limitation, vesicle-forming lipids having two hydrocarbon chains, typically acyl chains, and a polar head group. Included in this class are the phospholipids, such as phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidic acid (PA), phosphatidylinositol (PI), and sphingomyelin (SM), where the two hydrocarbon chains are typically between about 14-22 carbon atoms in length and have varying degrees of unsaturation. In some embodiments, the lipid is a relatively unsaturated phospholipid (having one, two or three double bonds in the hydrocarbon chain). In some embodiments, the lipid is a phosphatidylcholine. Phosphatidylcholine is a phospholipid that incorporates choline as a headgroup and combines a

glycerophosphoric acid with two fatty acids. In some embodiments, the phosphatidylcholine is a palmitoyl phosphatidylcholine or a oleoyl phosphatidylcholine or a 1-palmitoyl,2-oleoyl-phosphatidylcholine. More than one type of lipid may be used in preparing the liposome composition. The selection of lipids and proportions can be varied to achieve a desired degree of fluidity or rigidity, and/or to control stability. Where more than one type of lipid is used in preparing the liposome composition, a suitable amount of the relatively unsaturated lipid (such as PC) should be used in order to form stable liposomes. In some embodiments, at least 45-50 mol % of the lipids used in the formulation are PC. The liposomes may also include lipids derivatized with a hydrophilic polymer such as polyethylene glycol (PEG). Suitable hydrophilic polymers include polyvinylpyrrolidone, polyvinylmethylether, polymethyloxazoline, polyethyloxazoline, polyhydroxypropyloxazoline, polyhydroxypropylmethacrylamide, polymethacrylamide, polydimethylacrylamide, polyhydroxypropylmethacrylate, polyhydroxyethylacrylate, hydroxymethylcellulose, hydroxyethylcellulose, polyethyleneglycol, polyaspartamide, and hydrophilic peptide sequences. Methods of preparing lipids derivatized with hydrophilic polymers are known (see e.g. U.S. Pat. No, 5,395,619, which is incorporated herein by reference).

In some embodiments, the first population or second population of mesoporous silica particles further includes a cytokine. The cytokine may be, without limitation, IL-1, IL-2, IL-4, IL-5, IL-7, IL-10, IL-12, IL-15, IL-17, IL-21, or transforming growth factor beta (TGF-β), or an agonist thereof, a mimetic thereof, a variant thereof, a functional fragment thereof, or a combination thereof. In particular embodiments, the cytokine is conjugated to or adsorbed on the first or second population of mesoporous silica particles. In embodiments, where the cytokine is adsorbed on the second population of mesoporous silica particles, the second population of MSPs (e.g., MSRs) may be further covered by a lipid bilayer, as described above.

Methods

Aspects disclosed herein relate to a method of transducing cells in vivo comprising administering a biomaterial comprising a cell recruitment factor; an extended release agent, e.g., a first population of mesoporous silica particles; a viral vector; and, optionally, a cell activation agent to a subject. In some embodiments, the components are administered simultaneously or sequentially. In some embodiments, the biomaterial comprising the cell recruitment factor is

administered first. In some embodiments, the first population of mesoporous silica rods, the viral vector, and, optionally, the cell activation agent is administered simultaneously and, optionally, after the biomaterial.

Aspects disclosed herein relate to a method of transducing cells in vivo comprising administering a biomaterial and a cell recruitment factor; an extended release agent, e.g., a first population of mesoporous silica particles; a viral vector; and, optionally, a cell activation agent to a subject. In some embodiments, the components are administered simultaneously or sequentially. In some embodiments, the biomaterial and the cell recruitment factor are administered first. In some embodiments, the first population of mesoporous silica rods, the viral vector, and, optionally, the cell activation agent is administered simultaneously and, optionally, after the biomaterial and the cell recruitment factor.

In some embodiments, the method further comprises: contacting T lymphocytes with a composition comprising a first population of mesoporous silica particles (e.g., MSRs), a viral vector, and, optionally, a cell activation agent; wherein the viral vector comprises an expression vector comprising the recombinant polynucleotide comprising an expression control sequence operatively linked to a nucleotide sequence to be expressed.

In some embodiments of the presently described methods, the methods result in an increase in the proportion of T lymphocytes in the population. In some embodiments, method comprises delivering a viral vector to a desired site of action in a subject.

Further aspects relate to a method of treating a subject having a disease, disorder, or condition comprising administering a biomaterial comprising a cell recruitment factor; an extended release agent, e.g., a first population of mesoporous silica particles; a viral vector; and, optionally, a cell activation agent to a subject. In some embodiments, the components are administered simultaneously or sequentially. In some embodiments, the biomaterial comprising the cell recruitment factor is administered first. In some embodiments, the first population of mesoporous silica rods, the viral vector, and, optionally, the cell activation agent is administered simultaneously and, optionally, after the biomaterial.

Further aspects relate to a method of treating a subject having a disease, disorder, or condition comprising administering a biomaterial and a cell recruitment factor; an extended release agent, e.g., a first population of mesoporous silica particles; a viral vector; and, optionally, a cell activation agent to a subject. In some embodiments, the components are

administered simultaneously or sequentially. In some embodiments, the biomaterial and the cell recruitment factor are administered first. In some embodiments, the first population of mesoporous silica rods, the viral vector, and, optionally, the cell activation agent is administered simultaneously and, optionally, after the biomaterial and the cell recruitment factor.

In some embodiments, the subject has cancer. In some embodiments, the subject has cancer expressing one or more tumor antigen selected from the group consisting of: TSHR, CD19, CD123, CD22, CD30, CD171, CS-1, CLL-1, CD33, EGFRvIII , GD2, GD3, BCMA, Tn Ag, PSMA, ROR1, FLT3, FAP, TAG72, CD38, CD44v6, CEA, EPCAM, B7H3, KIT, IL-13Ra2, Mesothelin, IL-11Ra, PSCA, PRSS21, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, CD20, Folate receptor alpha, ERBB2 (Her2/neu), MUC1, EGFR, NCAM, Prostase, PAP, ELF2M, Ephrin B2, IGF-I receptor, CAIX, LMP2, gp100, bcr-abl, tyrosinase, EphA2, Fucosyl GM1, sLe, GM3, TGS5, HMWMAA, o-acetyl-GD2, Folate receptor beta, TEM1/CD248, TEM7R, CLDN6, GPRC5D, CXORF61, CD97, CD179a, ALK, Polysialic acid, PLAC1, GloboH, NY-BR-1, UPK2, HAVCR1, ADRB3, PANX3, GPR20, LY6K, OR51E2, TARP, WT1, NY-ESO-1, LAGE-1a, MAGE-A1, legumain, HPV E6,E7, MAGE A1, ETV6-AML, sperm protein 17, XAGE1, Tie 2, MAD-CT-1, MAD-CT-2, Fos-related antigen 1, p53, p53 mutant, prostein, survivin and telomerase, PCTA-1/Galectin 8, MelanA/MART1, Ras mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, TRP-2, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP-4, SSX2, RAGE-1, human telomerase reverse transcriptase, RU1, RU2, intestinal carboxyl esterase, mut hsp70-2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3, FCRL5, IGLL1, and any combination thereof.

In some embodiments, the method further comprises: administering to a subject a composition comprising a first population of mesoporous silica particles and a viral vector; wherein the viral vector comprises an expression vector comprising a recombinant polynucleotide comprising an expression control sequence operatively linked to a nucleotide sequence that expresses a chimeric antigen receptor (CAR) that is engineered to target the tumor antigen.

In some embodiments of the method, the composition further comprises a T cell stimulating compound or tumor antigen conjugated to or adsorbed on the first population of

mesoporous silica particles or a second population of mesoporous silica particles, or both populations of MSPs (e.g., MSRs). Alternatively, the method includes administering a second extended release agent, e.g., a second population of mesoporous silica particles in combination with, e.g., simultaneously or shortly after, administration of the first population of MSPs (e.g., MSRs). Alternatively, the second population of MSPs (e.g., MSRs) may be administered after a prolonged period of time after administration of the first population of MSPs.

In some embodiments, the extended release agent comprises a first population of MSPs and the second extended release agent comprises a second population of MSPs.

In some embodiments, the method comprises administering a cell activation agent, wherein the cell activation agent is conjugated to or adsorbed on the first or second population of mesoporous silica particles.

In some embodiments, the second population of MSPs (e.g., MSRs) is administered to the subject simultaneously (e.g., administered on the same day) with or shortly after administration (e.g., administered 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, or 7 days after administration) of the first population of MSPs. In other embodiments, the cytokine is administered to the subject after a prolonged period of time (e.g., e.g., at least 2 weeks, 3 weeks, 4 weeks, 6 weeks, 8 weeks, 10 weeks, or more) after administration of the first population of MSPs.

In some embodiments of any of the aforesaid methods or uses, the disease, disorder, or condition is associated with a tumor antigen, e.g., a tumor antigen described herein, selected from a proliferative disease such as a cancer or malignancy or a precancerous condition such as a myelodysplasia, a myelodysplastic syndrome or a preleukemia, or is a non-cancer related indication associated with expression of a tumor antigen described herein. In some embodiments, the disease is a cancer described herein, e.g., a cancer described herein as being associated with a target described herein. In some embodiments, the disease is a hematologic cancer. In some embodiments, the hematologic cancer is leukemia. In some embodiments, the cancer is selected from the group consisting of one or more acute leukemias including but not limited to B-cell acute lymphoid leukemia ("BALL"), T-cell acute lymphoid leukemia ("TALL"), acute lymphoid leukemia (ALL); one or more chronic leukemias including but not limited to chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL); additional hematologic cancers or hematologic conditions including, but not limited to B cell

prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, Marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin lymphoma, Hodgkin lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and "preleukemia" which are a diverse collection of hematological conditions united by ineffective production (or dysplasia) of myeloid blood cells, and to disease associated with expression of a tumor antigen described herein include, but not limited to, atypical and/or non-classical cancers, malignancies, precancerous conditions or proliferative diseases expressing a tumor antigen as described herein; and any combination thereof. In another embodiment, the disease associated with a tumor antigen described herein is a solid tumor.

In embodiments, the cancer is selected from the group consisting of colon cancer, rectal cancer, renal-cell carcinoma, liver cancer, non-small cell carcinoma of the lung, cancer of the small intestine, cancer of the esophagus, melanoma, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, cancer of the anal region, stomach cancer, testicular cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin's Disease, non-Hodgkin's lymphoma, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, solid tumors of childhood, cancer of the bladder, cancer of the kidney or ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers, combinations of said cancers, and metastatic lesions of said cancers.

In some embodiments, a cancer that can be treated with CAR-expressing cell of the present invention is multiple myeloma. Generally, myeloma cells are thought to be negative for a cancer associate antigen as described herein expression by flow cytometry. Thus, in some embodiments, a CD19 CAR, e.g., as described herein, may be used to target myeloma cells. In

some embodiments, cars of the present invention therapy can be used in combination with one or more additional therapies, e.g., lenalidomide treatment.

In various aspects, the immune effector cells (e.g., T cells, NK cells) generated by the methods described herein and administered to the patient, or their progeny, persist in the patient for at least four months, five months, six months, seven months, eight months, nine months, ten months, eleven months, twelve months, thirteen months, fourteen month, fifteen months, sixteen months, seventeen months, eighteen months, nineteen months, twenty months, twenty-one months, twenty-two months, twenty-three months, two years, three years, four years, or five years after administration of the T cell or NK cell to the patient.

The invention also includes a type of cellular therapy where immune effector cells (e.g., T cells, NK cells) are modified, e.g., by in vitro or in vivo transcribed RNA, to transiently express a chimeric antigen receptor (CAR). The resultant cells are able to kill tumor cells in the subject or patient. Thus, in various aspects, the immune effector cells (e.g., T cells, NK cells) are present for less than one month, e.g., three weeks, two weeks, one week, after administration of the compositions as described herein.

Without wishing to be bound by any particular theory, the anti-tumor immunity response elicited by the CAR-modified immune effector cells (e.g., T cells, NK cells) may be an active or a passive immune response, or alternatively may be due to a direct vs indirect immune response. In some aspects, the CAR transduced immune effector cells (e.g., T cells, NK cells) exhibit specific proinflammatory cytokine secretion and potent cytolytic activity in response to human cancer cells expressing the a cancer associate antigen as described herein, resist soluble a cancer associate antigen as described herein inhibition, mediate bystander killing and mediate regression of an established human tumor. For example, antigen-less tumor cells within a heterogeneous field of a cancer associate antigen as described herein-expressing tumor may be susceptible to indirect destruction by a cancer associate antigen as described herein-redirected immune effector cells (e.g., T cells, NK cells) that has previously reacted against adjacent antigen-positive cancer cells.

In some aspects, the fully human CAR-modified immune effector cells (e.g., T cells, NK cells) of the invention may be a type of vaccine for ex vivo immunization and/or in vivo therapy in a mammal. In some aspects, the mammal is a human.

In some aspects the CAR-expressing cells of the inventions may be used to treat a proliferative disease such as a cancer or malignancy or is a precancerous condition such as a myelodysplasia, a myelodysplastic syndrome or a preleukemia. Further a disease associated with a cancer associate antigen as described herein expression include, but not limited to, e.g., atypical and/or non-classical cancers, malignancies, precancerous conditions or proliferative diseases expressing a cancer associated antigen as described herein. Non-cancer related indications associated with expression of a cancer associate antigen as described herein include, but are not limited to, e.g., autoimmune disease, (e.g., lupus), inflammatory disorders (allergy and asthma) and transplantation.

In some aspects the CAR-expressing cells of the inventions may be used to treat an autoimmune disease, an inflammatory disease, or transplant. Exemplary autoimmune diseases include but are not limited to Addison's disease, agammaglobulinemia, alopecia areata, amyloidosis, ankylosing spondylitis, anti-GBM/anti-TBM nephritis, antiphospholipid syndrome (APS), autoimmune hepatitis, autoimmune inner ear disease (AIED), axonal & neuronal neuropathy (AMAN), Behcet's disease, Bullous pemphigoid, Castleman disease (CD), Celiac disease, Chagas disease, chronic inflammatory demyelinating polyneuropathy (CIDP), chronic recurrent multifocal osteomyelitis (CRMO), Churg-Strauss, Cicatricial pemphigoid/benign mucosal pemphigoid, Cogan's syndrome, Cold agglutinin disease, Congenital heart block, Coxsackie myocarditis, CREST syndrome, Crohn's disease, dermatitis herpetiformis, dermatomyositis, Devic's disease (neuromyelitis optica), Discoid lupus, Dressler's syndrome, endometriosis, eosinophilic esophagitis (EoE), eosinophilic fasciitis, erythema nodosum, essential mixed cryoglobulinemia, Evans syndrome, fibromyalgia, fibrosing alveolitis, giant cell arteritis (temporal arteritis), giant cell myocarditis, Glomerulonephritis, Goodpasture's syndrome, Granulomatosis with Polyangiitis, Graves' disease, Guillain-Barre syndrome, Hashimoto's thyroiditis, hemolytic anemia, Henoch-Schonlein purpura (HSP), herpes gestationis or pemphigoid gestationis (PG), hypogammalglobulinemia, IgA nephropathy, IgG4-related sclerosing disease, inclusion body myositis (IBM), interstitial cystitis (IC), juvenile arthritis, juvenile diabetes (Type 1 diabetes), juvenile myositis (JM), Kawasaki disease, Lambert-Eaton syndrome, leukocytoclastic vasculitis, Lichen planus, Lichen sclerosus, Ligneous conjunctivitis, linear IgA disease (LAD), lupus, Lyme disease chronic, Meniere's disease, microscopic polyangiitis (MPA), mixed connective tissue disease (MCTD), Mooren's ulcer, Mucha-

Habermann disease, multiple sclerosis (MS), Myasthenia gravis, Myositis, Narcolepsy, Neuromyelitis optica, neutropenia, ocular cicatricial pemphigoid, optic neuritis, palindromic rheumatism (PR), PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus), paraneoplastic cerebellar degeneration (PCD), Paroxysmal nocturnal hemoglobinuria (PNH), Parry Romberg syndrome, Pars planitis (peripheral uveitis), Parsonnage-Turner syndrome, Pemphigus, peripheral neuropathy, Perivenous encephalomyelitis, pernicious anemia (PA), POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes), polyarteritis nodosa, polymyalgia rheumatica, polymyositis, postmyocardial infarction syndrome, postpericardiotomy syndrome, primary biliary cirrhosis, primary sclerosing cholangitis, progesterone dermatitis, psoriasis, psoriatic arthritis, pure red cell aplasia (PRCA), pyoderma gangrenosum, Raynaud's phenomenon, Reactive Arthritis, Reflex sympathetic dystrophy, Reiter's syndrome, relapsing polychondritis, restless legs syndrome (RLS), retroperitoneal fibrosis, rheumatic fever, rheumatoid arthritis (RA), sarcoidosis, Schmidt syndrome, scleritis, scleroderma, Sjogren's syndrome, sperm & testicular autoimmunity, Stiff person syndrome (SPS), subacute bacterial endocarditis (SBE), Susac's syndrome, sympathetic ophthalmia (SO), Takayasu's arteritis, temporal arteritis/Giant cell arteritis, thrombocytopenic purpura (TTP), Tolosa-Hunt syndrome (THS), transverse myelitis, type 1 diabetes, ulcerative colitis (UC), undifferentiated connective tissue disease (UCTD), uveitis, vasculitis, vitiligo, or Wegener's granulomatosis (Granulomatosis with Polyangiitis (GPA)). In some embodiments, the CAR binds to a B cell antigen, e.g., CD 19, CD20, CD22, CD123, FcRn5, FcRn2, BCMA, CS-1 and CD138.

The CAR-modified immune effector cells (e.g., T cells, NK cells) of the present invention may be administered either alone, or as a pharmaceutical composition in combination with diluents and/or with other components such as IL-2 or other cytokines or cell populations.

Hematologic Cancer

Hematological cancer conditions are the types of cancer such as leukemia, lymphoma, and malignant lymphoproliferative conditions that affect blood, bone marrow and the lymphatic system.

Leukemia can be classified as acute leukemia and chronic leukemia. Acute leukemia can be further classified as acute myelogenous leukemia (AML) and acute lymphoid leukemia (ALL). Chronic leukemia includes chronic myelogenous leukemia (CML) and chronic lymphoid

leukemia (CLL). Other related conditions include myelodysplastic syndromes (MDS, formerly known as "preleukemia") which are a diverse collection of hematological conditions united by ineffective production (or dysplasia) of myeloid blood cells and risk of transformation to AML. Lymphoma is a group of blood cell tumors that develop from lymphocytes. Exemplary lymphomas include non-Hodgkin lymphoma and Hodgkin lymphoma.

The present invention also provides methods for inhibiting the proliferation or reducing a cancer associated antigen as described herein, the methods comprising contacting a population of cells comprising a cancer associated antigen as described herein with a composition comprising a mesoporous silica particles and a viral vector. In a specific aspect, the MSPs are surface modified as described herein. In other embodiments, the viral vector comprises an expression vector comprising a recombinant polynucleotide comprising an expression control sequence operatively linked to a nucleotide sequence to be expressed. Exemplary nucleotide sequences express a chimeric antigen receptor (CAR), engineered TCR, cytokines, chemokines, shRNA to block an inhibitory molecule, or mRNA to induce expression of a protein. In some aspects, a CAR-expressing T cell or NK cell of the invention reduces the quantity, number, amount or percentage of cells and/or cancer cells by at least 25%, at least 30%, at least 40%, at least 50%, at least 65%, at least 75%, at least 85%, at least 95%, or at least 99% in a subject with or animal model for myeloid leukemia or another cancer associated with a cancer associated antigen as described herein-expressing cells relative to a negative control. In some aspects, the subject is a human.

Combination Therapies

Administered "in combination", as used herein, means that two (or more) different treatments are delivered to the subject during the course of the subject□s affliction with the disorder, e.g., the two or more treatments are delivered after the subject has been diagnosed with the disorder and before the disorder has been cured or eliminated or treatment has ceased for other reasons. In some embodiments, the delivery of one treatment is still occurring when the delivery of the second begins, so that there is overlap in terms of administration. This is sometimes referred to herein as "simultaneous" or "concurrent delivery". In other embodiments, the delivery of one treatment ends before the delivery of the other treatment begins. In some embodiments of either case, the treatment is more effective because of combined administration.

For example, the second treatment is more effective, e.g., an equivalent effect is seen with less of the second treatment, or the second treatment reduces symptoms to a greater extent, than would be seen if the second treatment were administered in the absence of the first treatment, or the analogous situation is seen with the first treatment. In some embodiments, delivery is such that the reduction in a symptom, or other parameter related to the disorder is greater than what would be observed with one treatment delivered in the absence of the other. The effect of the two treatments can be partially additive, wholly additive, or greater than additive. The delivery can be such that an effect of the first treatment delivered is still detectable when the second is delivered.

In some embodiments, the methods or uses are carried out in combination with an agent that increases the efficacy of the immune effector cell, e.g., an agent as described herein.

In some embodiments of the methods or uses described herein, the mesoporous silica rod composition is administered in combination with an agent that increases the efficacy of the immune effector cell, e.g., one or more of a protein phosphatase inhibitor, a kinase inhibitor, a cytokine, an inhibitor of an immune inhibitory molecule; or an agent that decreases the level or activity of a T_{REG} cell.

In some embodiments of the methods or uses described herein, the protein phosphatase inhibitor is a SHP-1 inhibitor and/or an SHP-2 inhibitor.

In other embodiments of the methods or uses described herein, kinase inhibitor is chosen from one or more of a CDK4 inhibitor, a CDK4/6 inhibitor (e.g., palbociclib), a BTK inhibitor (e.g., ibrutinib or RN-486), an mTOR inhibitor (e.g., rapamycin or everolimus (RAD001)), an MNK inhibitor, or a dual P13K/mTOR inhibitor. In some embodiments, the BTK inhibitor does not reduce or inhibit the kinase activity of interleukin-2-inducible kinase (ITK).

In other embodiments of the methods or uses described herein, the agent that inhibits the immune inhibitory molecule comprises an antibody or antibody fragment, an inhibitory nucleic acid, a clustered regularly interspaced short palindromic repeats (CRISPR), a transcription-activator like effector nuclease (TALEN), or a zinc finger endonuclease (ZFN) that inhibits the expression of the inhibitory molecule.

In other embodiments of the methods or uses described herein, the agent that decreases the level or activity of the TREG cells is chosen from cyclophosphamide, anti-GITR antibody, CD25-depletion, or a combination thereof.

In some embodiments of the methods or uses described herein, the immune inhibitory molecule is selected from the group consisting of PD1, PD-L1, CTLA-4, TIM-3, LAG-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, TGFR beta, CEACAM-1, CEACAM-3, and CEACAM-5.

In other embodiments, the agent that inhibits the inhibitory molecule comprises a first polypeptide comprising an inhibitory molecule or a fragment thereof and a second polypeptide that provides a positive signal to the cell, and wherein the first and second polypeptides are expressed on the CAR-containing immune cells, wherein (i) the first polypeptide comprises PD1, PD-L1, CTLA-4, TIM-3, LAG3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, TGFR beta, CEACAM-1, CEACAM-3, and CEACAM-5 or a fragment thereof; and/or (ii) the second polypeptide comprises an intracellular signaling domain comprising a primary signaling domain and/or a costimulatory signaling domain. In some embodiments, the primary signaling domain comprises a functional domain of CD3 zeta; and/or the costimulatory signaling domain comprises a functional domain of a protein selected from 41BB, CD27, and CD28.
In other embodiments, cytokine is chosen from IL-7, IL-15, or IL-21, or combinations thereof.

In other embodiments, the immune effector cell comprising the CAR molecule and a second, e.g., any of the combination therapies disclosed herein (e.g., the agent that that increases the efficacy of the immune effector cell) are administered substantially simultaneously or sequentially.

In other embodiments, the immune cell comprising the CAR molecule is administered in combination with a molecule that targets GITR and/or modulates GITR function. In some embodiments, the molecule targeting GITR and/or modulating GITR function is administered prior to the CAR-expressing cell or population of cells, or prior to apheresis.

In some embodiments, lymphocyte infusion, for example allogeneic lymphocyte infusion, is used in the treatment of the cancer, wherein the lymphocyte infusion comprises at least one CAR-expressing cell of the present invention. In some embodiments, autologous lymphocyte infusion is used in the treatment of the cancer, wherein the autologous lymphocyte infusion comprises at least one CAR-expressing cell described herein.

In some embodiments, the cell is a T cell and the T cell is diaglycerol kinase (DGK) deficient. In some embodiments, the cell is a T cell and the T cell is Ikaros deficient. In some embodiments, the cell is a T cell and the T cell is both DGK and Ikaros deficient.

In embodiments of any of the aforesaid methods or uses, there may be a further administration of an agent that treats the disease associated with expression of the tumor antigen, e.g., any of the second or third therapies disclosed herein. Additional exemplary combinations include one or more of the following.

In another embodiment, there may be a further administration of another agent, e.g., a kinase inhibitor and/or checkpoint inhibitor described herein. For example, there may be a further administration of an agent which enhances the activity of a CAR-expressing cell.

For example, in some embodiments, the agent that enhances the activity of a CAR-expressing cell can be an agent which inhibits an inhibitory molecule (e.g., an immune inhibitor molecule). Examples of inhibitory molecules include PD1, PD-L1, CTLA-4, TIM-3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, and TGFR beta.

In some embodiments, the agent that inhibits the inhibitory molecule is an inhibitory nucleic acid is a dsRNA, a siRNA, or a shRNA. In embodiments, the inhibitory nucleic acid is linked to the nucleic acid that encodes a component of the CAR molecule. For example, the inhibitory molecule can be expressed on the CAR-expressing cell.

In another embodiment, the agent which inhibits an inhibitory molecule, e.g., is a molecule described herein, e.g., an agent that comprises a first polypeptide, e.g., an inhibitory molecule, associated with a second polypeptide that provides a positive signal to the cell, e.g., an intracellular signaling domain described herein. In some embodiments, the agent comprises a first polypeptide, e.g., of an inhibitory molecule such as PD-1, PD-L1, CTLA-4, TIM-3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, or TGFR beta, or a fragment of any of these (e.g., at least a portion of the extracellular domain of any of these), and a second polypeptide which is an intracellular signaling domain described herein (e.g., comprising a costimulatory domain (e.g., 41BB, CD27 or CD28, e.g., as described herein) and/or a primary signaling domain (e.g., a CD3 zeta signaling domain described herein). In some embodiments, the agent comprises a first polypeptide of PD1 or a fragment thereof (e.g., at least a portion of the extracellular domain of PD1), and a second polypeptide of an intracellular signaling domain described herein (e.g., a CD28 signaling domain described herein and/or a CD3 zeta signaling domain described herein).

In some embodiments, the CAR-expressing immune effector cell of the present invention, e.g., T cell or NK cell, is administered to a subject that has received a previous stem cell transplantation, e.g., autologous stem cell transplantation.

In some embodiments, the CAR–expressing immune effector cell of the present invention, e.g., T cell or NK cells, is administered to a subject that has received a previous dose of melphalan.

In some embodiments, the cell expressing a CAR molecule, e.g., a CAR molecule described herein, is administered in combination with an agent that increases the efficacy of a cell expressing a CAR molecule, e.g., an agent described herein.

In some embodiments, the cell expressing a CAR molecule, e.g., a CAR molecule described herein, is administered in combination with an agent that ameliorates one or more side effect associated with administration of a cell expressing a CAR molecule, e.g., an agent described herein.

In some embodiments, the cell expressing a CAR molecule, e.g., a CAR molecule described herein, is administered in combination with an agent that treats the disease associated with a cancer associated antigen as described herein, e.g., an agent described herein.

In some embodiments, a cell expressing two or more CAR molecules, e.g., as described herein, is administered to a subject in need thereof to treat cancer. In some embodiments, a population of cells including a CAR expressing cell, e.g., as described herein, is administered to a subject in need thereof to treat cancer.

In some embodiments of the methods or uses described herein, the CAR molecule is administered in combination with another agent. In some embodiments, the agent can be a kinase inhibitor, e.g., a CDK4/6 inhibitor, a BTK inhibitor, an mTOR inhibitor, a MNK inhibitor, or a dual PI3K/mTOR inhibitor, and combinations thereof. In some embodiments, the kinase inhibitor is a CDK4 inhibitor, e.g., a CDK4 inhibitor described herein, e.g., a CD4/6 inhibitor, such as, e.g., 6-Acetyl-8-cyclopentyl-5-methyl-2-(5-piperazin-1-yl-pyridin-2-ylamino)-8*H*-pyrido[2,3-*d*]pyrimidin-7-one, hydrochloride (also referred to as palbociclib or PD0332991). In some embodiments, the kinase inhibitor is a BTK inhibitor, e.g., a BTK inhibitor described herein, such as, e.g., ibrutinib. In some embodiments, the kinase inhibitor is an mTOR inhibitor, e.g., an mTOR inhibitor described herein, such as, e.g., rapamycin, a rapamycin analog, OSI-027. The mTOR inhibitor can be, e.g., an mTORC1 inhibitor and/or an mTORC2 inhibitor, e.g.,

an mTORC1 inhibitor and/or mTORC2 inhibitor described herein. In some embodiments, the kinase inhibitor is a MNK inhibitor, e.g., a MNK inhibitor described herein, such as, e.g., 4-amino-5-(4-fluoroanilino)-pyrazolo [3,4-*d*] pyrimidine. The MNK inhibitor can be, e.g., a MNK1a, MNK1b, MNK2a and/or MNK2b inhibitor. The dual PI3K/mTOR inhibitor can be, e.g., PF-04695102.

In some embodiments of the methods or uses described herein, the kinase inhibitor is a CDK4 inhibitor selected from aloisine A; flavopiridol or HMR-1275, 2-(2-chlorophenyl)-5,7-dihydroxy-8-[(3S,4R)-3-hydroxy-1-methyl-4-piperidinyl]-4-chromenone; crizotinib (PF-02341066; 2-(2-Chlorophenyl)-5,7-dihydroxy-8-[(2*R*,3*S*)-2-(hydroxymethyl)-1-methyl-3-pyrrolidinyl]- 4*H*-1-benzopyran-4-one, hydrochloride (P276-00); 1-methyl-5-[[2-[5-(trifluoromethyl)-1*H*-imidazol-2-yl]-4-pyridinyl]oxy]-*N*-[4-(trifluoromethyl)phenyl]-1*H*-benzimidazol-2-amine (RAF265); indisulam (E7070); roscovitine (CYC202); palbociclib (PD0332991); dinaciclib (SCH727965); N-[5-[[(5-*tert*-butyloxazol-2-yl)methyl]thio]thiazol-2-yl]piperidine-4-carboxamide (BMS 387032); 4-[[9-chloro-7-(2,6-difluorophenyl)-5*H*-pyrimido[5,4-*d*][2]benzazepin-2-yl]amino]-benzoic acid (MLN8054); 5-[3-(4,6-difluoro-1H-benzimidazol-2-yl)-1H-indazol-5-yl]-N-ethyl-4-methyl-3-pyridinemethanamine (AG-024322); 4-(2,6-dichlorobenzoylamino)-1H-pyrazole-3-carboxylic acid N-(piperidin-4-yl)amide (AT7519); 4-[2-methyl-1-(1-methylethyl)-1*H*-imidazol-5-yl]-*N*-[4-(methylsulfonyl)phenyl]- 2-pyrimidinamine (AZD5438); and XL281 (BMS908662).

In some embodiments of the methods or uses described herein, the kinase inhibitor is a CDK4 inhibitor, e.g., palbociclib (PD0332991), and the palbociclib is administered at a dose of about 50 mg, 60 mg, 70 mg, 75 mg, 80 mg, 90 mg, 100 mg, 105 mg, 110 mg, 115 mg, 120 mg, 125 mg, 130 mg, 135 mg (e.g., 75 mg, 100 mg or 125 mg) daily for a period of time, e.g., daily for 14-21 days of a 28 day cycle, or daily for 7-12 days of a 21 day cycle. In some embodiments, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or more cycles of palbociclib are administered.

In some embodiments of the methods or uses described herein, the kinase inhibitor is a BTK inhibitor selected from ibrutinib (PCI-32765); GDC-0834; RN-486; CGI-560; CGI-1764; HM-71224; CC-292; ONO-4059; CNX-774; and LFM-A13. In some embodiments, the BTK inhibitor does not reduce or inhibit the kinase activity of interleukin-2-inducible kinase (ITK), and is selected from GDC-0834; RN-486; CGI-560; CGI-1764; HM-71224; CC-292; ONO-4059; CNX-774; and LFM-A13.

In some embodiments of the methods or uses described herein, the kinase inhibitor is a BTK inhibitor, e.g., ibrutinib (PCI-32765), and the ibrutinib is administered at a dose of about 250 mg, 300 mg, 350 mg, 400 mg, 420 mg, 440 mg, 460 mg, 480 mg, 500 mg, 520 mg, 540 mg, 560 mg, 580 mg, 600 mg (e.g., 250 mg, 420 mg or 560 mg) daily for a period of time, e.g., daily for 21 day cycle, or daily for 28 day cycle. In some embodiments, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or more cycles of ibrutinib are administered.

In some embodiments of the methods or uses described herein, the kinase inhibitor is a BTK inhibitor that does not inhibit the kinase activity of ITK, e.g., RN-486, and RN-486 is administered at a dose of about 100 mg, 110 mg, 120 mg, 130 mg, 140 mg, 150 mg, 160 mg, 170 mg, 180 mg, 190 mg, 200 mg, 210 mg, 220 mg, 230 mg, 240 mg, 250 mg (e.g., 150 mg, 200 mg or 250 mg) daily for a period of time, e.g., daily a 28 day cycle. In some embodiments, 1, 2, 3, 4, 5, 6, 7, or more cycles of RN-486 are administered.

In some embodiments of the methods or uses described herein, the kinase inhibitor is an mTOR inhibitor selected from temsirolimus; ridaforolimus (1*R*,2*R*,4*S*)-4-[(2*R*)-2 [(1*R*,9*S*,12*S*,15*R*,16*E*,18*R*,19*R*,21*R*, 23*S*,24*E*,26*E*,28*Z*,30*S*,32*S*,35*R*)-1,18-dihydroxy-19,30-dimethoxy-15,17,21,23, 29,35-hexamethyl-2,3,10,14,20-pentaoxo-11,36-dioxa-4-azatricyclo[30.3.1.$0^{4,9}$] hexatriaconta-16,24,26,28-tetraen-12-yl]propyl]-2-methoxycyclohexyl dimethylphosphinate, also known as AP23573 and MK8669; everolimus (RAD001); rapamycin (AY22989); simapimod; (5-{2,4-bis[(3**S**)-3-methylmorpholin-4-yl]pyrido[2,3-**d**]pyrimidin-7-yl}-2-methoxyphenyl)methanol (AZD8055); 2-amino-8-[*trans*-4-(2-hydroxyethoxy)cyclohexyl]-6-(6-methoxy-3-pyridinyl)-4-methyl-pyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PF04691502); and N^2-[1,4-dioxo-4-[[4-(4-oxo-8-phenyl-4*H*-1-benzopyran-2-yl)morpholinium-4-yl]methoxy]butyl]-L-arginylglycyl-L-α-aspartylL-serine- (SEQ ID NO: 692), inner salt (SF1126); and XL765.

In some embodiments of the methods or uses described herein, the kinase inhibitor is an mTOR inhibitor, e.g., rapamycin, and the rapamycin is administered at a dose of about 3 mg, 4 mg, 5 mg, 6 mg, 7 mg, 8 mg, 9 mg, 10 mg (e.g., 6 mg) daily for a period of time, e.g., daily for 21 day cycle, or daily for 28 day cycle. In some embodiments, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or more cycles of rapamycin are administered. In some embodiments, the kinase inhibitor is an mTOR inhibitor, e.g., everolimus and the everolimus is administered at a dose of about 2 mg, 2.5 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7 mg, 8 mg, 9 mg, 10 mg, 11 mg, 12 mg, 13 mg, 14 mg, 15 mg

(e.g., 10 mg) daily for a period of time, e.g., daily for 28 day cycle. In some embodiments, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 or more cycles of everolimus are administered.

In some embodiments of the methods or uses described herein, the kinase inhibitor is an MNK inhibitor selected from CGP052088; 4-amino-3-(p-fluorophenylamino)-pyrazolo [3,4-*d*] pyrimidine (CGP57380); cercosporamide; ETC-1780445-2; and 4-amino-5-(4-fluoroanilino)-pyrazolo [3,4-*d*] pyrimidine.

In some embodiments of the methods or uses described herein, the kinase inhibitor is a dual phosphatidylinositol 3-kinase (PI3K) and mTOR inhibitor selected from 2-Amino-8-[trans-4-(2-hydroxyethoxy)cyclohexyl]-6-(6-methoxy-3-pyridinyl)-4-methyl-pyrido[2,3-d]pyrimidin-7(8H)-one (PF-04691502); N-[4-[[4-(Dimethylamino)-1-piperidinyl]carbonyl]phenyl]-N□-[4-(4,6-di-4-morpholinyl-1,3,5-triazin-2-yl)phenyl]urea (PF-05212384, PKI-587); 2-Methyl-2-{4-[3-methyl-2-oxo-8-(quinolin-3-yl)-2,3-dihydro-1*H*-imidazo[4,5-c]quinolin-1-yl]phenyl}propanenitrile (BEZ-235); apitolisib (GDC-0980, RG7422); 2,4-Difluoro-N-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide (GSK2126458); 8-(6-methoxypyridin-3-yl)-3-methyl-1-(4-(piperazin-1-yl)-3-(trifluoromethyl)phenyl)-1H-imidazo[4,5-c]quinolin-2(3H)-one Maleic acid (NVP-BGT226); 3-[4-(4-Morpholinylpyrido[3□,2□:4,5]furo[3,2-d]pyrimidin-2-yl]phenol (PI-103); 5-(9-isopropyl-8-methyl-2-morpholino-9H-purin-6-yl)pyrimidin-2-amine (VS-5584, SB2343); and N-[2-[(3,5-Dimethoxyphenyl)amino]quinoxalin-3-yl]-4-[(4-methyl-3-methoxyphenyl)carbonyl]aminophenylsulfonamide (XL765).

In some embodiments of the methods or uses described herein, there may be a further administration of a protein tyrosine phosphatase inhibitor, e.g., a protein tyrosine phosphatase inhibitor described herein. In some embodiments, the protein tyrosine phosphatase inhibitor is an SHP-1 inhibitor, e.g., an SHP-1 inhibitor described herein, such as, e.g., sodium stibogluconate. In some embodiments, the protein tyrosine phosphatase inhibitor is an SHP-2 inhibitor.

In some embodiments of the methods or uses described herein, there may be a further administration of another agent, and the agent is a cytokine. The cytokine can be, e.g., IL-7, IL-15, IL-21, or a combination thereof. In another embodiment, the CAR molecule is administered in combination with a checkpoint inhibitor, e.g., a checkpoint inhibitor described herein. For example, in some embodiments, the check point inhibitor inhibits an inhibitory molecule selected

from PD-1, PD-L1, CTLA-4, TIM-3, CEACAM (e.g., CEACAM-1, CEACAM-3 and/or CEACAM-5), LAG-3, VISTA, BTLA, TIGIT, LAIR1, CD160, 2B4, and TGFR beta.

In other embodiments of the methods or uses described herein, there may be a further administration of an agent that ameliorates one or more side effects associated with a cell expressing a CAR molecule. Side effects associated with the CAR-expressing cell can be chosen from cytokine release syndrome (CRS) or hemophagocytic lymphohistiocytosis (HLH).

The present invention also provides methods for preventing, treating and/or managing a disease associated with a cancer associated antigen as described herein-expressing cells (e.g., a hematologic cancer or atypical cancer expressing a cancer associated antigen as described herein), the method comprising administering to a subject a composition comprising a first population of mesoporous silica particles and a viral vector, and wherein the viral vector comprises an expression vector comprising a recombinant polynucleotide comprising an expression control sequence operatively linked to a nucleotide sequence that expresses a chimeric antigen receptor (CAR) that is engineered to target the tumor antigen. In some aspects, the subject is a human. Non-limiting examples of disorders associated with a cancer associated antigen as described herein-expressing cells include autoimmune disorders (such as lupus), inflammatory disorders (such as allergies and asthma) and cancers (such as hematological cancers or atypical cancers expressing a cancer associated antigen as described herein).

The present invention also provides methods for preventing, treating and/or managing a disease associated with a cancer associated antigen as described herein-expressing cells, the methods comprising administering to a subject a composition comprising a first population of mesoporous silica particles and a viral vector, and wherein the viral vector comprises an expression vector comprising a recombinant polynucleotide comprising an expression control sequence operatively linked to a nucleotide sequence that expresses a chimeric antigen receptor (CAR) that is engineered to target the tumor antigen. In some aspects, the subject is a human.

The present invention provides methods for preventing relapse of cancer associated with a cancer associated antigen as described herein-expressing cells, the methods comprising administering to a subject a composition comprising a first population of mesoporous silica particles and a viral vector, and wherein the viral vector comprises an expression vector comprising a recombinant polynucleotide comprising an expression control sequence operatively

linked to a nucleotide sequence that expresses a chimeric antigen receptor (CAR) that is engineered to target the tumor antigen.

When "an immunologically effective amount," "an anti-tumor effective amount," "a tumor-inhibiting effective amount," or "therapeutic amount" is indicated, the precise amount of the compositions of the present invention to be administered can be determined by a physician with consideration of individual differences in age, weight, tumor size, extent of infection or metastasis, and condition of the patient (subject).

In some aspects, it may be desired to administer activated immune effector cells (e.g., T cells, NK cells) to a subject and then subsequently redraw blood (or have an apheresis performed), activate and expand immune effector cells (e.g., T cells, NK cells) according to the present invention, and reinfuse the patient with these activated and expanded immune effector cells (e.g., T cells, NK cells). This process can be carried out multiple times every few weeks. In some aspects, immune effector cells (e.g., T cells, NK cells) can be activated from blood draws of from 10cc to 400cc. In some aspects, immune effector cells (e.g., T cells, NK cells) are activated from blood draws of 20cc, 30cc, 40cc, 50cc, 60cc, 70cc, 80cc, 90cc, or 100cc.

The administration of the subject compositions may be carried out in any convenient manner, including by aerosol inhalation, injection, ingestion, transfusion, implantation or transplantation. The compositions described herein may be administered to a patient trans arterially, subcutaneously, intradermally, intratumorally, intranodally, intramedullary, intramuscularly, by intravenous (i.v.) injection, or intraperitoneally. In some aspects, the MSP (e.g., MSR) compositions of the present invention are administered to a patient by intradermal or subcutaneous injection. In some aspects, the T cell compositions of the present invention are administered parenterally. The term "parenteral" administration of an T cell composition includes, e.g., intrathecal, epidural, intracranial, subcutaneous (s.c.), intravenous (i.v.), intramuscular (i.m.), or intrasternal injection, intratumoral, or infusion techniques. In particular embodiments, the T cell composition is administered intravenously. In some embodiments, the compositions of MSPs (e.g., MSRs) and viral vectors may be injected directly into a tumor, lymph node, or site of infection.

EXAMPLES

Example A. Synthesis and post-functionalization of mesoporous silica particles

Unless otherwise noted, all reagents were obtained from commercial sources and used as is.

1. Exemplary synthesis of mesoporous silica particles

Poly(ethylene glycol)-*block*-poly(propylene glycol)-*block*-poly(ethylene glycol) avg Mn ~5,800 (Pluronic P-123, 80.0 g, 487 mmol; Sigma) surfactant was dissolved in 3L of 1.6M HCl at room temperature, heated to 40 degrees Celsius in a 5L jacketed flask, and was mechanically stirred via and overhead stirrer at a rate of 0-600 rpm (but most commonly 300 rpm). Tetraethyl orthosilicate (TEOS, 184 mL, 826 mmol; Sigma) was added in one portion over <5min and was heated at 40 degrees Celsius with maintained stirring for at least 2 hours but most commonly 20 hours. The resulting slurry was heated to 80-130 degrees Celsius (most commonly 100 degrees Celsius) for 6-72 hours (but most commonly 24 hours) for hydrothermal treatment before being cooled to room temperature. The slurry was filtered in a Buchner funnel and was washed with deionized water followed by ethanol and air dried at room temperature. The resulting silica material was calcined in a furnace with a slow ramp temperature from room temperature to 550 degrees Celsius over 8 hours and then maintaining at 550 degrees Celsius for another 8 hours before cooling to room temperature to afford 47g of mesoporous silica particles.

Changes in the stir rate may have changes in the microparticle aspect ratio. Varying the conditions of the hydrothermal temperature and duration are common pore size controllers for mesoporous materials. For more information, see *J. Chem. Educ.* **2017**, *94*, 91−94 and references within.

Final mesoporous materials were characterized by light microscopy, Malvern Morphologi G3, scanning electron microscopy (SEM), thermal gravimetric analysis (TGA).

2. Post-modification of silica microparticles

Example 2(a): Diethyl ethylphosphonate functionalized microparticles

Diethyl ethylphosphonate functionalized silica microparticles were prepared by a modified method reported in *New J. Chem.*, **2014**, *38*, 3853, with some modifications. Diethylphosphatoethyltriethoxysilane (4.15 mL, 13.03 mmol) was added to a slurry of 2.0 g of mesoporous silica microparticles suspended in 300 mL of toluene. The slurry was stirred and refluxed at 110 degrees Celsius for 14 hours before cooling to room temperature and filtered.

The particles were washed with deionized water followed by ethanol and then dried in an oven at 100 degrees Celsius for 20 hours to afford diethyl ethylphosphonate functionalized particles.

Example 2(b): Ethylphosphonic acid functionalized microparticles

Ethylphosphonic acid functionalized microparticles were prepared by a modified method to the procedure reported in *New J. Chem.*, **2014**, *38*, 3853. Trimethylsilylchlorosilane (1.388 mL, 10.86 mmol) was added to a slurry of 2.0 g of diethyl ethylphosphonate functionalized microparticles suspended in 150 mL of toluene and heated to 110 degrees Celsius for 24 hours. The slurry was cooled to room temperature and filtered, washing with dionized water and ethanol before drying in a oven at 100 degrees Celsius for 24 hours. The mesoporous silica particles were then suspended in 100 mL of 12M HCl and heated to 100 degrees Celsius for 18 hours. The slurry was cooled to room temperature, filtered and washed with deionized water and ethanol before drying in an oven at 100 degrees Celsius for 24 hours to afford ethylphosphonic acid functionalized microparticles.

Example 2(c): Propylamine functionalized microparticles

Propylamine functionalized microparticles were prepared by a modified method to the procedure reported in *Langmuir* **2015**, *31*, 6457-6462. (3-aminopropyl)trimethoxysilane (3.05 ml, 19.54 mmol; APTMS, Sigma) was added to a slurry of 3.0 grams of mesoporous silica microparticles in 150 mL of reagent grade ethanol. The slurry was refluxed at 75 degrees Celsius for 7 hours. After cooling to room temperature and the slurry was filtered and the particles were washed with deionized water followed by ethanol and then dried in an oven at 100 degrees Celsius for 24 hours.

Example 2(d): Biotin functionalized microparticles

(+)-Biotin N-succinimidyl ester (246 mg, 0.720 mmol) was added to a slurry of 1.0 g of propylamine-functionalized microparticles in 10.0 mL of pH 7.4 adjusted PBS buffer and stirred at room temperature for 18 hours. The slurry was filtered and washed with deionized water and ethanol before drying in an oven at 100 degrees Celsius for 24 hours to afford Biotin-functionalized microparticles.

Example 2(e): Biotin-PEG4 functionalized microparticles

PEG4-Biotin N-hydroxysuccinimide (106 mg, 0.180 mmol; ThermoFischer EZ-Link NHS-PEG4-biotin) was added to a slurry of 0.25 g of propylamine-functionalized microparticles in 2.5 mL of pH 7.4 adjusted PBS buffer and stirred at room temperature for 18 hours. The slurry was filtered and washed with deionized water and ethanol before drying in an oven at 100 degrees Celsius for 24 hours to afford Biotin-PEG4 functionalized microparticles.

Example 2(f): 3(2-pyridyldithio)propionamido)hexanoate functionalized microparticles

Succinimidyl 6-(3(2-pyridyldithio)propionamido)hexanoate (112 mg, 0.360 mmol; LC-SPDP, ThermoFischer) was added to a slurry of 0.50 g of propylamine-functionalized microparticles in 2.5 mL of pH 7.4 adjusted PBS buffer and stirred at room temperature for 18 hours. The slurry was filtered and washed with deionized water and ethanol before drying in an oven at 100 degrees Celsius for 24 hours to afford 3(2-pyridyldithio)propionamido)hexanoate-functionalized microparticles.

Example 2(g): 4-oxo-4-(propylamino)butanoic acid functionalized microparticles

Succinic anhydride (4 g, 40.0 mmol) was added to a slurry of 1.0 g of propylamine-functionalized microparticles in anhydrous DMF and was stirred at room temperature for 24 hours. The slurry was filtered and washed with deionized water and ethanol before drying in an oven at 100 degrees Celsius for 24 hours to afford 4-oxo-4-(propylamino)butanoic acid functionalized microparticles.

Example 2(h): Propyldiethylenetriamine functionalized microparticles

Trimethoxysilylpropyldiethylenetriamine (1.678 mL, 6.51 mmol) was added to 1.0 g of mesoporous silica microparticles were suspended in 150 mL of reagent grade ethanol. The slurry was stirred at 75 degrees Celsius for 7 hours. After cooling to room temperature and the slurry was filtered and the particles were washed with deionized water followed by ethanol and then dried in an oven at 100 degrees Celsius for 20 hours to afford propyldiethylenetriamine functionalized microparticles.

Example 2(i): 3-propyldihydrofuran-2,5-dione functionalized microparticles (succinic anhydride)

3-(3-(triethoxysilyl)propyl)dihydrofuran-2,5-dione (4.94 mL, 17.37 mmol) was added to a slurry of 3.0 g of mesoporous silica microparticles in 300mL of toluene. The slurry was heated to 110 degrees Celsius for 20 hours and was then cooled to room temperature, filtered and washed with dionizied water and ethanol. The functionalized microparticles were dried in an oven at 100 degrees Celsius for 24 hours.

Example 2(j): Branched, polyethylenimine functionalized microparticles

Polyethylenimine (25.1 g, 47.0 mmol; Branched, avg Mw ~25,000, Sigma) was dissolved in 600 mL of anhydrous DMF and 6.0 g of 3-propyldihydrofuran-2,5-dione functionalized microparticles were added and stirred at room temperature for 20 hours. The slurry was filtered, and the particles were washed with deionized water followed by ethanol and then dried in an oven at 100 degrees Celsius for 20 hours to afford branched, polyethylenimine functionalized microparticles.

Example 2(k): *N,N,N*-trimethylpropan-1-ammonium functionalized microparticles

Trimethoxysilylpropyltrimethylammonium chloride (3.61 mL, 6.51 mmol; 50% solution in methanol) was added to a slurry of 1.0 g mesoporous silica microparticles in 150 mL reagent ethanol and was heated to 75 degrees Celsius for 7 hours. After cooling to room temperature and the slurry was filtered and the particles were washed with deionized water followed by ethanol and then dried in an oven at 100 degrees Celsius for 20 hours to afford *N,N,N*-trimethylpropan-1-ammonium functionalized microparticles.

The procedure above was repeated at varying ratios of trimethoxysilylpropyltrimethylammonium chloride to silica microparticles (0.25 mmol trimethoxysilyltrimethylammonium chloride per gram of microparticles) to affect varying ratios of functional density.

Example 2(l): Octyl functionalized microparticles

Triethyoxy(octyl)silane (2.05 mL, 6.51 mmol) was added to a slurry of 1.0 g mesoporous silica microparticles in 150 mL reagent ethanol and was heated to 75 degrees Celsius for 7 hours. After cooling to room temperature and the slurry was filtered and the particles were washed with deionized water followed by ethanol and then dried in an oven at 100 degrees Celsius for 20 hours to afford octyl functionalized microparticles.

Example 2(m): Hexadecyl functionalized microparticles

Hexadecyltrimethoxysilane (2.54 mL, 6.51 mmol) was added to a slurry of 1.0 g mesoporous silica microparticles in 150 mL reagent ethanol and was heated to 75 degrees Celsius for 7 hours. After cooling to room temperature and the slurry was filtered and the particles were washed with deionized water followed by ethanol and then dried in an oven at 100 degrees Celsius for 20 hours to afford hexadecyl functionalized microparticles.

Example 2(n): 11-azidoundecyl functionalized microparticles

(11-azidoundecyl)trimethoxysilane (1.0 g, 3.15 mmol) was added to a slurry of 1.0 g mesoporous silica microparticles in 150 mL reagent ethanol and was heated to 75 degrees Celsius for 7 hours. After cooling to room temperature and the slurry was filtered and the particles were washed with deionized water followed by ethanol and then dried in an oven at 100 degrees Celsius for 20 hours to afford 11-azidoundecyl functionalized microparticles.

Example 2(o): 3-azidopropyl functionalized microparticles

(3-azidopropyl)trimethoxysilane (1.0 g, 4.87 mmol) was added to a slurry of 1.0 g mesoporous silica microparticles in 150 mL reagent ethanol and was heated to 75 degrees Celsius for 7 hours. After cooling to room temperature and the slurry was filtered and the particles were washed with deionized water followed by ethanol and then dried in an oven at 100 degrees Celsius for 20 hours to afford 3-azidopropyl functionalized microparticles.

Example 2(p): 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl functionalized microparticles

Triethoxy(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)silane (2.499 mL, 6.51 mmol) was added to a slurry of 1.0 g mesoporous silica microparticles in 150 mL reagent ethanol and was heated to 75 degrees Celsius for 7 hours. After cooling to room temperature and the slurry was filtered and the particles were washed with deionized water followed by ethanol and then dried in an oven at 100 degrees Celsius for 20 hours to afford 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl functionalized microparticles.

Example B. Testing MSR surface modifications for virus binding

To test the binding of lentivirus to MSPs, a variety of MSPs was prepared with varying surface chemistries **(FIG. 1)**. Dry MSR batches were resuspended at 10 mg/ml in ice-cold Tris-NaCl-EDTA buffer pH 7.5 (NTE buffer). A stock solution of green fluorescent protein (GFP) expressing lentivirus (FCT067, Kerafast) was diluted in ice-cold NTE buffer to a titer of $3x10^6$/ml. The MSR suspension and the diluted virus were combined at ratios of 1:1 vol/vol and incubated on ice for 30 minutes. Control particles were incubated 1:1 vol/vol with NTE buffer without virus. Following the incubation, samples were washed once with 1% bovine serum albumin (BSA) in phosphate buffered saline (PBS) at 4 °C, and then with PBS at 4 °C. Samples were then fixed with 4.2% paraformaldehyde in PBS. Samples were stained with an antibody against the viral envelope (anti-VSV-G from Kerafast, 8G5F11; 1:50 dilution) followed by an anti-mouse IgG labeled with Dylight-488 (Invitrogen). Samples were washed twice with PBS and imaged using an Evos fluorescent microscope equipped with a GFP LED light cube **(FIG. 2)**. Imaging showed no detectable binding of the staining reagents to MSRs bearing no virus. Virus-conjugated rods show varying levels of quantitative binding, with the trimethylammonium and amine functionalities showing maximum binding.

Example C. In vitro assay for T cell transduction with GFP lentivirus using MSR

A schematic representation of the use of MSRs for virus transduction of T cells is shown in **FIG. 3**. Naïve human T cells were stimulated with Dynabead T cell activator beads at a 3:1 bead:cell ratio for two days. Beads were removed using a magnet, and cells were transferred to fresh culture medium. Virus-conjugated MSRs were prepared as noted above and resuspended at 80 µg/ml in cell culture medium. Serial dilutions of this were made as indicated in FIG. 3. This suspension was combined 1:1 with T cells $5x10^5$/ml and incubated for four days. GFP expression was assessed in live, singlet, cells in culture to assess the transduction efficiency. Results **(FIG. 4)** indicate that the transduction of MSR-conjugated virus occurred at greater levels than virus given in culture media only. The trimethylammonium functionalized MSRs provided the highest level of transduction.

Example D. Interaction of T cells with MSRs presenting CD3/CD28 agonistic antibodies, EGFRvIII peptides, or BCMA protein;

MSRs with surface-immobilized ligands were prepared as described in Cheung, A. S., et al., Scaffolds that mimic antigen-presenting cells enable ex vivo expansion of primary T cells. *Nature Biotechnology*, *36*(2), 160–169. A schematic of this process is shown in **FIG. 5**.

Briefly, liposomes primarily composed of POPC with 1 mol% PE-biotin were formed using a thin film rehydration method and extrusion through a 100 nm polycarbonate membrane. Hydroxyl functionalized MSRs were incubated with the liposomes to allow the formation of a supported lipid bilayer on the MSR surface (**FIG. 6**). To functionalize the MSRs with CD3 and CD28 agonistic antibodies, MSRs were washed several times with PBS, incubated with streptavidin, and then tethered with biotinylated CD3 and CD28 antibodies. For MSR-immobilization of EGFRvIII CAR-binding peptides, a biotinylated EGFRvIII CAR-binding peptide was used (**FIG. 7**). For BCMA CART stimulation, recombinant BCMAFc protein was biotinylated using biotin-NHS and similarly coupled to the MSR surface.

After incubation with the desired ligands, MSRs were washed several times with PBS and resuspended in culture medium at various concentrations and incubated with T cells. T cell proliferation was read out using CFSE labeling of the T cells and assessing dye dilution by flow cytometry. Cytokine production was assessed using a multiplex cytokine analysis method (Mesoscale Delivery V-Plex).

EGFRvIII CARTs produced interferon gamma and IL-2 in response to EGFRvIII CAR-binding peptide bound to the surface of the MSRs, while free EGFRvIII CAR-binding peptide in solution, a non-stimulating peptide (OVA) presented on the MSRs, or undecorated MSRs gave no response from the CARTs (**FIG. 8**). In another experiment, the proliferation of EGFRvIII CARTs were monitored in response to various stimuli using cell counting **(FIG. 9)**.

To further analyze the phenotype expansion of different T cell subsets, proliferation of EGFRvIII CARTs was assessed using flow cytometry. CARTs were stained with CFSE and monitored for dye dilution to indicate proliferation by flow cytometry **(FIG. 10)**. Similar experiments were conducted using MSRs functionalized with BCMAFc protein antigen present on the MSR surface **(FIG. 11)**.

To test the simultaneous stimulation and transduction of T cells with virus using two types of MSRs (MSRs bearing stimulatory cues, and MSRs mixed with lentivirus), the experimental

schema shown in **FIG. 12** was used. One population of MSRs were coated with a lipid bilayer and grafted with anti-CD3/CD28 antibodies as described above. A second population of MSRs were incubated with lentivirus. Results shown in **FIG. 13** indicated a superior transduction level when T cells were stimulated with anti-CD3/CD28 agonistic antibodies and were exposed to virus that was incubated with PEI-MSRs compared to free virus in solution.

To test the simultaneous stimulation and transduction of T cells with both cues on the same population of MSRs, T cells were exposed to either (1) anti-CD3/CD28 agonistic antibody-bearing lipid-coated stimulating MSRs, and virus in media, (2) anti-CD3/CD28 agonistic antibody-bearing lipid-coated stimulating MSRs, and PEI-MSRs pre-incubated with virus, or (3) PEI MSRS adsorbed with anti-CD3/CD28 agonistic antibodies, and then incubated with virus. After three days of culture, T cells were assessed for transduction efficiency. **FIG. 14** shows the effect of stimulatory MSR concentration on the MSRs of conditions (1) and (2) above at various amounts of virus. As shown in the **FIG. 14**, overall transduction is enhanced under condition (2) where PEI-MSRs are incubated with virus.

FIG. 15 compares all three conditions, where conditions (1) and (2) are at the highest concentration of stimulatory MSRs. As seen in FIG. 15, condition (3) where stimulatory cues are bound to the PEI-MSRs produces the highest relative transduction efficiency. The same formulations were used to study MSR-mediated transduction with human peripheral blood mononuclear cells (PBMCs). In **FIG. 16**, the transduction in various cell populations as a function of virus concentration is shown at the highest level of stimulation for conditions (1) and (2). **FIG. 17** shows the proportion of each cell population present in the total GFP+ transduced cell fraction, and in the total cell population collected at the highest level of stimulation for conditions (1) and (2).

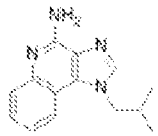
Example E. In vivo study of MSR induced T cell transduction.

A composition of mesoporous silica particle conjugated to viral vectors is injected under the skin of mice. Approximately 5-7 days later, MSRs adsorbed with a virus encoding an anti-mouse CD19 CAR is injected at this site. The depletion of CD19+ B cells in the blood of mice will be monitored as an indication that anti-CD19 CARTs have been generated. The presence of these CARTs is confirmed in the blood and bone marrow. Detailed histological assessment of the

injection site as well as draining lymph nodes, the spleen, and liver, using *in situ* hybridization for the CAR transgene is conducted to assess the leakage of the virus to unwanted sites.

Example F. Drug loading onto mesoporous silica microparticles

A variety of drugs may be loaded onto the mesoporous silica microparticles.



Imiquimod

1. Example 1: Loading of TLR7 agonist onto mesoporous silica microparticles.

A solution of Imiquimod, in chloroform is added to a slurry of 100 mg silica microparticles in 2.0 mL chloroform (a concentration of 100-500 µg of imiquimod per 10 mg of mesoporous silica particles) and shake at 500 rpm at 40 degrees Celsius for 72 hours. The MSPs are centrifuged at 1000 rpm for 3 min and the remaining solution is removed. The MSPs are washed with 2.0 mL of chloroform followed by centrifugation and removal of the supernatant. The wash steps are repeated with ethanol to remove excess and unabsorbed imiquimod. The final microparticles are slurried in water and lyophilized.

2. Example 2: *In Vitro* Drug release from mesoporous silica particles.

10.0 mg (or the equivalent of 300 µg of drug-loaded material) drug-loaded MSPs are suspended in 1.0 mL of pH 7.4 (0.0067M) phosphate buffer and left at 37 degrees Celsius. Samples are collected at 1h, 3h, 6h, 24h, 2 days, and 5 days; analysis of these samples is performed by UPLC and plotted to a standard analytical curve. Supernatant is removed and replaced with fresh buffer at each timepoint.

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the constructs deposited, since the deposited embodiments are intended to illustrate only certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this

invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.

It is understood that the application of the teachings of the present invention to a specific problem or situation will be within the capabilities of one having ordinary skill in the art in light of the teachings contained herein.

The disclosures of each and every citation in the specification are expressly incorporated herein by reference.

Example G. In vivo study of MSR induced CAR-T generation

Mice engrafted with human T cells and B cells (human CD34+ stem cell humanized mice or human peripheral blood mononuclear cell-injected mice) are established using known methods. A composition of mesoporous silica particle conjugated to CAR19 lentivirus is injected under the skin of mice to transduce T cells. The presence of CAR19-expressing T cells (using anti-CAR19 idiotype antibody staining) and the depletion of CD19+ B cells in the blood of mice treated with MSR-CAR19 lentivirus conjugates is monitored using flow cytometry on serial blood collection samples (day 0 pre-injection and twice weekly between day 1 to day 21 following MSR-virus injection) and compared to control mice injected with MSR-GFP lentivirus as an indication that anti-CD19 CARTs have been generated and are functional in killing their target. The concentration of human interferon-gamma and tumor necrosis factor alpha is determined from the same blood samples as a second biomarker for CD19 CAR T cell generation and activation. Detailed histological assessment of the injection site as well as lymph nodes, bone marrow, the spleen, and liver using *in situ* hybridization for the CAR transgene is conducted to assess the leakage of the virus to unwanted sites and study trafficking of the generated CAR19 T cells to these sites.

In another experiment, human T and B cell-containing mice are intravenously injected with a CD19-expressing Nalm6 leukemia tumor that expresses a luciferase reporter gene. Cohorts of

mice are injected under the skin with a single injection of a composition of mesoporous silica particles conjugated to CAR19 or GFP lentivirus from 7 days before to 7 days following tumor injection to transduce T cells. The Nalm6 tumor burden is monitored by luciferase signal on IVIS imaging to study anti-tumor efficacy of the generated anti-CD19 CARTs. The presence of CAR19-expressing T cells and the depletion of CD19+ B cells in the blood of mice treated with MSR-CAR19 lentivirus conjugates is monitored on serial blood collection samples (day 0 pre-injection and twice weekly between day 1 to day 21 following MSR-virus injection) and compared to control mice injected with MSR-GFP lentivirus. The concentration of human interferon-gamma and tumor necrosis factor alpha is determined from the same blood samples as a second biomarker for CD19 CAR T cell generation and activation.

These studies are repeated with MSR-lentivurs conjugates for other cancer/tumor targets, including but not limited to BCMA, CD20, CD22, CD123, EGFRvIII, CLL-1, and combinations thereof (with each other and/or CD19).

EXAMPLE H: Functional Analysis of Compositions Comprising A Cryogel Comprising VEGF-C and MSRS with Conjugated Viral Vector and Absorbed Cell Activation Agent

Example 1: Generation of VEGF-C

HEK Production

DNA was synthesized at GeneArt (Regensburg, Germany) and cloned into a mammalian expression vector using restriction enzyme-ligation based cloning techniques. The resulting plasmid was transfected into HEK293T cells. For transient expression of proteins, vectors for wild-type or engineered variants were transfected into suspension-adapted HEK293T cells using Polyethylenimine (PEI; Cat# 24765 Polysciences, Inc.). The recombinant expression vectors were then introduced into the host cells and the construct produced by further culturing of the cells for a period of 7 days to allow for secretion into the culture medium.

The produced constructs were then purified from cell-free supernatant, using immobilized metal ion affinity chromatography (IMAC).

His-tagged proteins were captured by IMAC. The resin was washed before the protein was eluted.

Finally, eluted fractions were polished by using size exclusion chromatography (allowing separation of aggregates, monomers and dimers. Purification analysis was done using SDS-PAGE and aggregation content was determined using analytical size exclusion chromatography method.

Table 21: Production yield of VEGF-C variants in HEK293T cell line

Variant	**Physical state**	**Final yield after IMAC and SEC (ug/L)**
1	Dimer	117
2	Dimer	405
	Monomer	714
7	Dimer	1120
	Monomer	623
8	Dimer	1190
9	Dimer	869
	Monomer	125

CHO Production

A CHO MaKO manufacturing expression system was used to produce VEGF-C variant 8. The gene encoding the target protein was introduced into an expression cassette driven by a CMV promoter in a plasmid expression vector. The vector was transfected in triplicate into CHO MaKO cells. For each transfection, 0.5 µg of plasmid were transfected into viable cells in medium. The transfected cells were seeded into cell culture medium with low concentration of folic acid in shake flasks. Cells were grown in a humidified shaker incubator. On day 3 post transfection, selection for stable transfectants was started. The cells went into a selection crisis and recovered within 21 days. Then vials of the selected stable pools were frozen.

For production of the VEGF-C variant 8 a fed-batch approach was used. A vial of the frozen cells was thawed. After recovery from thawing, cells were seeded into production cell culture medium in shake flasks. Cultures were grown in a humidified shaker incubator. Growth temperature was decreased on day 5 after seeding the culture. Feed solutions were added on day 3, 4, 5, 6, 7 and 10 after seeding. The culture was harvested on day 11 after seeding. Cells were separated from the cell culture medium by centrifugation and sterile filtering. The target protein was purified from the clarified cell culture supernatant and characterized as above.

Table 22: Production yield of VEGF-C variant 8 in CHO MaKO cell line

Variant	Physical state	Final yield after IMAC and SEC (mg/L)
8	Dimer	17.5

Example 2: Generation of Cryogel

Alginate conjugations were formulated based on a previously described protocol (Koshy et al. 2018).

Norbornene Alginate (Alg-Nb)

One gram of Pronova UP MVG alginate was dissolved in 100ml of 0.1 M 2-(N-morpholino)ethanesulfonic acid (MES) buffer overnight at room temperature under constant stirring. 280µl of 5-norbornene-2-methylamine (norbornene) was then added to the alginate solution. 1464mg of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (EDC) and 1085mg of N-hydroxysuccinimide (NHS) were separately dissolved in 20ml of MES buffer and added to the alginate-norbornene solution and allowed to react for 24 hours at room temperature. After 24 hours the solution was dialyzed in sequential 5L salt baths (7, 6, 5, 4, 3, 2, 1, 0, 0, 0 g/L NaCl) for 3 hours at each concentration. Solution was then filtered twice (0.22m vacuum) and frozen at -80C overnight. Frozen solutions were then lyophilized for 5 days and stored at -20C until use in experiments.

Tetrazine Alginate (Alg-Tz)

One gram of Pronova UP MVG alginate was dissolved in 0.1 M 2-(N-morpholino)ethanesulfonic acid (MES) buffer overnight at room temperature under constant stirring. 126mg of (4-(1,2,4,5-

tetrazin-3-yl)phenyl methanamine hydrochloride (tetrazine) was then added to the alginate solution. 1464mg of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (EDC) and 1085mg of N-hydroxysuccinimide (NHS) were separately dissolved in 20ml of MES buffer and added to the alginate-tetrazine solution and allowed to react for 24 hours at room temperature. After 24 hours, solution was quenched with 311mg of hydroxylamine for 30 min and centrifuged at maximum RPM for 10 minutes. Solution was then filtered (0.22uM filter) and dialyzed in sequential 5L salt baths (7, 6, 5, 4, 3, 2, 1, 0, 0, 0 g/L NaCl) for 3 hours at each concentration. Solution was then filtered twice (0.22uM filter) and frozen at -80C overnight. Frozen solutions were then lyophilized for 5 days and stored at -20C until use in experiments.

Cryogel Formulation (Figure 21A)

Alg-Tz and Alg-Nb were dissolved in DIH_2O at 20mg/ml with a Thermomixer (37C, 2000rpm) for 1 hour. Separately, laponite was dissolved for 1 hour at 5mg/ml concentration in DI-H_2O under constant mixing at room temperature. Solutions were then filtered (0.22uM filter) under sterile conditions. VEGF-C (3mg/ml stock) and laponite (Laponite XLG) (5mg/ml stock) solutions were incubated together at room temperature for 1 hour. Alg-Tz solution and Alg-Nb solutions were then added in a 1:1 ratio and diluted to a final concentration of 10mg/ml (0.25 mg/ml final concentration of laponite, 10µg VEGF-C/gel). 50ul of mixture was immediately pipetted into PEEK molds and frozen at -20C overnight. Prior to injection, gels were thawed at room temperature in the molds and then placed into 16ga syringe needles. Needles with gels were then placed on 1ml syringes with 100ul of sterile PBS.

Example 3: VEGF-C Release Analysis

In vitro VEGF-C release assay from alginate cryogels (Figure 21)

VEGF-C cryogels (10µg protein + 0.25 mg/ml laponite) were incubated at 37C in 1ml of release buffer (1% BSA solution in PBS). Release buffer was completely removed and replaced at various timepoints throughout the experiment. Samples of release buffer were stored at -80C until thawed for use in a VEGF-C ELISA.

Example 4: MSR Synthesis

Poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) avg Mn ~5,800 (Pluronic P-123, 80.0 g, 487 mmol; Sigma) surfactant was dissolved in 3L of 1.6M HCl at room temperature, heated to 40C in a 5L jacketed flask, and mechanically stirred via and overhead stirrer at a rate of 0-600 rpm. Tetraethyl orthosilicate (TEOS, 184 mL, 826 mmol; Sigma) was added in one portion over <5min and was heated at 40C with maintained stirring for at least 2 hours but most commonly 20 hours. The resulting slurry was heated to 80-130C for 6-72 hours for hydrothermal treatment before being cooled to room temperature. The slurry was filtered in a Buchner funnel and was washed with deionized water followed by ethanol and air dried at room temperature. The resulting silica material was calcined in a furnace with a slow ramp temperature from room temperature to 550C over 8 hours and then maintaining at 550C for another 8 hours before cooling to room temperature to afford 47g of mesoporous silica particles.

Changes in the stir rate may have changes in the microparticle aspect ratio. Varying the conditions of the hydrothermal temperature and duration are common pore size controllers for mesoporous materials.

Final mesoporous materials were characterized by light microscopy, Malvern Morphologi G3, scanning electron microscopy (SEM), thermal gravimetric analysis (TGA).

N,N,N-trimethylpropan-1-ammonium functionalized microparticles

Trimethoxysilylpropyltrimethylammonium chloride (3.61 mL, 6.51 mmol; 50% solution in methanol) was added to a slurry of 1.0 g mesoporous silica microparticles in 150 mL reagent ethanol and was heated to 75 degrees Celsius for 7 hours. After cooling to room temperature and the slurry was filtered and the particles were washed with deionized water followed by ethanol and then dried in an oven at 100 degrees Celsius for 20 hours to afford N,N,N-trimethylpropan-1-ammonium functionalized microparticles, referred to herein as “trimethylammonium MSRs”.

MSR size reduction

Stock MSR variants were roughly 100-200µm in length after synthesis. To improve injectability through a 28.5ga insulin syringe, dry MSRs were homogenized in a MP FastPrep-24 5G bead beating grinder and lysis system for 80 seconds **(Figure 30)**. MSRs were then autoclaved and stored at room temperature until used in experiments.

Loading of lentivirus onto MSRs and characterization of complex

Homogenized MSR batches were resuspended at 10 mg/ml in ice-cold Tris-NaCl-EDTA buffer pH 7.5 (NTE buffer). The desired lentivirus stock was diluted in ice-cold NTE buffer to the desired total amount of transducing units (TU) for loading. The MSR suspension and the diluted virus were combined at ratios of 1:1 vol/vol and incubated on ice for 30 minutes. At least two wash steps in excess DPBS were performed to remove excess virus prior to functional in vitro tests, or in vivo use. For loading and retention studies (**Figures 27-28**), a 2.5mg/ml MSR suspension was mixed 1:1 with of a solution containing the indicated amount of virus in the figures and incubated for 30 minutes on ice. Virus amounts in loading solutions, bound to the MSRs, and released from the MSRs was quantified using a commercially available kit. For release studies, the MSR-lentivirus complex was incubated in the media at 37C, and the supernatant was collected at the indicated timepoints for qPCR analysis.

MSR loading with virus and STARTERS for in vivo use

Construct 2 (**Table 20, FIG. 48A-48B**) and trimethylammonium MSRs were co-incubated to allow adsorption of the cell activation agent onto the MSR surface. Construct 2 was added to 1 an 8 mg/ml trimethylammonium MSR suspension and incubated for 1 hour at 4C. Loaded MSRs were washed three times and resuspended in DPBS to a final concentration of 15 mg/ml MSRs.

NTE buffer solution containing CD19 CAR encoding (also referred to as CAR19) lentivirus was mixed with a 10 mg/ml trimethylammonium MSR suspension and incubated for 30 minutes at 4C. MSRs were washed twice and resuspended in DPBS to a final concentration of 15 mg/ml MSRs.

Finally, MSRs were vigorously pipetted up and down, back loaded into insulin syringes, and immediately injected intradermally into mice.

Example 5: Transduction of cells and functional testing

In vitro T cell transduction

Human T cells were isolated from leukopaks using the Miltenyi Human Pan T cell isolation kit and frozen prior to use. Cells were thawed and plated in complete OpTmizer medium in the

presence of the format 4 construct (**Table 20, FIGs. 48A-48B**). CD19 CAR encoding (also referred to as CAR19) virus, either as free virus or MSR-virus complexes were added into the culture, followed by one day of incubation. Cells were washed and plated for a further three days prior to use in characterization and functional tests (**FIG. 29-30**).

*CAR T cell characterization and functional testing (**Figure 29**)*

CAR T cells were analyzed for expression of the CAR receptor by staining with a CD19 CAR anti-idiotype antibody conjugated to PE and analysis by flow cytometry. Nalm6 (RRID: CVCL_0092) is a human acute lymphoblastic leukemia (ALL) cell line. Cells were grown in RPMI medium containing 10% fetal bovine serum and both grow in suspension. Cells were modified to express luciferase (Nalm6-Luc), so that their presence in co-cultures could be assessed by luciferase signal. Nalm6-Luc cells were co-cultured at various cellular ratios with CD19-CARTs produced using free virus of MSR-virus complexes (**Figure 29**). The luciferase signal at the end of a 1-day coculture was used to calculate the percentage of input Nalm6 that had been killed by the CARTs. Interferon-gamma levels in the supernatant at the end of the co-culture were quantified using a commercially available kit.

Example 6: Analysis of results

*Tube Assay (**Figure 20**)*

Human Dermal Lymphatic Endothelial Cells (HDLECs) were seeded (p0) and passaged at 75% confluence until p4 or enough cells were obtained for experiments. One ml was then aliquoted into Eppendorf tubes, treated with 600µg of VEGF-C protein, and vortexed. Each treatment was added to warmed media in a 6 well plate and incubated overnight at 37C (5% CO_2). For imaging analysis cells were washed and then fixed with 3.7% formalin-0.05%Triton X-100 solution (fixing buffer), then washed and coated with 0.1% Triton X-100 solution (permeabilization buffer). After washing twice with PBS cells were coated with 0.05% Triton X-100 in 1% BSA solution (blocking buffer). DAPI and phalloidin staining was performed according to known protocols. After staining cells were washed twice with PBS and imaged.

*Proliferation Assay (**Figure 20**)*

WST-8 media was prepared by diluting WST-8 solution 1:10 into MV media. Culture media was removed, and cells were incubated in WST-8 media. Following incubation, media was removed in triplicate from each well and added to a 96 well plate. Absorbance of each well at 450nm was read using a spectrophotometer.

Tissue Processing after in vivo experiments

Tissues were harvested from mice, weighted, and cut into very fine pieces with scissors. Samples were then enzymatically digested under constant stirring in of digestion media containing collagenase 4 and DNAse 1. Samples were then pipetted up and down. Following pipetting, digestion media containing collagenase D and DNAse 1 was added to the samples. Samples were pipetted up and down for 3 cycles. EDTA was added (5mM) and cells were filtered through 70µm filters and 40uM mesh and resuspended in Fc blocking buffer. Cells were washed and stained for FACS analysis.

*H&E and ISH staining (**Figures 32-33**)*

Skin/cryogel tissues, adjacent skin and draining lymph node were collected at necropsy, submersion fixed in 10% neutral buffered formalin and processed to paraffin. Sections were stained with hematoxylin and eosin (H&E) for histological evaluation. In situ hybridization to detect CAR transcript as well as Hs-PPIB (positive control and tissue quality control) and DAPB (negative control) genes was performed on formalin fixed paraffin embedded tissue sections. Positive PPIB and negative DAPB control probe sets were included to optimize preconditioning and ensure mRNA quality and specificity, respectively. The hybridization method followed known protocols using a 3,3'-Diaminobenzidine (DAB) chromogen. Briefly, 5 µm thick tissue sections were placed on glass slides, baked for 60 minutes and used for hybridization. The deparaffinization and rehydration protocol was performed using a stainer. Off-line manual pretreatment in 1X retrieval buffer was conducted. Optimization was performed by first evaluating PPIB and DAPB hybridization signal and subsequently using the same conditions for all slides. Following pre-treatment, the slides were transferred to a autostainer to complete the hybridization procedure including protease pretreatment; hybridization followed by amplification; and detection with HRP and hematoxylin counter stain. Slides were digitalized using a slide scanner and representative images captured.

Further Results

Cryogels (0.25mg/ml laponite) containing 10µg of different VEGF-C constructs were injected superficially into the dermis mice (N=5/group) at day 0. At day 14 mice were euthanized and the skin/cryogel (combined) were dissected for digestion and FACS analysis. Representative FACS plots of LECs ($CD31^+$, $PDPN^+$) are pre-gated on FSC-A/SSC-A, and $CD45^-$(**Figure 22**).

The results of **Figure 23** bear on the delivery of VEGF-C. Mice were injected with VEGF-C (N=12) or blank cryogels (N=10) synthesized as previously mentioned. Skin/gels from mice were harvested at timepoints day 7, 14, and 21, digested, and stained for FACS. LECs were gated on $CD45^-$ $CD31^+$ $PDPN^+$. BECs were gated on $CD45^-$ $CD31^+$ $PDPN^-$. CD4 and CD8 T Cells were gated on $CD45^+$ $CD11b^-$ $CD11c^-$ $Thy1^+$.

In **Figure 25A** C57Bl6 Mice were injected with either VEGF-C cryogels (N=5) or blank cryogels (N=5) and evaluated for lymphangiogenesis at day 14. Additionally, NSG mice were injected with VEGF-C cryogels (N=5) to compare LEC proliferation between immunocompetent mice (C57Bl6) and immune-compromised mice (NSG). For **Figure 25B**, NSG mice were injected on day 0 with either VEGF-C cryogels (N=5) or blank cryogels (N=5). On day 10, all mice were injected with PBMCs via their lateral tail vein. Seven days after PBMC injection skin/gel tissue was collected for digestion and FACS analysis. LECs were gated from human $CD45^-$ mouse $CD11b^-$ mouse $CD31^+$ mouse $PDPN^+$. CD4 and CD8 T cells were gated from human $CD45^+$ mouse $CD11b^-$ human $CD3^+$. B Cells were gated human $CD45^+$ mouse $CD11b^-$ human $CD3^-$ human CD19+.

In **Figure 34**, NSG mice (N=45) were injected with VEGF-C cryogels at day 0 and PBMCs at day 10 via tail vein injection. At day 17 mice were intradermally injected with either 1) PBS (N=15 total/ 5 for endpoint FACS analysis), 2) MSR with Construct 2 (10µl injection of 15 mg/ml MSR equivalent) followed by free CD19 CAR encoding lentivirus (10µl injection containing 4.26e6 TU of virus at 1 hour post STARTERS injection) (N=15 total / 6 for endpoint FACS analysis) or 3) MSR bound CD19 CAR encoding lentivirus mixed 1:1 with MSR with Construct 2 (20ul single injection of 15 mg/ml MSRs) (N=15 total / 5 for endpoint FACS analysis). On day 14, 3 or 4 mice group mice were euthanized and analyzed for

lymphangiogenesis in the skin/gel area, while on day 20 and 35, mice were euthanized and skin/gel and spleen were collected for histological analysis to look for local and systemic transduced cells (N=3/group/timepoint). Mice were periodically bled for FACS analysis of circulating CD19 CAR+ cells (D25, 30, 35). Finally, mice were euthanized for FACS analysis of skin/gel and spleen on day 35 to look for CART expansion and B cell depletion.

EXAMPLE I: Functional Analysis of In Vivo CART Manufacturing

Summary

This Example describes an *in vivo* CART manufacturing process involving localized delivery of a cell recruitment factor to induce lymphangiogenesis and/or attract T cells, e.g., naïve T cells, that can be subsequently activated and transduced with a viral vector encoding a CAR to generate functional CART cells *in vivo* (**FIG. 18**). In some embodiments, a subject is administered (for example, locally) a cell recruitment factor via a cryogel, wherein the cell recruitment factor is VEGF-C (e.g., a slow-releasing VEGF-C protein cryogel formulation). Without wishing to be bound by theory, release of VEGF-C induces lymphangiogenesis of pre-existing skin lymphatic capillaries, activating lymphatic endothelial cells (LECs). The activated LECs secrete chemokines such as CCL21, which in turn recruit immune cells, e.g., naïve T cells, to the site of administration, e.g., to the site in the dermis on top of the gel. In some embodiments, after a period of 7 to 21 days, e.g., 14 days, the subject is administered (for example, locally) a viral vector encoding a CAR and a cell activation agent, delivered by mesoporous silica rods (MSRs), for transduction of T cells and generation of CART cells *in vivo*. Without wishing to be bound by theory, brief CD3 and CD28 activation, for example, using anti-CD3/anti-CD28 (for example, a bispecific antibody), promotes efficient transduction of T cells. Without wishing to be bound by theory, in some embodiments, these transduced T cells will return into systemic circulation via the skin lymphatics, lymph nodes and thoracic duct and will further expand in response to tumor antigen.

Example 1: Generation and Characterization of VEGF-C Protein and Functional Variants

This Example describes the generation and characterization of various cell recruitment factors, including VEGF-C and functional variants thereof. Cell recruitment factors described in

this Example may, for example, be used in cryogels for promoting lymphangiogenesis in a site in a subject prior to administration of a viral vector encoding a CAR.

As shown in FIG. 19A, VEGF-C can exist in natural and modified forms. Immature VEGF-C (**FIG. 19A**, #1) is typically found intracellularly with N-terminal and C-terminal propeptide sequences. Once released, VEGF-C protein undergoes proteolytic cleavage and is present in the extracellular space as a major or minor mature form (**FIG. 19A,** #2 (SEQ ID NO: 731) or #7 (SEQ ID NO: 733), respectively) that is either a dimer or monomer. Stabilized dimers of the major mature (**FIG. 19A,** #9 (SEQ ID NO: 737)) and minor mature (**FIG. 19A,** #8 (SEQ ID NO: 735)) form of VEGF-C were engineered by inserting the C137A mutation into the sequences. As compared to the major mature forms of VEGF-C, the minor mature forms comprise an additional, short propeptide sequence (TEETIKFAA (SEQ ID NO: 740)) on the minor mature form N-terminus. Without wishing to be bound by theory, in some embodiments, this additional short propeptide boosts dimer formation as well as protein expression in both HEK293T and CHO MaKo cells.

HEK Production of VEGF-C Protein and Functional Variants

DNA was synthesized at GeneArt (Regensburg, Germany) and cloned into a mammalian expression vector using restriction enzyme-ligation based cloning techniques. The resulting plasmid was transfected into HEK293T cells. For transient expression of proteins, vectors for wild-type or engineered variants were transfected into suspension-adapted HEK293T cells using Polyethylenimine (PEI; Cat# 24765 Polysciences, Inc.). The recombinant expression vectors were then introduced into the host cells and the construct produced by further culturing of the cells for a period of 7 days to allow for secretion into the culture medium. The produced constructs were then purified from cell-free supernatant, using immobilized metal ion affinity chromatography (IMAC). His-tagged proteins were captured by IMAC. The resin was washed before the protein was eluted. Finally, eluted fractions were polished by using size exclusion chromatography (allowing separation of aggregates, monomers and dimers). Purification analysis was done using SDS-PAGE (**FIG. 19B-19C**) under reducing and non-reducing

conditions and aggregation content was determined using analytical size exclusion chromatography method.

As shown in **FIG. 19B-19C**, the immature VEGF-C with the full length propeptide (**FIG. 19A**, #1 (SEQ ID NO: 727)) was produced as a dimer (wells 2 and 3) and the removal of the propeptide led to the production of two major mature VEGF-C forms (#2 (SEQ ID NO: 731)), one non-covalent dimer form (wells 5, 6) and a monomeric form (wells 8, 9). A short N-terminal propeptide was left attached to the protein to generate a minor mature, wild type VEGF-C form (#7 (SEQ ID NO: 733)) in non-covalent dimer (wells 11,12) or in monomeric form (wells 15,16). Addition of the mutation C137A into the #2 major mature form of VEGF-C to generate the #9 major mature form with mutation of VEGF-C (SEQ ID NO: 737) led to the production of a covalent dimer (well 21, 22) and a monomer form (well 24, 25). Introduction of the C137A mutation to the #7 minor mature VEGF-C form to generate the #8 minor mature with mutation form of VEGF-C (SEQ ID NO: 735) led to the detectable production of a VEGF-C dimer only (wells 18,19). Without wishing to be bound by theory, in some embodiments, this #8 minor mature with mutation form of VEGF-C (SEQ ID NO: 736 or 735) may be suitable for large scale production.

Overall production yield using HEK cells was calculated and summarized in **Table 21**.

Table 21: Production yield of VEGF-C variants in HEK293T cell line

Variant	**Physical state**	**Final yield after IMAC and SEC (ug/L)**
1	Dimer	117
2	Dimer	405
	Monomer	714
7	Dimer	1120
	Monomer	623
8	Dimer	1190
9	Dimer	869
	Monomer	125

CHO Production of the VEGF-C #8 Minor Mature Variant

A CHO MaKO manufacturing expression system was then used to produce the VEGF-C variant #8 (minor mature form with mutation, SEQ ID NO: 736 or 735). The gene encoding the target protein was introduced into an expression cassette driven by a CMV promoter in a plasmid expression vector. The vector was transfected in triplicate into CHO MaKO cells. For each transfection, 0.5 µg of plasmid were transfected into viable cells in medium. The transfected cells were seeded into cell culture medium with low concentration of folic acid in shake flasks. Cells were grown in a humidified shaker incubator. On day 3 post transfection, selection for stable transfectants was started. The cells went into a selection crisis and were recovered within 21 days. Then vials of the selected stable pools were frozen.

For production of the VEGF-C variant #8 (minor mature form with mutation, SEQ ID NO: 736 or 735), a fed-batch approach was used. A vial of the frozen cells was thawed. After recovery from thawing, cells were seeded into production cell culture medium in shake flasks. Cultures were grown in a humidified shaker incubator. Growth temperature was decreased on day 5 after seeding the culture. Feed solutions were added on day 3, 4, 5, 6, 7 and 10 after seeding. The culture was harvested on day 11 after seeding. Cells were separated from the cell culture medium by centrifugation and sterile filtering. The target protein was purified from the clarified cell culture supernatant and characterized as above. The production yield of the VEGF-C variant #8 (minor mature form with mutation, SEQ ID NO: 736 or 735) is summarized in **Table 22**.

Table 22: Production yield of VEGF-C variant 8 in CHO MaKO cell line

Variant	**Physical state**	**Final yield after IMAC and SEC (mg/L)**
8	Dimer	17.5

Investigation of the in vitro activity of VEGF-C

The *in vitro* biological activity of VEGF-C and the variant forms produced above were investigated. The impact of VEGF-C on human dermal lymphatic endothelial cells (HDLECs), including sprouting and proliferation (**FIG. 20A-20C**), was measured. The various VEGF-C variants investigated in this example include: the immature VEGF-C with the full length propepitde (#1); the major mature form #2 as a monomer (2M) or a dimer (2D); minor mature

form #7 as a monomer (7M) or a dimer (7D); the major mature form with mutation (C137A) #9 as a monomer (9M) or a dimer (9D); and the minor mature form with mutation (C137A) #8 as a monomer (8M) or a dimer (8D).

An overview of the experimental setup of the *in vitro* sprouting assay on HDLECs to test the biological activity of VEGF-C variants is shown in **FIG. 20A**. HDLECs were first seeded (p0) and passaged at 75% confluence until p4 or enough cells were obtained for experiments. About 1mL of the HDLECs was then aliquoted into Eppendorf tubes, treated with 600µg of VEGF-C protein, and vortexed. Each treatment was added to warmed media in a 6 well plate and incubated overnight at 37C (5% CO_2). For imaging analysis, cells were washed and then fixed with 3.7% formalin-0.05%Triton X-100 solution (fixing buffer), then washed and coated with 0.1% Triton X-100 solution (permeabilization buffer). After washing twice with PBS, cells were coated with 0.05% Triton X-100 in 1% BSA solution (blocking buffer). DAPI and phalloidin staining was performed according to known protocols. After phalloidin staining, cells were washed twice with PBS, and imaged for tube formation.

In order to measure proliferation, a WST-8 assay was performed (**FIG 20B**), in which WST-8 media was first prepared by diluting WST-8 solution 1:10 into MV media. Culture media was removed, and cells were incubated in WST-8 media. Following incubation, media was removed in triplicate from each well and added to a 96 well plate. Absorbance of each well at 450nm was read using a spectrophotometer.

As shown in **FIG. 20B**, all VEGF-C mature forms (wild-type or mutant major and minor mature forms) led to similar levels of proliferation of HDLECs, which was improved relative to proliferation of HDLECs incubated with the immature VEGF-C with the full length propeptide (#1). As shown in **FIG. 20C**, the tube formation images show that the major and minor mature forms that are wild-type (#2 and #7, respectively) or comprise the C137A mutation (#9 and #8, respectively) stimulate better sprouting of HDLECs than the immature form (#1). Further, the dimeric forms (D) of the various VEGF-C forms appeared to demonstrate good *in vitro* activity (**FIG. 20B-20C**). Without wishing to be bound by theory, in some embodiments, the dimeric forms of the major and minor mature forms that are wild-type (#2D and #7D, respectively) or comprise the C137A mutation (#9D and #8D, respectively) comprise enhanced sprouting activity as compared to the monomeric forms.

Example 2: Generation and Characterization of Cryogel containing VEGF-C

A cryogel containing VEGF-C or functional variants was generated and investigated. Laponite was added to the cryogel formation to result in a slow, more controlled release of VEGF-C.

To form the cryogel, alginate conjugates were formulated based on a previously described protocol (Koshy et al., Acta Biomater. 2018 Jan;65:36-43) and mixed.

Norbornene Alginate (Alg-Nb)

One gram of Pronova UP MVG alginate was dissolved in 100ml of 0.1 M 2-(N-morpholino)ethanesulfonic acid (MES) buffer overnight at room temperature under constant stirring. 280µl of 5-norbornene-2-methylamine (norbornene) was then added to the alginate solution. 1464mg of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (EDC) and 1085mg of N-hydroxysuccinimide (NHS) were separately dissolved in 20ml of MES buffer and added to the alginate-norbornene solution and allowed to react for 24 hours at room temperature. After 24 hours the solution was dialyzed in sequential 5L salt baths (7, 6, 5, 4, 3, 2, 1, 0, 0, 0 g/L NaCl) for 3 hours at each concentration. Solution was then filtered twice (0.22m vacuum) and frozen at -80°C overnight. Frozen solutions were then lyophilized for 5 days and stored at -20C until use in experiments.

Tetrazine Alginate (Alg-Tz)

One gram of Pronova UP MVG alginate was dissolved in 0.1 M 2-(N-morpholino)ethanesulfonic acid (MES) buffer overnight at room temperature under constant stirring. 126mg of (4-(1,2,4,5-tetrazin-3-yl)phenyl methanamine hydrochloride (tetrazine) was then added to the alginate solution. 1464mg of 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (EDC) and 1085mg of N-hydroxysuccinimide (NHS) were separately dissolved in 20ml of MES buffer and added to the alginate-tetrazine solution and allowed to react for 24 hours at room temperature. After 24 hours, solution was quenched with 311mg of hydroxylamine for 30 min and centrifuged at maximum RPM for 10 minutes. Solution was then filtered (0.22uM filter) and dialyzed in sequential 5L salt baths (7, 6, 5, 4, 3, 2, 1, 0, 0, 0 g/L NaCl) for 3 hours at each concentration. Solution was then filtered twice (0.22uM filter) and frozen at -80°C

overnight. Frozen solutions were then lyophilized for 5 days and stored at -20C until use in experiments.

Cryogel Formulation

The Alg-Tz and Alg-Nb were then dissolved in DIH_2O at 20mg/ml with a Thermomixer (37C, 2000rpm) for 1 hour. Separately, laponite was dissolved for 1 hour at 5mg/ml concentration in DI-H_2O under constant mixing at room temperature. Solutions were then filtered (0.22uM filter) under sterile conditions.

For cryogels not containing laponite, the Alg-Tz solution and Alg-Nb solutions were then added together in a 1:1 ratio along with the desired amount of VEGF-C and diluted to a final concentration of 10mg/ml (10µg VEGF-C/gel).

For cryogel formulations containing laponite, VEGF-C (3mg/ml stock) and laponite (Laponite XLG) (5mg/ml stock) solutions were incubated together at room temperature for 1 hour. Alg-Tz solution and Alg-Nb solutions were then added in a 1:1 ratio and diluted to a final concentration of 10mg/ml (0.25 mg/ml final concentration of laponite, 10µg VEGF-C/gel).

50µl of the cryogel and VEGF-C mixture with or without laponite was immediately pipetted into PEEK molds and frozen at -20°C overnight. Prior to injection, gels were thawed at room temperature in the molds and then placed into 16ga syringe needles. Needles with gels were then placed on 1ml syringes with 100µl of sterile PBS.

In vitro VEGF-C release from alginate cryogels

The release rate of VEGF-C from alginate cryogel formations comprising laponite was investigated *in vitro*. As described above, alginate liquid prepolymer is mixed with laponite and VEGF-C, then frozen and thawed again before injection to generate porous matrix (**FIG. 21A**).

First, the release of VEGF-C from alginate cryogels with and without laponite was measured. Different types of alginate gels containing VEGF-C (10µg protein) were formed for use in the VEGF-C release assay: alginate nanoporous (gelification occurs without cryogelation so no macro-scale pores are formed), alginate cryogel (after freeze and cryogelation, porous), and alginate cryogel with 0.25% laponite. To perform the release assay, VEGF-C cryogels (10µg protein ± 0.25 mg/ml laponite) were incubated at 37°C in 1ml of release buffer (1% BSA solution in PBS). Release buffer was completely removed and replaced at various timepoints

throughout the experiment, ranging from 0 to more than 500 hours following the addition of the release buffer. Samples of release buffer that were collected were stored at -80°C until thawed for use in a VEGF-C ELISA. As shown in **FIG. 21B**, the alginate cryogel with 0.25% laponite showed the most controlled and longest-lasting release of VEGF-C *in vitro*.

Next, the modulation of VEGF-C release *in vitro* from a 0.25% laponite alginate cryogel loaded with 10µg or 50µg VEGF-C, or a 0.5% laponite alginate cryogel loaded with 50µg VEGF-C were measured. As demonstrated in **FIG. 21C**, about 30% of the total VEGF-C was released from the gels and the 0.25% laponite alginate cryogel showed the most controlled release profile.

A cryogel was injected subcutaneously in mice using a 16G needle. **FIG. 21D** demonstrates successful implantation of the cryogel in the skin of a mouse.

Investigation of VEGF-C cryogels in vivo

The ability of VEGF-C delivered via cryogel (0.25mg/ml laponite) to implant and induce lymphangiogenesis and recruit T cells *in vivo* was investigated in mice. These series of experiments investigate the ability of different VEGF-C variants including those comprising a C137A mutation and VEGF-C variants produced by different methods to induce lymphangiogenesis. The ability of varying amounts of VEGF-C cryogel to induce lymphangiogenesis and recruit T cells in wild type mice and immunocompromised NSG mice injected with human peripheral blood mononuclear cells (PBMCs) was also investigated.

First, cryogels (0.25mg/ml laponite) containing 10µg of different VEGF-C forms, including the dimeric forms of the major and minor mature forms that are wild-type (#2 and #7, respectively) and the major and minor mature forms that comprise the C137A mutation (#9 and #8, respectively), were injected superficially into the dermis of mice (N=5/group) at day 0. At day 14 mice were euthanized and the skin/cryogel (combined) were dissected for digestion and FACS analysis (**FIG. 22A**). Specifically, tissues were harvested from mice, weighted, and cut into very fine pieces with scissors. Samples were then enzymatically digested under constant stirring of digestion media containing collagenase 4 and DNAse 1. Samples were then pipetted up and down. Following pipetting, digestion media containing collagenase D and DNAse 1 was added to the samples. Samples were pipetted up and down for 3 cycles. EDTA was added (5mM)

and cells were filtered through 70μm filters and 40μM mesh and resuspended in Fc blocking buffer. Cells were washed and stained for FACS analysis.

Representative FACS plots of lymphatic endothelial cells (LECs) ($CD31^+$, $PDPN^+$) isolated on day 14 post-injection of the cryogel were pre-gated on FSC-A/SSC-A, and $CD45^-$ (**FIG. 22B**) and show that *in vivo* lymphangiogenesis was induced. The amount of lymphangiogenesis in mouse skin was quantified as LEC counts per mg of tissue, as shown in **FIG. 22C**. The covalent dimers of the major and minor mature forms that comprise the C137A mutation (#9 and #8, respectively) resulted in higher amounts of LECs compared to the dimers of the major and minor mature forms that are wild-type (#2 and #7, respectively), and thus led to higher levels of *in vivo* lymphangiogenesis following cryogel implantation (**FIG. 22C**).

In addition, the functionality of the VEGF-C variant #8 (minor mature form with C137A mutation) produced in CHO MaKo cells as described above was investigated *in vivo* and compared to the same mutant form produced in HEK cells. Both #8 variants showed comparable activity in an *in vitro* HDLECs sprouting assay despite being produced in different cell types.

The VEGF-C variant #8 produced in CHO MaKo cells was able to induce lymphangiogenesis *in vivo* as shown in **FIG. 24B**, as compared to a blank cryogel control which does not comprise VEGF-C. Comparable bioactivity of the two #8 variants produced by the different cell types was then also confirmed *in vivo* by staining LECs after skin digestion 14 days after cryogel delivery (**FIG. 24C**). Lymphangiogenesis was quantified as total LECs counts/mg tissue in mice injected with a blank cryogel (no VEGF-C) or cryogel loaded with the #8 VEGF-C variant produced in HEK cells (#8HEK) or the #8 VEGF-C variant produced in MaKo cells (#8CHO). Blood vascular endothelial cells (BECs) (CD45-CD31+PDPN-) were not affected by the #8 variant VEGF-C delivery regardless of which cell type it was produced in. It was also observed that peak lymphangiogenesis corresponded to elevated LEC levels and peak immune infiltration of CD4 and CD8 T cells (CD45+) in the skin on top of the cryogels on day 14 after cryogel delivery with the #8 variant VEGF-C delivery regardless of which cell type it was produced in.

In addition, the response of skin lymphatics to 10μg VEGF-C delivered by alginate cryogels was measured. Mice were injected with VEGF-C alginate cryogels (N=12) or blank cryogels (does not comprise VEGF-C) (N=10) synthesized as previously mentioned. Skin/gels from mice were harvested as described above, at timepoints day 7, 14, and 21, digested, and

stained for FACS. LECs were gated on $CD45^-$ $CD31^+$ $PDPN^+$. BECs were gated on $CD45^-$ $CD31^+$ $PDPN^-$. CD4 and CD8 T Cells were gated on $CD45^+$ $CD11b^-$ $CD11c^-$ $Thy1^+$. The number of cells per mg of tissue were also quantified.

FIG. 23A depicts the *in vivo* dose response of VEGF-C loaded into alginate cryogels (1, 10, 20, 50 μg) and lymphangiogenesis induction (represented as total lymphatic endothelial cells (LECs) counts/mg tissue, upper graph) and time course of lymphangiogenesis after delivery of 10μg VEGF-C (lower graph). These results indicated that 10μg of VEGF-C induced high *in vivo* lymphangiogenesis and that peak lymphangiogenesis was observed 14 days after subcutaneous cryogel delivery. Representative plots of LECs (CD45-CD31+PDPN+) and blood endothelial cells (BECs, CD45-CD31+PDPN-) staining isolated after skin digestion of C57/BL6 mice 14 days after gel implant (**FIG. 23B**) as well as quantification of endothelial cells as total cell counts/mg tissue (**FIG. 23C**) also indicated that 10μg of VEGF-C induced high *in vivo* lymphangiogenesis compared to blank gel controls that did not comprise VEGF-C. Further, quantification represented as total cell counts/mg tissue of CD4+ T cells and CD8+ T cells demonstrated that T cell infiltration was also increased following 10μg of VEGF-C alginate cryogel delivery, and LECs counts correlated with T cells infiltrates especially those of a naïve phenotype (CD62L+, CD44-). As shown in **FIG. 23E**, peak lymphangiogenesis was observed 14 days after subcutaneous VEGF-C alginate cryogel delivery, and peak T cell infiltrates were also observed on day 14.

The ability of VEGF-C to induce lymphangiogenesis in immunocompromised NSG mice and the ability of mouse LECs to efficiently recruit human peripheral blood mononuclear cells (PBMCs) was investigated. In **FIG. 25A**, C57B6 mice were injected with either VEGF-C cryogels/0.25% laponite (N=5) or blank cryogels (N=5) and evaluated for lymphangiogenesis at day 14. Additionally, NSG mice were injected with VEGF-C cryogels (N=5) to compare LEC proliferation between immunocompetent mice (C57Bl6) and immune-compromised mice (NSG). Representative flow cytometry plots of skin LECs and BECs staining in NSG, C57/BL6 mice 14 days after VEGF-C or blank cryogel delivery demonstrated increased LECs and thus higher *in vivo* lymphangiogenesis following delivery of VEGF-C cryogels in NSG and C57B6 mice (**FIG. 25A**). In **FIG. 25B**, NSG mice were injected on day 0 with either VEGF-C cryogels (N=5) or blank cryogels (N=5). On day 10, all mice were injected with PBMCs via their lateral tail vein. Seven days after PBMC injection, skin/gel tissue was collected for digestion and FACS analysis.

LECs were gated on human $CD45^-$ mouse $CD11b^-$ mouse $CD31^+$ mouse $PDPN^+$. CD4 and CD8 T cells were gated on human $CD45^+$ mouse $CD11b^-$ human $CD3^+$. B Cells were gated on human $CD45^+$ mouse $CD11b^-$ human $CD3^-$ human CD19+. These data demonstrate that CD3+ T cells, CD4+ T cells, CD8+ T cells, and B cells were all increased in the skin of the NSG mice administered the VEGF-C cryogels compared to the blank cryogel controls (no VEGF-C), and that T cells were the main cell type of PBMCs recruited in NSG mice.

Taken together, these data indicate that alginate cryogels comprising VEGF-C with or without laponite were capable of locally inducing lymphangiogenesis and T cell recruitment to the site of cryogel administration *in vivo*.

Example 3: MSR Synthesis for Transduction of T cells to generate CART cells

This Example describes the synthesis of mesoporous silica rods (MSRs). Mesoporous silica particles (MSPs) such as MSRs may be used, e.g., to assist with delivery of a viral vector encoding a CAR to a site in a patient that has undergone lymphangiogenesis due to administration of a VEGF-C cryogel described above.

MSR synthesis was performed by first dissolving poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) avg Mn ~5,800 (Pluronic P-123, 80.0 g, 487 mmol; Sigma) surfactant in 3L of 1.6M HCl at room temperature, which was then heated to 40C in a 5L jacketed flask, and mechanically stirred via and overhead stirrer at a rate of 0-600 rpm. Tetraethyl orthosilicate (TEOS, 184 mL, 826 mmol; Sigma) was added in one portion over <5min and was heated at 40C with maintained stirring for at least 2 hours but most commonly 20 hours. The resulting slurry was heated to 80-130C for 6-72 hours for hydrothermal treatment before being cooled to room temperature. The slurry was filtered in a Buchner funnel and was washed with deionized water followed by ethanol and air dried at room temperature. The resulting silica material was calcined in a furnace with a slow ramp temperature from room temperature to 550C over 8 hours and then maintaining at 550C for another 8 hours before cooling to room temperature to afford 47g of mesoporous silica particles.

Changes in the stir rate may have changes in the microparticle aspect ratio. Varying the conditions of the hydrothermal temperature and duration are common pore size controllers for mesoporous materials.

Final mesoporous materials were characterized by light microscopy, Malvern Morphologi G3, scanning electron microscopy (SEM), thermal gravimetric analysis (TGA).

N,N,N-trimethylpropan-1-ammonium functionalized microparticles

Trimethoxysilylpropyltrimethylammonium chloride (3.61 mL, 6.51 mmol; 50% solution in methanol) was added to a slurry of 1.0 g mesoporous silica microparticles in 150 mL reagent ethanol and was heated to 75 degrees Celsius for 7 hours. After cooling to room temperature and the slurry was filtered and the particles were washed with deionized water followed by ethanol and then dried in an oven at 100 degrees Celsius for 20 hours to afford N,N,N-trimethylpropan-1-ammonium functionalized microparticles, referred to herein as "trimethylammonium MSRs".

MSR size reduction

Stock MSR variants were roughly 100-200μm in length after synthesis. MSRs were homogenized to reduce their size and improve injectability. In particular, to improve injectability through a 28.5ga insulin syringe, dry MSRs were homogenized in a MP FastPrep-24 5G bead beating grinder and lysis system for 80 seconds **(FIG. 30A)**. In **FIG. 30A**, size reduction was observed in terms of MSR length, which allows for injection through a smaller diameter needle into the intradermal space. MSRs were then autoclaved and stored at room temperature until use.

Loading of lentivirus onto MSRs and characterization of the MSR + Viral Vector

Homogenized MSR batches were resuspended at 10 mg/ml in ice-cold Tris-NaCl-EDTA buffer pH 7.5 (NTE buffer). The desired lentivirus stock (described below) was diluted in ice-cold NTE buffer to the desired total amount of transducing units (TU) for loading. The MSR suspension and the diluted virus were combined at ratios of 1:1 vol/vol and incubated on ice for 30 minutes. At least two wash steps in excess DPBS were performed to remove excess virus prior to functional in vitro tests, or in vivo use. For loading and retention studies (**FIGs. 27-28**), a 2.5mg/ml MSR suspension was mixed 1:1 with a solution containing the indicated amount of virus in the figures and incubated for 30 minutes on ice. Virus amounts in loading solutions, bound to the MSRs, and released from the MSRs was quantified using a commercially available kit, e.g., a qRTPCR based kit, e.g., Lenti-X qRT-PCR Titration Kit. For release studies, the

MSR-lentivirus complex was incubated in the media at 37°C, and the supernatant was collected at the indicated timepoints for qPCR analysis.

First, the loading capacity of MSRs with a GFP-encoding lentivirus was measured. Trimethylammonium MSRs were co-incubated with a GFP-expressing lentivirus at various amounts according to functional titers as determined by cell-based transduction assays. The amount of virus in three fractions was characterized, which include the viral loading solution (initial input added to the MSRs), MSR-bound virus (amount remaining bound to the MSRs after incubation and washing), and unbound virus (the amount in the solution remaining after co-incubation of MSRs and virus). MSR and virus were co-incubated for 30 minutes on ice, the supernatant was removed (Unbound Virus) and the MSRs were washed twice prior to assessing MSR-bound virus. The untouched viral loading solutions from each condition were also analyzed. As shown in **FIG. 27A**, the majority of the virus in the input viral loading solution was retained in the MSR-bound virus fraction after adsorption and washing as compared to the unbound virus. The amount of virus adsorbed to the MSRs also increased with the amount of virus in the viral loading solution. As depicted in **FIG. 27B** which graphs the percentage of viral loading solution versus the functional titer of virus, the calculated fraction of MSR-bound virus relative to the viral loading solution had a strong efficiency of loading and retention on the MSRs following adsorption and washing.

Next, retention of virus on MSRs was characterized. Specifically, lentivirus and MSRs were co-incubated for 30 minutes on ice, and the MSRs were washed twice. MSRs were then cultured in R10 medium containing 10% FCS or OpTmizer serum-free medium, and the input virus stock was incubated in media as well. The supernatant was removed at the indicated times after the start of incubation and analyzed for total virus content. As demonstrated in **FIG. 28**, the results indicated that the MSRs release only a fraction of the input virus over the first 18 hours (MSR-Virus in R10 media and MSR-Virus in OpTmizer media), compared to unbound virus controls (virus in R10 media and virus in OpTmizer media).

Example 4: Transduction of T cells with MSR and viral vector, and optionally STARTERS, and functional testing

This Example describes the transduction of T cells in vitro using a viral vector encoding a CAR. Without wishing to be bound by theory, the viral vector was administered together with

MSR (to promote controlled release of the vector), and optionally also STARTERS (to promote activation of the T cells).

In vitro T cell transduction with MSR +viral vector +optionally STARTERS

Human T cells were isolated from leukopaks using the Miltenyi Human Pan T cell isolation kit and frozen prior to use. Cells were thawed and plated in complete OpTmizer medium in the presence of STARTERS Construct 4 (**Table 20, FIG. 48A**). CD19 CAR encoding (also referred to as CAR19) virus, either as free virus or MSR-virus complexes were added into the culture, followed by one day of incubation. Cells were washed and plated for three additional days prior to use in characterization and functional tests.

CAR T cell characterization and functional testing

CAR T cells were analyzed for expression of the CAR receptor by staining with a CD19 CAR anti-idiotype antibody conjugated to PE and analysis by flow cytometry.

To measure CD19 CAR expression, the percentage of CAR+ cells was quantified at day 4 after transduction (**FIG. 29A**). Transduction efficiency of T cells *in vitro* was comparable for those T cells transduced with CAR-MSR or CAR-free (unbound virus) **(FIG. 29A)**.

To measure function of CD19 CAR T cells transduced with MSR-bound virus or unbound virus, a Nalm6-Luc cell specific killing assay and an interferon-γ (IFN-γ) release assay were used. Nalm6 (RRID: CVCL_0092) is a human acute lymphoblastic leukemia (ALL) cell line. Cells were grown in RPMI medium containing 10% fetal bovine serum and were grown in suspension. Cells were modified to express luciferase (Nalm6-Luc), so that their presence in co-cultures could be assessed by luciferase signal. Nalm6-Luc cells were co-cultured at various cellular ratios (Effector to Target rations (E:T Ratio)) with CD19-CARTs produced using free virus or MSR-virus complexes (**FIG. 29B-29C**). The luciferase signal at the end of a 1-day co-culture was used to calculate the percentage of input Nalm6 that had been killed by the CARTs. IFN-γ levels in the supernatant at the end of the co-culture were quantified using a commercially available kit.

Results from these assays indicate that specific killing activity (**FIG. 29B**) and IFN-γ release (**FIG. 29C**) during the co-incubation for 24 hours were comparable between CART cells transduced with the MSR-bound virus (CAR-MSR) and CART cells transduced with the free

virus (CAR-free), showing that transduction by formulation with MSRs produced equivalently functional CARTs *in vitro* compared to conventional free virus transduction.

Next, the transduction efficiency of MSRs following homogenization was assessed. MSRs were homogenized as described above to allow for injection through a smaller diameter needle (**FIG. 30A**). As shown in **FIG. 30B**, standard trimethylammonium MSRs or homogenized MSRs were adsorbed with lentivirus and a dilution series of this complex was created and used to transduce T cells with a GFP-encoding lentivirus. Homogenization of MSRs did not substantially alter transduction performance *in vitro*.

Administration of cryogel/laponite followed by MSR+ viral vector in vivo

An experiment was designed to investigate localization and distribution of a cryogel injected into mice followed by injection of MSR-virus complexes. Blank alginate cryogels were injected subcutaneously and 7 days later viral particles (4e6 TU) free or bound to MSRs were injected in the intradermal space on top of the gel with insulin syringe (for MSR-virus group) or Hamilton syringe (for free virus). 72h after viral delivery, mice were euthanized, and tissues (skin and draining lymph node) were harvested for immunohistochemistry analysis. Skin/cryogel tissues, adjacent skin and draining lymph node were collected at necropsy, submersion fixed in 10% neutral buffered formalin and processed to paraffin. Sections were stained with hematoxylin and eosin (H&E) for histological evaluation. Slides were digitalized using a slide scanner and representative images captured. **FIG. 31A-31B** depict the hematoxylin and eosin (H&E) stained section of skin containing adjacent cryogel and MSRs.

In **FIG. 31A**, H&E stained sections demonstrated the location of the subcutaneous cryogel superficial to the panniculus muscle in the hypodermis. The MSRs appeared as lightly eosinophilic granular material admixed with mononuclear cells positioned at the dermal-hypodermal junction adjacent to the implanted cryogel (**FIG. 31B** for close up image).

FIGs. 32A-32B show in situ hybridization for CAR mRNA on sections of isolated mouse skin. In situ hybridization to detect CAR transcript as well as Hs-PPIB (positive control and tissue quality control) and DAPB (negative control) genes was performed on formalin fixed paraffin embedded tissue sections. Positive PPIB and negative DAPB control probe sets were included to optimize preconditioning and ensure mRNA quality and specificity, respectively. The hybridization method followed known protocols using a 3,3'-Diaminobenzidine (DAB)

chromogen. Briefly, 5 µm thick tissue sections were placed on glass slides, baked for 60 minutes and used for hybridization. The deparaffinization and rehydration protocol was performed using a stainer. Off-line manual pretreatment in 1X retrieval buffer was conducted. Optimization was performed by first evaluating PPIB and DAPB hybridization signal and subsequently using the same conditions for all slides. Following pre-treatment, the slides were transferred to an autostainer to complete the hybridization procedure including protease pretreatment; hybridization followed by amplification; and detection with HRP and hematoxylin counter stain. Slides were digitalized using a slide scanner and representative images captured.

As shown in **FIG. 32A,** in situ hybridization to detect CAR mRNA transcript demonstrated robust signal within regions corresponding to the injected MSR in mice injected with MSR-bound virus. As depicted in **FIG. 32B**, in situ hybridization detected diffuse signal in cells infiltrating the cyrogel, as well as cells adjacent to it in the free virus condition. These data appear to support the notion that MSRs may maintain the virus localized in the dermis where the T cells are infiltrating the skin.

FIGs. 33A-33B show a mouse injected with MSR-virus had less CAR mRNA transcript positive cells in draining lymph node compared to the free virus group. In situ hybridization for CAR mRNA was performed as described above on sections of draining lymph node (dLN). This in situ hybridization detected only one CAR mRNA transcript positive cell within the dLN of mice injected with MSR-bound virus (**FIG. 33A**), while mice injected with free-virus showed a few CAR mRNA transcript positive cells in the subcapsular sinus consistent with local drainage of the virus or the cells from the site of cryogel implantation (**FIG. 35B**). This study demonstrated that MSP-virus formulations limited virus drainage to the draining lymph node, thereby decreasing potential off-site transduction and improving safety.

MSR loading with virus and STARTERS for in vivo use

STARTERS (specifically, STARTERS Construct 2, shown in **Table 20, FIG. 37A**) and trimethylammonium MSRs were co-incubated to allow adsorption of the cell activation agent onto the MSR surface. STARTERS Construct 2 protein was added to an 8 mg/ml trimethylammonium MSR suspension and incubated for 1 hour at 4°C. Loaded MSRs were washed three times and resuspended in DPBS to a final concentration of 15 mg/ml MSRs. NTE buffer solution containing CD19 CAR encoding lentivirus was mixed with a 10 mg/ml

trimethylammonium MSR suspension and incubated for 30 minutes at 4°C. MSRs were washed twice and resuspended in DPBS to a final concentration of 15 mg/ml MSRs. Finally, MSRs were vigorously pipetted up and down, back loaded into insulin syringes, and immediately injected intradermally into mice.

Taken together, these data indicate that MSR-bound virus, together with a STARTERS construct, was capable of efficiently transducing T cells to produce functional CART cells. Accordingly, contemplated herein is VEGF-C delivery in mouse skin generating a secondary priming site for T cells to be educated and transduced after injection of viral particles bound to mesoporous silica rods (MSRs) in combination with MSR-bound STARTERS (**FIG. 26A**), or free virus in combination with MSR-bound STARTERS (**FIG. 26B**).

Example 5: *In vivo* CART Manufacturing

A study was performed to demonstrate viral transduction of human T cells with a CD19 CAR encoding lentivirus in an *in vivo* mouse model. Specifically, a VEGF-C cryogel (0.25mg/ml laponite) was administered to mice to promote lymphangiogenesis and recruitment of T cells. Next, a combination of a viral vector encoding CD19 CAR, MSR, and STARTERS was administered to activate and transduce the T cells in the area that underwent lymphangiogenesis.

Methods

Mouse study and flow cytometry analysis

NSG mice (N=45) were injected with VEGF-C cryogels at day 0 and PBMCs at day 10 via tail vein injection. Seven days later at day 17, mice were intradermally injected with either: 1) PBS (N=15 total/ 5 for endpoint FACS analysis), 2) MSR with STARTERS Construct 2 (10µl injection of 15 mg/ml MSR equivalent, produced as described above) followed by free CD19 CAR encoding lentivirus (10µl injection containing 4.26e6 TU of virus at 1 hour post STARTERS injection) (N=15 total / 6 for endpoint FACS analysis) or 3) MSR bound CD19 CAR encoding lentivirus mixed 1:1 with MSR with STARTERS Construct 2 (20µl single injection of 15 mg/ml MSRs) (N=15 total / 5 for endpoint FACS analysis) (**FIG. 34A**). MSR-STARTERS was used for promoting T cell activation and T cell transduction. On day 14, 3 or

4 mice per group were euthanized and analyzed for lymphangiogenesis in the skin/cryogel injection area. On day 35, mice were euthanized and the spleen and blood were collected to determine if *in vivo* CD19 CAR encoding viral delivery elicited transduction of those T cells recruited by VEGF-C induced lymphangiogenesis and to look for local and systemic transduced cells (N=3/group/timepoint). Mice were periodically bled for FACS analysis of circulating CD19 CAR+ cells on days 25, 30, 35. Finally, mice were euthanized for FACS analysis of skin/cryogel and spleen on day 35 to look for CART expansion and B cell depletion. B cells depletion and CAR-T cells were also quantified in the spleen of the mice in all groups.

ISH staining of CAR

In situ hybridization using RNAscope 2.5 VS probe CAR 3UTR (catalog #438289) to detect CAR mRNA transcripts as well as 2.5 VS probe Hs-PPIB (positive control and tissue quality control (catalog #313909)) and 2.5 VS probe DAPB (negative control (catalog #3120390) was performed on blocks using reagents and equipment supplied by Advanced Cell Diagnostics (ACDBio) (Hayward, CA) and Ventana Medical Systems (Roche, Tuscon AZ). Positive PPIB and negative DAPB control probe sets were included to ensure mRNA quality and specificity, respectively. The hybridization method followed protocols established by ACDBio and Ventana systems using a 3,3'-Diaminobenzidine (DAB) chromogen and optimized for study tissues. Briefly, 5 µm sections were baked at 60 degrees for 60 minutes and used for hybridization. The deparaffinization and rehydration protocol was performed using a Sakura Tissue-Tek DR5 stainer with the following steps: 3 times xylene for 3 minutes each; 2 times 100% alcohol for 3 minutes; air dried for 5 minutes. Off-line manual pretreatment in 1X retrieval buffer at 98 to 104 degrees C was conducted for 15 minutes. Optimization was performed by first evaluating PPIB and DAPB hybridization signal and subsequently using the same conditions for all slides. Following pretreatment the slides were transferred to a Ventana Ultra autostainer to complete the ISH procedure including protease pretreatment; hybridization at 43 degrees C for 2 hours followed by amplification; and detection with HRP and hematoxylin counter stain.

IHC staining for T cells

Immunohistochemistry staining for CD3 including the deparaffinization and antigen retrieval steps were performed on a Ventana Discovery XT autostainer using standard Ventana

Discovery XT reagents (Ventana, Indianapolis, IN) using a rabbit monoclonal antibody clone 2GV6 (Ventana catalog # 790-431). Slides were deparaffinized then submitted to heat-induced antigen retrieval by covering them with Cell Conditioning 1 (CC1/pH8) solution according to the standard Ventana retrieval protocol. Slides were incubated with the primary antibody or a non-immune isotype-matched negative control. Visualization was obtained by incubation with Ventana Discovery OmniMap HRP reagent followed by Ventana Discovery ChromoMap 3,3'-Diaminobenzidine (DAB). Counterstaining was performed using Ventana Hematoxylin and Ventana Bluing reagent for 4 minutes each. Slides were dehydrated, cleared and coverslipped with a synthetic mounting medium.

IF staining protocol – mouse tissue for in vivo CART- multiplexing

On day 1, slides were washed and then blocked overnight at 4°C. On day 2, slides were incubated with AffiniPure Fab fragment goat anti-mouse IgG (H+L) and then with Alexa Fluor® 647-labeled anti-CD19 antibody overnight at 4°C. On day 3, slides were washed and then incubated with Alexa Fluor® 488-labeled anti-CD3 zeta antibody overnight at 4°C. On day 4, the slides were washed, counterstained with DAPI, and then washed again. Slides were mounted with cover glass, placed in the fridge for at least 24 hours before imaging.

Results

As demonstrated in **FIG. 38**, T cells were recruited efficiently around the implant site in the mouse skin and surrounding the gel. Results from the CAR ISH study showed that some mononuclear cells (from the phenotype likely T cells) in the area were transduced with the lentiviral vector that encodes CAR (**FIG. 39**). The expression of CAR RNA was also observed in some endothelial cells (likely lymphatics) (**FIG. 39**). However, CD19 CAR protein expression on the cell surface, analyzed by flow cytometry, was confirmed to be almost exclusively on T cells, with the exception of few human monocytic cells, indicating that there was minimal transduction of non-T cells by the free virus and MSR-virus (**FIG. 35**).

The locally generated CAR-T cells migrated to the spleen (**FIG. 40**). As shown in **FIG. 34B**, CAR-T cells as well as significant reduction of B cells were detected in those mice that received (a) free virus and MSR bound with STARTERS Construct 2 or (b) MSR bound CD19 CAR encoding lentivirus mixed 1:1 with MSR with STARTERS Construct 2. The number of B

cells in the spleen inversely correlated with the number of CAR-T cells (which were mainly CD8+) in the spleen (**FIGs. 34C and 36A**) as well as in the blood (**FIG. 36B**), supporting that B cell depletion was caused by CD19-specific CAR-T cells generated *in vivo*. As shown in **FIGs. 41A-41B**, B cells in close proximity with T cells had a shrunken and unhealthy shape indicating cell death, while B cells that did not enter yet in contact with CD19 specific T cells showed a healthy phenotype (round and bigger cells with CD19 staining only at the cell surface). T cells stained with CD3 antibody (dotted staining) were likely CART cells, even though co-stain with CAR probe was not performed.

This study demonstrates that functional CART cells can be generated *in vivo*, following local administration of cryogel containing a growth/cell recruitment factor, e.g., VEGF-C, for induction of lymphangiogenesis and recruitment of T cells, which are then subsequently transduced by MSR-bound virus or free virus and MSR-bound STARTERS.

Example 6: Additional Study Testing *In vivo* CART Manufacturing

In this example, an additional study as laid out in **FIG. 42A** was conducted to test in vivo CART manufacturing. The methods are similar to the ones described in Example 5. Briefly, NSG mice were subcutaneously injected with VEGF-C cryogel (0.25mg/ml laponite) at Day -24 and human PBMCs at Day -14. At Day 0, mice were intradermally injected with: 1) free virus and MSP with STARTERS Construct 2 (referred to as the free virus group), 2) MSP with virus and MSP with STARTERS Construct 2 (referred to as the MSP-virus group), or 3) PBS and MSP with STARTERS Construct 2 (referred to as the PBS group). A fourth group of mice received blank cryogel at Day -24 and free virus as well as blank MSPs at Day 0 (referred to as the free virus control group). The first two groups (the free virus group and the MSP-virus group) are referred to as full combination groups or groups receiving full combination treatments. The viral dose was increased from 4e6 TU (Example 5, FIG. 34A) to 1.1e7 TU (Example 6, FIG. 42A).

As shown in **FIG. 42B**, human CD45 circulating cells increased in number over time. Full combination treatments (solid line box, white and black circles) further boosted T cell expansion, particularly CD8+ T cells, compared to control mice (dotted line box, grey triangles, white rhombus). Different from the study described in Example 5 (virus injection 17 days after VEGF-C injection and 7 days after PBMC injection), in this new study, virus injection was

postponed to 24 days after VEGF-C injection and 14 days after PBMC injection. This modification led to a higher consistency of CART cell generation, likely due to the higher density of T cells around the VEGF-C cryogel implant at this later time point (day 24).

As shown in **FIG. 43A**, in vivo generated human CD3+ CAR+ T cells increased in number over time in mice treated with the full combination treatments (solid line box, white and black circles), particularly CAR-T cells of the CD8 phenotype, compared to control mice (dotted line box, grey triangles, white rhombus). Corresponding to an increase in CAR-T cell number, a decrease of B cells in the circulation was observed over time compared to PBS control (**FIG. 43B**, upper panel). The MSP-virus and free-virus groups performed similarly, while the free virus control group (**FIG. 43B**, lower panel) also showed partial B cells depletion, although not to the same extent as the full combination groups. Indeed, the number of circulating CAR-T cells in the mice from the free virus control group was not as high as the number in the full combination groups.

Consistent with results described in Example 5, this new study also showed a strong correlation between CAR-T cell expansion and B cell depletion in the blood (**FIG. 44A**) and in the spleen (**FIG. 44B**). While the free virus control group showed an intermediate level of B cell depletion in the circulation (**FIG. 44A**), this control treatment did not lead to effective B cell depletion in the spleen (**FIG. 44B**). The presence of CAR-T cells, especially from the CD8 phenotype, corresponded to B cells depletion in the spleen (**FIGs. 45A-45B**) and in the skin (**FIGs. 46A-46C**) of the treated mice. In the skin, CART cell expansion also correlated with lymphangiogenesis as measured by the number of lymphatic endothelial cells (LECs) (**FIG. 46D**).

In summary, this study demonstrates that the in vivo CART manufacturing methods described herein can be used to generate functional CARTs, the expansion of which correlates with B cell depletion.

Example 7: Co-delivery of virus and STARTERS using MSP.

This example examines co-delivery of virus and STARTERS using the same MSP. Briefly, MSPs were simultaneously co-incubated with a lentiviral vector that encodes GFP and STARTERS Construct 1 (**Table 20**, **FIG. 48A**). After co-incubation and washing, the virus and STARTERS-loaded MSPs were serially diluted prior to incubation with T cells in a 96 well flat-

bottom plate. As shown in **FIG. 47**, co-delivery of virus and STARTERS using MSP led to successful transgene expression in primary pan T cells.

Example 8: Generation of STARTERS molecules

This example describes the generation of multispecific molecules that comprise an anti-CD3 binding domain and a costimulatory molecule binding domain. In some embodiments, the costimulatory molecule binding domain binds to CD28, CD2, CD25, CD27, IL6Ra, IL6Rb, ICOS, or 41BB. Such molecules are referred to as STARTERS molecules.

A variety of configurations of anti-CD3 x anti-CD28 or anti-CD3 x anti-CD2 bispecific antibodies and multimer conjugates thereof were generated. Schema for these molecules are provided in **FIGs. 48A-48B** (Constructs 1-17, also referred to as F1 to F17; first generation STARTERS molecules). The sequences of Constructs 1-17 and their binding domains are disclosed in **Table 19** and **Table 20**.

In addition, second generation STARTERS molecules were generated to test binders targeting different co-stimulatory molecules (e.g., CD25, IL6Rb, CD27, 41BB, ICOS, or CD2). Different anti-CD3 binders (binders based on ANTI-CD3 (1) or ANTI-CD3 (2)) were also compared. All the second generation STARTERS molecules (**FIG. 49A**) have the configuration shown in **FIG. 49B**. The sequences of the different binders of second generation STARTERS molecules can be found in **Table 19**.

Without wishing to be bound by theory, reducing the binding of STARTERS molecules to FcR may decrease or prevent unwanted killing of FcR-expressing cells by T cells. Third generation STARTERS molecules were generated by introducing D265A/N297A/P329A substitutions (EU numbering according to Kabat) ("DANAPA") in the IgG1 Fc region. In addition, different anti-CD3 binders (binders based on ANTI-CD3 (1), ANTI-CD3 (2), or ANTI-CD3 (3)) and different anti-CD28 binders (binders based on ANTI-CD28 (1) or ANTI-CD28 (2)) were also compared (**FIG. 50A**). All the third generation STARTERS molecules have the configuration shown in **FIG. 50B**. The sequences of third generation STARTERS molecules and their binding domains can be found in **Table 19** and **Table 20**.

The STARTERS molecules were shown to mediate transduction of T cells with a lentiviral vector that encodes a CAR.

Exemplary methods for assaying STARTERS activity are disclosed, e.g., in Examples 16-19 and 22-23 of PCT/US2021/019889, incorporated by reference herein in its entirety.

Example J: Use of a STARTERS molecule in in vivo CART manufacturing

This example describes the characterization of a STARTERS molecule for use in *in vivo* CART manufacturing. This STARTERS molecule is an anti-CD3/anti-CD28 bispecific molecule comprising an anti-CD28 antibody fused to an anti-CD3 scFv (FIG. 51A). This STARTERS molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 726 and a light chain comprising the amino acid sequence of SEQ ID NO: 728. The Fc region of this STARTERS molecule comprises L234A/L235A/S267K/P329A mutations, numbered according to the Eu numbering system.

In a first in vitro study, the STARTERS molecule was tested for its ability to mediate T cell activation and transduction, when delivered via MSPs. Briefly, isolated T cells were thawed and resuspended at 1e6 cells/mL in serum-free T cell media with 100 units/mL of IL2 before being added to a 96-well plate. 20 mg of each MSP batch was resuspended at 30mg/mL in Dulbecco's PBS (Thermo: # 14190144) and 1.5 mg of MSP (or equal volume of DPBS) was added to Eppendorf tubes. To the same Eppendorf tubes, 2.1 µg of STARTERS was added. Lentivirus was thawed on ice and diluted to 1.4e8 TU/mL with DPBS before 7e7 TU of virus was added to each of the aforementioned tubes. After the mixtures were incubated at 4°C for one hour, they were serially diluted with T cell media before being administered to plated T cells. Components were co-cultured with T cells for three days before T cell activation and transduction were evaluated using flow cytometry.

Two independently produced batches of MSPs were loaded with lentivirus and the STARTERS molecule prior to co-culturing with T cells in vitro. Delivering the STARTERS molecule bound to MSPs enhanced activation and transduction as compared to soluble delivery of the molecule, particularly in more dilute conditions (FIGs. 51B and 51C). The MSP-virus-STARTERS complexes were co-cultured with T cells for three days before a flow cytometry analysis was performed to examine CD25 expression as an activation readout (FIG. 51B) and GFP expression to measure transduction (FIG. 51C). The data show that complexes formed with either batch of MSPs were capable of activating T cells and mediating T cell transduction. It is worth noting that activation and transduction with MSPs shows a bell-shaped response. Without wishing to be bound by theory, high concentrations of MSPs in T cell cultures can have negative

impacts on the T cell viability, and subsequently, can hamper activation and transduction efficiency.

A second in vitro study tested whether size reduction of MSPs, through either sonication or bead homogenization, would impact MSP performance. Isolated T cells were thawed and resuspended at 1e6 cells/mL in serum-free T cell media with 100 units/mL of IL-2 before being added to a 96-well plate. 60 mg of MSPs were resuspended at 30mg/mL in DPBS. A portion of MSP solution was size-reduced by bead homogenization. Additionally, 30 mg of MSPs were resuspended at 5 mg/mL in sterile water, and then sonicated using a Q125 system (qSonica) sonication probe at an amplitude of 40% for a duration of two minutes (sonication performed in 15sec intervals with 30sec breaks). After sonication, MSPs were centrifuged to aspirate water and resuspended at 30 mg/mL in DPBS. 1.5 mg of full-sized or size-reduced MSPs were added to fresh Eppendorf tubes and an equal volume of DPBS was added to a separate Eppendorf tube as a soluble virus control. Then, 1.6 μg of the STARTERS molecule was added to MSPs or DPBS before 8e7 TU of thawed virus was added. The mixtures were incubated at 4°C for one hour before serially diluted with T cell media and added to plated T cells. Components were co-cultured with T cells for three days before T cell activation and transduction were evaluated using flow cytometry.

GFP-encoding lentivirus and the STARTERS molecule were loaded onto full-size or size-reduced MSPs, where size reduction was achieved using bead homogenization or sonication of MSPs. The MSP-virus-STARTERS complexes were co-cultured with T cells for three days before flow cytometry analysis was performed for CD25 expression (activation) and GFP expression (transduction). Size reduction of MSPs did not negatively impact in vitro potency with respect to T cell activation (FIG. 52A) and transduction (FIG. 52B), and sonicated MSPs demonstrated the greatest peak transduction efficiency of MSP conditions tested.

Next, an in vivo study (FIG. 53A) was conducted to examine the use of the STARTERS molecule in in vivo CART manufacturing. Briefly, VEGF-C loaded cryogels ("injectable 1" in FIG. 53A) were injected at day -16 followed by a 20e6 human PBMC injection at day -14. 14 days later, different combinations of CD19 CAR-encoding virus and STARTERS molecules co-loaded onto MSPs ("injectable 2" in FIG. 53B) were injected intradermally above the cryogel location. Flow cytometry analysis was performed on blood from weekly bleeds and expansion of lymphocyte populations was assessed. On day 18, mice with significant CAR-T expansion were

euthanized and circulating lymphocytes were harvested via cardiac puncture, analyzed for CAR% and cell count, pooled within the groups, and adoptively transferred into mice which had been challenged with 1e6 NALM6 cells 4 days prior. Weekly bleeds and bi-weekly luminescence imaging of tumors were performed until end of study. The aims of this study were to 1) elucidate the necessity of single components within each injectable, and 2) demonstrate the ability of in vivo manufactured CAR-Ts to control tumor burden.

As shown in FIG. 53C, in vivo manufactured CAR-Ts, when adoptively transferred into NALM6 tumor bearing mice, were able to recognize their target CD19 receptor and deplete B cells in these mice. As shown in FIG 53D, tumors treated with transferred PBMCs from donor mice with no CARTs ("PBMC control" in FIG. 53D) showed comparable growth kinetics compared to untreated NALM6 tumors ("NALM6" in FIG. 53D). Mice treated with a dose of 3e5 CAR-Ts manufactured using free virus ("Free virus" in FIG. 53D) or MSP-delivered virus ("MSP virus" in FIG. 53D) show reduced tumor burden. These data show that in vivo-generated CARTs demonstrated strong anti-tumor activity in vivo.

Furthermore, expansion of in vivo-generated CARTs in circulation was examined. 13 days after intradermal injection of injectable 2 at the cryogel site, mice treated with a combination of VEGF-C cryogel, virus (MSP-deliver or free), and MSP-STARTERS showed comparable CART, shown by similar CAR percentage in total circulating T cells (FIG. 53E) and counts/μl of CART cells in blood (FIG. 53F). Mice treated without full treatment combination showed lower levels of CAR-T number and CAR+ % (FIGs. 53E and 53F).

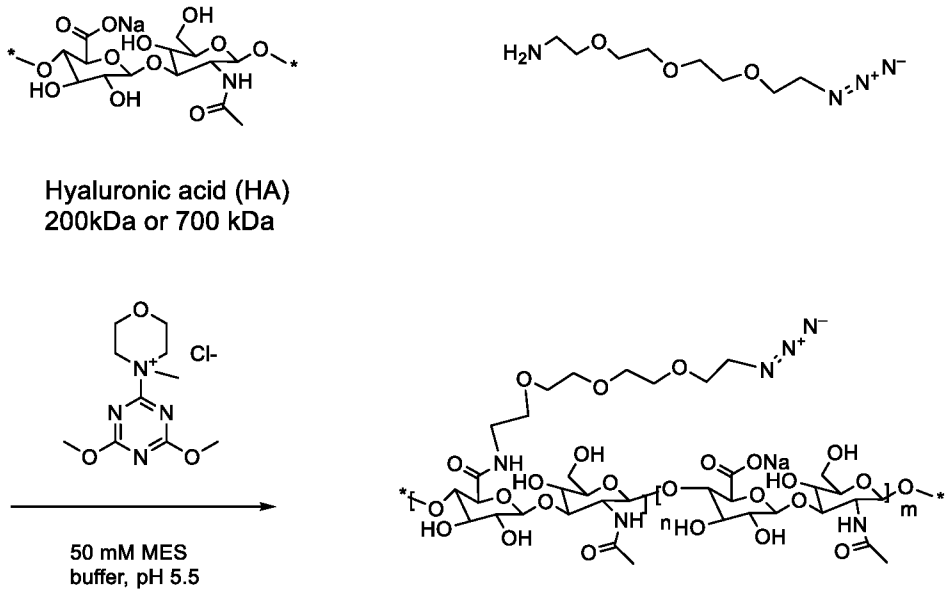
18 days after intradermal injection of injectable 2, despite similar amount of circulating T cells (FIG. 53H), mice treated with virus and STARTERS co-loaded onto MSPs had a higher CAR-T number (FIG. 53I) and CAR+% (FIG. 53J) compared to mice treated with MSP-delivered STARTERS in combination with free virus. The day-18 data were used to determine the CAR+ cell number after pooling of blood lymphocytes to determine the number of cells dosed into mice bearing Nalm6 tumors.

FIGs. 53K and 53L show results from combined flow cytometry analysis of blood from mice used for adoptive transfer and remaining mice enrolled in the study. No significant difference in the number of circulating T cells was observed between groups (FIG. 53K). Full combination of injectable 1 and injectable 2 induced the highest absolute counts of CARTs in circulation (FIG. 53L).

Example K: Use of HA-hydrogel for sustained release of VEGF-C

This example describes the use of hyaluronic acid (HA)-hydrogel for sustained release of VEGF-C protein to achieve lymphangiogenesis and T-cell localization at an injection site.

Example 1: Functionalization of hyaluronic acid



This example describes the synthesis of an azide functionalized hyaluronic acid, which is reacted with a crosslinking moiety to form a hydrogel.

Synthesis of hyaluronic acid intermediate [HA-N_3]

Hyaluronic acid sodium salt is a linear polymer consisting of repeating dimeric units of glucuronic acid and N-acetylgalactosamine, with a repeating unit molecular weight of 401.3 Da. In this example the moles of hyaluronic acid reported refers to the moles of repeating unit and the equivalents of reagents used in the reaction with hyaluronic acid are reported relative to the moles of hyaluronic acid repeating unit. The average molecular weight of the polymer determines the average number of repeat units per polymer strand. Hyaluronic acid sodium salt was obtained from supplier Lifecore Biomedical with label HA700K-5 having a nominal average molecular weight of 700kDa and may vary from batch to batch.

Synthesis of 700KD [HA-N_3]-16%

A solution of hyaluronic acid, sodium salt (nominal average molecular weight 700 kDa; 258.9 mg, 0.62 mmol; Lifecore Biomedical, LLC; product number HA700K-5) was fully dissolved

in 37.5 mL of MES buffer (50 mM, pH 5.5). To this solution was added 4-(4',6'-dimethoxy-1',3',5'-triazin-2'-yl)-4-methylmorpholin-4-ium chloride (DMTMM, 298.1 mg, 1.077 mmol, 1.736 eq), followed after 5 min by addition of 11-azido-3,6,9-trioxaundecan-1-amine (201 mg, 0.921 mmol). The reaction was stirred overnight. A crude reaction mixture was filled into a dialysis membrane (MWCO 50 kDa), and dialyzed 1–3 days against 0.25 M NaCl, with several changes of the dialysis solution, followed by 1–3 day's dialysis against deionized water, also with multiple changes of the dialysis solution. Upon completion, the sample was removed from the dialysis tubing, flash-frozen, and lyophilized to get **700kDa [HA-N_3]-16%**.

^{1}H NMR (400 MHz, D_2O) δ 4.45 (bs, 1.71H), 4.0–3.1 (m, 16H), 1.95 (s, 3H).

DOSY-NMR. One dimensional diffusion ordered NMR spectra (DOSY) were collected using the stimulated echo with one spoil gradient pulse sequence (stegp1s1d) on a Bruker AVANCE III 400 MHz (for ^{1}H-NMR) instrument with 5 mm DCH cryoprobe. The diffusion time and the diffusion gradient time were set to 50 ms and 4 ms, respectively. Two spectra were collected with gradient strength (gpz6) set to 2% and 95%. Comparison of the two spectra showed no differences apart from the solvent peak, indicating no small molecule impurities were present in the polymer.

Elemental analysis of a purified sample showed the following elemental content - C: 38.9%: H: 5.42%; N: 4.85%.

The degree of substitution of the **[HA-N_3]** is defined as the % of repeat units in which the carboxylate moiety has undergone reaction to give the depicted amide. Elemental analysis was used to determine the degree of substitution. The [%C/%N] ratio determined by elemental analysis of a purified sample is entered into the following formula to provide the degree of substitution. Where y = [(%C) / (%N)]) then:

Degree of substitution =

$$100 \times \frac{\frac{14 \times 12.01}{14.01 \times y} - 1}{4 - \frac{8 \times 12.01}{14.01 \times y}}$$

In this example, the degree of substitution (DS) of **[HA-N_3]** was 16%.

This 700 kDa hyaluronic acid, functionalized with 16% of the azide linker is labeled **700kDa [HA-N_3]-16%**.

Synthesis of 200KD [HA-N_3]-24%

In another aspect, hyaluronic acid, sodium salt (nominal average molecular weight 200 kD) was reacted as described above in example 1.

^{1}H NMR (400 MHz, D_2O) δ 4.45 (bs, 2H), 4.0–3.1 (m, 18H), 1.95 (s, 3H).

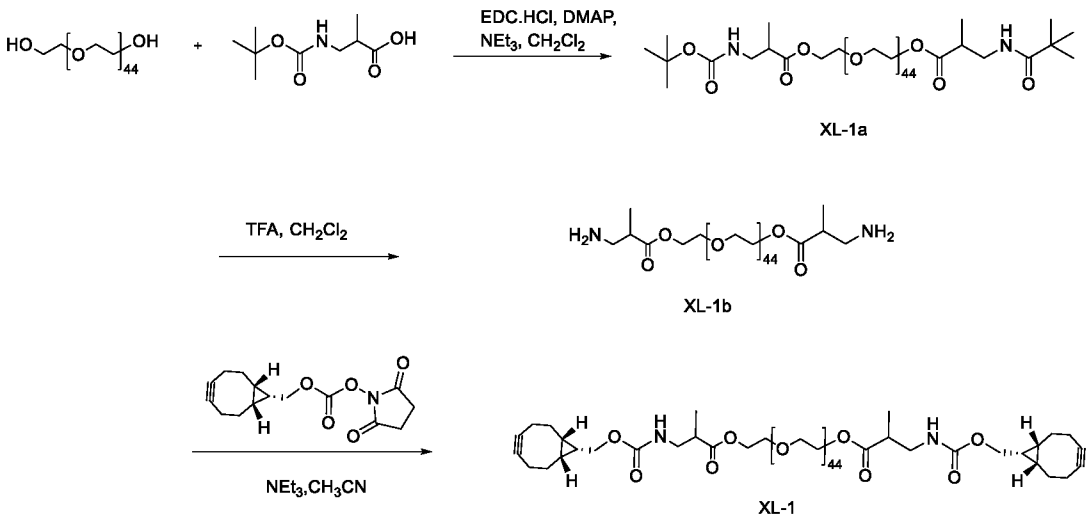
Elem. Anal: C: 39.94%: H: 5.53%; N: 5.73%.

In the rest of the examples, a 700 kDa and 200kDa hyaluronic acid, functionalized with X% of the azide linker is labeled **700kDa [HA-N_3]-X%** and **200kDa [HA-N_3]-X%** respectively.

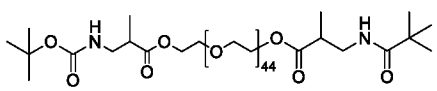
[HA-N_3] intermediates may also be purified by tangential flow filtration. The reaction mixture diluted with 25 mL of 0.25 M NaCl solution and purified by tangential flow filtration. Tangential flow filtration was carried out using a 30 kDa MWCO Vivaflow-50R Hydrosart cartridge (Sartorius), eluting with 400 mL of 0.25 M NaCl solution, then 400 mL of water. The product was flash frozen and lyophilized to get final product.

Example 2: Synthesis of crosslinkers (XL)

XL-1 synthesis

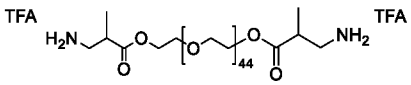


XL-1a. PEG(2000)-bis-3-((tert-butoxycarbonyl)amino)-2-methylpropanoate



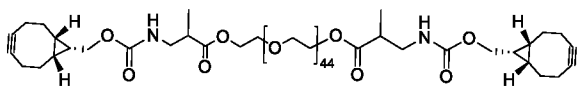
3-((tert-butoxycarbonyl)amino)propanoic acid (0.152 g, 0.75 mmol) and Mn ~ 2 kDa PEG (0.5 g, 0.250 mmol) was dissolved in 15 mL dichloromethane. Dimethylaminopyridine (0.015 g, 0.125 mmol) and EDC·HCl (0.192 g, 1.003 mmol) were added and the reaction mixture was stirred at room temperature overnight. The crude product was purified by flash column chromatography on silica with a 0–15% dichloromethane : methanol gradient. The product containing fractions were combined and reduced to dryness to provide **XL-1a**. ^{1}H NMR (400 MHz, methanol-d4) δ 4.23 (m, 4H), 3.63 (m, 170H), 3.22 (m, 4H) 2.66 (m, 2H), 1.43 (s, 18H), 1.13 (m, 6H).

XL-1b. PEG (2000)-bis-[methyl-3-amino-2-methylpropanoate], bis-trifluoroacetic acid



XL-1a (260 mg, 0.108 mmol) was dissolved in dichloromethane (3 mL). Trifluoroacetic acid was added (0.415 mL) and the reaction mixture was stirred at room temperature for 4h. The solvent was removed under reduced pressure. The crude product was triturated with Et_2O twice, then dried under vacuum to provide **XL-1b**. ^{1}H NMR (400 MHz, Methanol-d4) δ 4.45 (m, 2H), 4.22 (m, 2H), 3.59 (m, 177H), 3.12 (m, 4H), 2.87 (m, 2H), 1.22 (m, 6H).

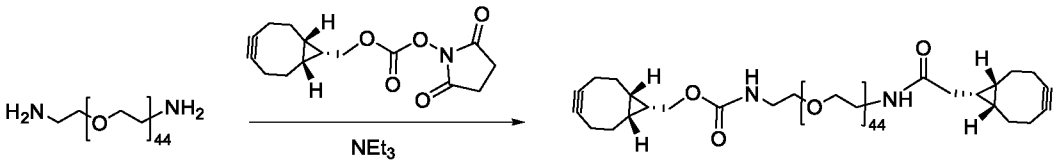
XL-1. PEG (2000)-bis 3-(((((1R,8S,9s)-bicyclo[6.1.0]non-4-yn-9-yl)methoxy)carbonyl)amino)-2-methylpropanoate



XL-1b (200 mg, 0.086 mmol) was dissolved in acetonitrile (3 mL). Triethylamine (0.599 mL, 4.30 mmol) was added, followed by ((1*R*,8*S*,9s)-bicyclo[6.1.0]non-4-yn-9-yl)methyl (2,5-dioxopyrrolidin-1-yl) carbonate (200 mg, 0.688 mmol) and the reaction mixture was stirred at room temperature for 4 h. The reaction mixture was directly purified by preparative reverse phase HPLC with ELSD triggered fraction collection (method below). The product containing fractions were pooled, frozen and lyophilized to provide **XL-1**. For storage purposes, **XL-1** was

kept as an acetonitrile, DMSO, or methanol solution in a freezer. Analytical HPLC-CAD (method below): retention time = 2.75 min. 1H NMR (400 MHz, methanol-d4) δ 4.23 (m, 4H), 4.14 (m, 4H), 3.63 (m, 188H), 2.68 (m, 2H), 2.22 (m, 12H), 1.60 (m, 4H), 1.37 (m, 2H), 1.14 (m, 6H), 0.94 (m, 4H).

XL-2 synthesis



Mn ~ 2 kDa PEG diamine hydrochloride (JenKem Technology, 300 mg, 0.148 mmol) was dissolved in acetonitrile (3 mL). Triethylamine (0.413 mL, 2.96 mmol) was added, followed by ((1R,8S,9s)-bicyclo[6.1.0]non-4-yn-9-yl)methyl (2,5-dioxopyrrolidin-1-yl) carbonate (345 mg, 1.184 mmol) and the reaction mixture was stirred at room temperature for 4 h. The reaction mixture was directly purified by preparative reverse phase HPLC with ELSD triggered fraction collection (method below). The product containing fractions were pooled, frozen and lyophilized to provide **XL-2**. For storage purposes, **XL-2** was kept as an acetonitrile, DMSO, or methanol solution in a freezer. Analytical HPLC-CAD (method below): retention time = 2.61 min. 1H NMR (400 MHz, methanol-d4) δ 4.14 (m, 4H), 3.63 (br s, 186H), 3.54 (m, 4H), 2.22 15 (m, 12H), 1.61 (m, 4H), 1.38 (m, 2H), 0.94 (m, 4H).

Preparative HPLC conditions: Waters XBridge C18; particle size: 5 μm; column size: 19 × 250 mm; eluent/gradient: 5% CH_3CN/H_2O/0.5 min, 5–95% CH3CN/H2O/12.5 min, 95% CH_3CN/H_2O/3 min; flow rate: 30 mL/min; column temperature: room temperature.

Analytical HPLC-CAD conditions: Waters ACQUITY UPLC BEH C18; particle size: 1.7 μm; column size: 2.1 × 50 mm; eluent/gradient: 2% CH_3CN/H_2O/0.5 min, 2–98% CH_3CN/H_2O/5min (CH_3CN containing 0.1% formic acid and H_2O containing 0.1% formic acid); flow rate: 1 mL/min; column temperature: 50 °C.

Example 3: Preparation of HA-hydrogel formulations for in vitro and in vivo studies

The crosslinker solution (50mg/mL) prepared in Example 2 was dried under reduced pressure to remove the ACN (acetonitrile). The same amount of 1X PBS was added to the dry

residue to get 50 mg/mL concentration of crosslinker in 1X PBS buffer. This freshly prepared solution was used for preparation of formulations for in vitro and in vivo studies.

H1a. *In situ* forming HA-hydrogel synthesis

200kDa [HA-N3]-24% (122.4 mg, degree of substitution = 24 %) was dissolved in 7.26 mL 1× PBS buffer pH 7.4 (16.9 mg/mL, as weighed concentration) and stirred at room temperature overnight while protected from light. The molecular weight of the unsubstituted carboxylate sodium salt repeat dimer unit is 401.3 Da. The MW of the azidylated repeat dimer unit is 579.6 Da. The average MW of a dimer unit for the sodium salt form of **200kDa [HA-N_3]-24%** is 444.1 Da = ((401.3 × 0.76) + (579.6 × 0.24)). Using the average MW of a sodium salt dimer unit, the total moles of repeat dimer unit is 276 µmol and the number of moles of azidylated repeat dimer unit is 66.2 µmol. 200 µL of 200kDa HA-N_3 -24% (3.38mg, 7.61 µmol) was aliquoted from a stock solution and gelation was carried out by adding 10.4 µl of **XL-2** crosslinker (0.52 mg, 0.221 µmol of reagent, 0.442 µmol of reactive functionality, 50 mg/mL in 1X PBS). This resulted in a solution with predicted crosslinking of 6.7 % of the **200kDa [HA-N_3]-24%** repeat units by the **XL-2** ((0.442 µmol [XL-2-reactive functionality]/66.2 µmol [HAunits)× 100 = 6.7%) The mixture was vortexed and 50 µl aliquot of the mixed solution was quickly added to an Eppendorf tube and stored at room temperature for overnight. The next day, visual inspection showed formation of **H1a** gel.

H2a hydrogel synthesis

VEGF-C protein was mixed with **200 kDa [HA-N_3]-24%** solution and a gelation reaction was performed with the crosslinker **XL-2** as described above to prepare **H2a** gel.

H3a hydrogel synthesis

VEGF-C protein was mixed with **200kDa [HA-N_3]-24%** solution and a gelation reaction was performed with the 2X amount of crosslinker **XL-1** as described above to prepare **H3a** gel.

H4a hydrogel synthesis

VEGF-C protein was mixed with **700kDa [HA-N_3]-16%** solution and a gelation reaction was performed with the 2X amount of crosslinker **XL-2** as described above to prepare **H4a** gel.

H5a hydrogel synthesis

VEGF-C protein was complexed with laponite XLG (BYK additives) prior to addition to **700kDa [HA-N_3]-16%** solution with laponite conc. 0.25 mg/mL in final gel. A gelation reaction

was performed with the 2X amount of crosslinker **XL-2** as described above to prepare **H5a** gel.

H6a hydrogel synthesis

VEGF-C protein was complexed with laponite XLG (BYK additives) prior to addition to **700kDa [HA-N_3]-16%** solution with laponite conc. 1 mg/mL in final gel. A gelation reaction was performed with the 2X amount of crosslinker **XL-2** as described above to prepare **H6a** gel.

H3b. HA hydrogel particles synthesis

200 µL of **H3a** gel prepared as described above was forced through a 100 mesh stainless steel screen disc into a 1mL syringe, yielding coarse gel particles. 100µL of 1× PBS was added to this syringe, followed by vortexing to mix. The syringe was held at room temperature for 6 h to allow swelling of the hydrogel. The swollen, coarse gel particles of **H3a** were forced 20 times through a 200-mesh stainless steel screen disc, yielding fine gel particles to get **H3b** product.

H5b hydrogel synthesis

H5a gel was extruded to fine gel particles to get final **H5b** product.

H6b hydrogel synthesis

H6a gel was extruded to fine gel particles to get final **H6b** product.

In vitro release study set up

950 µl PBS-2%BSA buffer was added to the 50 µL aliquot of hydrogel and incubated at 37°C on 300rpm shaking. 800 µl aliquots were taken out at different time points and no gel was removed at those time points. The study samples were replenished with same amount of 1X PBS-2%BSA buffer to keep the volume of study sample same. The release samples were then analyzed with ELISA for VEGF-C content.

In vivo study set up

After all the components for preparation of **H3a** gel was mixed, the tube was vortexed and quickly filled in the back of insulin syringe. The sample was pushed inside the syringe with a plunger and any air bubbles formed was removed. 30 µL was injected intradermally in mice within 2-3 minutes of mixing.

Results

Sustained release of VEGF-C was achieved in vitro using different compositions of HA-hydrogels (FIGs. 54A-54D). No difference was observed in the release curves for HA-hydrogels prepared with **700kDa [HA-N_3]-16%** and **200kDa [HA-N_3]-24%** (FIG. 54A). The VEGF-C release from HA-hydrogel formulations can be tuned by the addition of laponite. The laponite containing HA-hydrogel formulations provided concentration-dependent slower release of VEGF-C protein as compared to the formulations containing no laponite (FIG. 54B). The laponite containing in situ forming hydrogel and HA-hydrogel particles provided a similar release profile for VEGF-C protein (FIGs. 54C and 54D).

The in vivo study was performed with intradermal injection of H1a and H3a in situ forming hydrogels in mice. The VEGF-C containing formulation (H3a) showed an increase in lymphatic endothelial cells (LECs) and T4 cells after day 7 analysis as compared to the control (H1a) formulation (FIGs. 55A and 55B).

EQUIVALENTS

The disclosures of each and every patent, patent application, and publication cited herein are hereby incorporated herein by reference in their entirety. While this invention has been disclosed with reference to certain embodiments, it is apparent that further embodiments and variations of this invention may be devised by others skilled in the art without departing from the true spirit and scope of the invention. The appended claims are intended to be construed to include all such embodiments and equivalent variations.

What is claimed is:

1. A plurality of compositions, comprising:

a first composition comprising:

a biomaterial and a cell recruitment factor; and

a second composition comprising:

a viral vector.

2. A first composition, comprising:

a biomaterial and a cell recruitment factor,

wherein the biomaterial comprises a hydrogel, e.g., a cryogel (e.g., an alginate cryogel) or a hyaluronic acid hydrogel (HA hydrogel), and

wherein the cell recruitment factor comprises an amino acid sequence according to SEQ ID NO: 741, or an amino acid sequence with at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto, provided that the amino acid at position 26 of SEQ ID NO: 741 is not Cysteine (C), optionally wherein the amino acid at position 26 of SEQ ID NO: 741 is Alanine (A).

3. A method of transducing cells of a subject in vivo or treating a disease, disorder, or condition in a subject, the method comprising:

administering a biomaterial and a cell recruitment factor to a site (e.g., high subcutaneous space or subcutaneous space adjacent to dermis) in the subject, and

administering a viral vector or a nucleic acid comprising a transgene to the subject;

thereby transducing cells of the subject with the transgene.

4. The method of claim 3, wherein the biomaterial and the cell recruitment factor are comprised in a first composition, and the viral vector or nucleic acid is comprised in a second composition.

5. The plurality of compositions of claim 1, or the method of any one of claims 3-4, wherein the biomaterial:

(i) comprises a hydrogel;

(ii) comprises a cryogel, e.g., an alginate cryogel;

(iii) comprises a hyaluronic acid hydrogel (HA hydrogel);

(iv) comprises a gelatin, hyaluronic acid, collagen, alginate, laminin, chitosan, silk fibroin, agarose, poly(ethylene glycol), poly-vinyl alcohol, and/or hydroxyethyl methylacrylate;

(v) comprises alginate hydrogel, optionally wherein the alginate hydrogel further comprises norbornene and/or tetrazine, optionally wherein the norbornene and/or tetrazine is covalently associated with, e.g., chemically linked to, or non-covalently associated with, e.g., adsorbed on, the alginate; and/or

(vi) comprises pores between about 10 μm to about 300 μm, e.g., between about 50 μm to about 300 μm, in diameter, or no pores; and/or

(vii) is chemically crosslinked.

6. The plurality of compositions, the first composition, or the method of any one of the preceding claims, wherein the first composition comprising the biomaterial further comprises laponite; or wherein the biomaterial is comprised within a first composition that further comprises laponite; optionally wherein the laponite is present at a concentration of about 0.15 mg/mL to about 0.35 mg/mL, e.g., about 0.25 mg/mL.

7. The plurality of compositions, the first composition, or the method of any one of the preceding claims, wherein the cell recruitment factor is:

(i) noncovalently associated with, e.g., adsorbed on, the biomaterial; or

(ii) covalently associated with, e.g., conjugated to, the biomaterial.

8. The plurality of compositions, the first composition, or the method of any one of the preceding claims, wherein the cell recruitment factor:

(i) induces lymphangiogenesis;

(ii) induce growth of lymphatic endothelial cells; and/or

(ii) recruits immune cells, optionally wherein the immune cells comprise T-cells and/or NK-cells.

9. The plurality of compositions, the first composition, or the method of claim 8, wherein induction of lymphangiogenesis:

(i) comprises an increase in the level of lymphatic endothelial cells (LECs) (e.g., CD45-CD31+PDPN+ cells), optionally wherein the level of LECs is increased by at least 10%, 20%, 30%, 40%, 50%, 60, 70%, 75%, 80%, 85%, 90%, 95%, 100%, or 200% as compared to a reference level (e.g., the level of LECs at a site in a subject prior to injection of the plurality of compositions or the first composition), when measured by an assay, e.g., a flow cytometry assay, e.g., as described in Example H or I; and/or

(ii) results in at least 50 LECs (e.g., at least 75, 100, 125, 150, 200, 225, or 250 LECs) per milligram of tissue when measured by an assay, e.g., a flow cytometry assay, e.g., as described in Example H or I.

10. The plurality of compositions, the first composition, or the method of any one of the preceding claims, wherein the cell recruitment factor recruits T cells, optionally wherein the T cells comprise naïve T cells (e.g., CD45RA+CD62L+ T cells or CD45RA+CD62L+CCR7+CD27+CD95+ T cells).

11. The plurality of compositions, the first composition, or the method of claim 10, wherein recruitment of T cells comprises an increase in the level of T cells, optionally wherein the level of T cells is increased by at least 10%, 20%, 30%, 40%, 50%, 60, 70%, 75%, 80%, 85%, 90%, 95%, 100%, 200%, or 300% as compared to a reference level (e.g., the level of T cells at a site in a subject prior to injection of the plurality of compositions or the first composition), when measured by an assay, e.g., a flow cytometry assay, e.g., as described in Example H or I.

12. The plurality of compositions of any one of claims 1 or 5-11, or the method of any one of claims 3-11, wherein the cell recruitment factor is chosen from VEGF-C, IL-2, IL-7, IL-15 (e.g., hetIL-15 (IL15/sIL-15Ra)), GM-CSF, CXCL12, CXC3L1, CCL19, CCL21, CXCL10, or CXCL11.

13. The plurality of compositions of any one of claims 1 or 5-12, or the method of any one of claims 3-12, wherein the cell recruitment factor comprises VEGF-C, optionally wherein the VEGF-C:

(i) comprises a mature VEGF-C peptide, optionally the minor or major mature form or a mutated variant thereof;

(ii) is a monomer or dimer; and/or

(iii) is present in an effective amount, optionally, in an amount of less than or about 1 mg, less than or about 10 mg, greater than or about 10 μg, greater than or about 1 μg, between about 1 μg and 1 mg, between about 10 μg and 1 mg, between about 1 μg and 10 mg, or between about 10 μg and 10 mg.

14. The plurality of compositions or the method of claim 13, wherein the VEGF-C comprises:

(i) an amino acid sequence of any one of the sequences provided in Table 18 or a sequence with at least 95% sequence identity thereto, optionally wherein the sequence comprises or does not comprise a linker (e.g., a glycine-serine linker) and/or a his tag; and/or

(ii) the amino acid substitution of C137A, numbered according to SEQ ID NO: 725.

15. The plurality of compositions of any one of claims 1 or 5-14 or the method of any one of claims 3-14, wherein the cell recruitment factor comprises:

(i) an amino acid sequence according to SEQ ID NO: 741, or an amino acid sequence with at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto, provided that the amino acid at position 26 of SEQ ID NO: 741 is not Cysteine (C), optionally wherein the amino acid at position 26 of SEQ ID NO: 741 is Alanine (A);

(ii) the amino acid sequence according to SEQ ID NO: 743 or a sequence an amino acid sequence with at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto;

(iii) the amino acid sequence according to SEQ ID NO: 740 or an amino acid sequence with at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto;

(iv) the amino acid sequence according to SEQ ID NO: 736, or an amino acid sequence with at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto;

(v) a linker, e.g., wherein the linker has a sequence of Gly-Ser, wherein optionally the linker is C-terminal of SEQ ID NO: 743 or a sequence having at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto;

(vi) the amino acid sequence according to SEQ ID NO: 735, or an amino acid sequence with at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto;

(vii) the amino acid sequence according to SEQ ID NO: 734, or an amino acid sequence with at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto; and/or

(viii) the amino acid sequence according to SEQ ID NO: 733, or an amino acid sequence with at least 80%, 85%, 90%, 95%, or 99% sequence identity thereto.

16. The plurality of compositions of any one of claims 1 or 5-15 or the method of any one of claims 3-15, wherein the cell recruitment factor comprises VEGF-C or a functional variant thereof; IL-15 (e.g., hetIL-15 (IL15/sIL-15Ra)) or a functional variant thereof; IL-7 or a functional variant thereof; or a combination thereof.

17. The plurality of compositions of any one of claims 1 or 5-16, or the method of any one of claims 4-16, wherein the second composition further comprises a particle.

18. The plurality of compositions or the method of claim 17, wherein the particle is a mesoporous particle, a silica particle and/or a mesoporous silica particle, optionally wherein the mesoporous silica particle is a mesoporous silica rod.

19. A second composition comprising:

a mesoporous silica particle;

a viral vector; and

a cell activation agent.

20. The plurality of compositions or the method of claim 18, or the second composition of claim 19, wherein the mesoporous silica particle:

(i) comprises a surface modification, optionally wherein the surface modification comprises:

(a) a –OH (hydroxyl), amine, carboxylic acid, phosphonate, halide, azide, alkyne, epoxide, sulfhydryl, polyethyleneimine, a hydrophobic moiety, or salts thereof, optionally using a C_1 to C_{20} alkyl or $(-O(CH2-CH_2-)_{1-25}$ linker;

(b) a primary, secondary, tertiary, or quaternary amine; and/or

(c) a polyethyleneimine having an average molecular weight of about 1000 to 20,000 Da, about 1,200 to 15,000 Da, about 1,500 to 12,000 Da, about 2,000 Da, about 3,000 Da, about 4,000 Da, about 5,000 Da, about 6,000 Da, about 7,000 Da, about 8,000 Da, about 9,000 Da, or about 10,000 Da, as measured by gel permeation chromatography (GPC);

(ii) is a trimethylammonium functionalized mesoporous silica particle, e.g., a N,N,N-trimethylpropan-1-ammonium functionalized mesoporous silica particle;

(iii) comprises a plurality of pores, optionally wherein the pores are between 2-50 nm in diameter; and/or

(iv) comprises a surface area of at least about 100 m^2/g.

21. The plurality of compositions of any one of claims 1, 5-18, or 20, the second composition of claim 19 or 20, or the method of any one of claims 3-18 or 20, wherein:

(i) the viral vector is noncovalently, e.g., electrostatically, or covalently associated with the mesoporous silica particle; and/or

(ii) the cell activation agent is noncovalently or covalently associated with the mesoporous silica particle.

22. A method of transducing cells of a subject in vivo or treating a disease, disorder, or condition in a subject, the method comprising:

administering a viral vector or a nucleic acid comprising a transgene to a site in the subject,

wherein the subject has previously been administered a biomaterial and a cell recruitment factor in an amount sufficient to induce lymphangiogenesis and/or recruitment of T cells to the site in the subject;

thereby transducing the cells.

23. The method of claim 22, wherein the viral vector is noncovalently, e.g., electrostatically, or covalently associated with a particle, e.g., a mesoporous silica particle.

24. The plurality of compositions of any one of claims 1, 5-18, or 20-21, the second composition of any one of claims 19-21, or the method of any one of claims 3-18, or 20-23, wherein the viral vector comprises:

(i) a lentivirus, retrovirus, adenovirus, adeno-associated virus, or herpes virus; and/or

(ii) an expression vector comprising a recombinant polynucleotide comprising an expression control sequence operatively linked to a nucleotide sequence to be expressed.

25. The plurality of compositions, the second composition, or the method of claim 24, wherein the nucleotide sequence encodes: a chimeric antigen receptor (CAR), an engineered TCR, a cytokine, a chemokine, an shRNA, or a polypeptide engineered to target a tumor antigen.

26. The plurality of compositions, the second composition, or the method of claim 25, wherein the tumor antigen is selected from the group consisting of: TSHR, CD19, CD123, CD22, CD30, CD171, CS-1, CLL-1, CD33, EGFRvIII , GD2, GD3, BCMA, Tn Ag, PSMA, ROR1, FLT3, FAP, TAG72, CD38, CD44v6, CEA, EPCAM, B7H3, KIT, IL-13Ra2, Mesothelin, IL-11Ra, PSCA, PRSS21, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, CD20, Folate receptor alpha, ERBB2 (Her2/neu), MUC1, EGFR, NCAM, Prostase, PAP, ELF2M, Ephrin B2, IGF-I receptor, CAIX, LMP2, gp100, bcr-abl, tyrosinase, EphA2, Fucosyl GM1, sLe, GM3, TGS5, HMWMAA, o-acetyl-GD2, Folate receptor beta, TEM1/CD248, TEM7R, CLDN6, GPRC5D, CXORF61, CD97, CD179a, ALK, Polysialic acid, PLAC1, GloboH, NY-BR-1, UPK2, HAVCR1, ADRB3, PANX3, GPR20, LY6K, OR51E2, TARP, WT1, NY-ESO-1, LAGE-1a, MAGE-A1, legumain, HPV E6,E7, MAGE A1, ETV6-AML, sperm protein 17, XAGE1, Tie 2, MAD-CT-1, MAD-CT-2, Fos-related antigen 1, p53, p53 mutant, prostein, survivin and telomerase, PCTA-1/Galectin 8, MelanA/MART1, Ras mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, TRP-2, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP-4, SSX2, RAGE-1, human telomerase reverse transcriptase, RU1, RU2, intestinal carboxyl esterase, mut hsp70-2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3, FCRL5, IGLL1, and any combination thereof.

27. The plurality of compositions of any one of claims 1, 5-18, 20-21, or 24-26, the second composition of any one of claims 19-21 or 24-26, or the method of any one of claims 3-18 or 20-26, wherein the viral vector encodes a CAR that comprises an antigen binding domain, a transmembrane domain, a costimulatory signaling region, and a signaling domain, wherein:

(i) the antigen binding domain binds an antigen selected from the group consisting of CD19, CD123, CD22, CD20, EGFRvIII , BCMA, Mesothelin, CD33, CLL-1, and any combination thereof;

(ii) the transmembrane domain comprises a CD8 hinge;

(iii) the costimulatory signaling region is selected from a 4-1BB or CD28 costimulatory signaling domain; and/or

(iv) the signaling domain comprises a CD3 zeta signaling domain.

28. The plurality of compositions of any one of claims 1, 5-18, 20-21, or 24-27, or the method of any one of claims 4-18 or 20-27, wherein the second composition further comprises a cell activation agent.

29. The plurality of compositions or the method of claim 28, the second composition of any one of claims 19-21 or 24-27, wherein the cell activation agent:

(a) comprises an agent that stimulates CD3/TCR complex and/or an agent that stimulates a costimulatory molecule and/or growth factor receptor;

(b) is a multispecific binding molecule comprising: (i) an anti-CD3 binding domain, and (ii) a costimulatory molecule binding domain (e.g., an anti-CD2 binding domain or an anti-CD28 binding domain);

(c) the amino acid sequence of any heavy chain provided in Table 20, or an amino acid sequence with at least 95% sequence identity thereto; and/or the amino acid sequence of any light chain provided in Table 20, or an amino acid sequence with at least 95% sequence identity thereto; and/or

(d) is conjugated to or adsorbed on the particle, e.g., mesoporous silica particle.

30. The plurality of compositions, the method, or the second composition of claim 29, wherein:

(i) the anti-CD3 binding domain, e.g., an anti-CD3 scFv, is situated N-terminal of the costimulatory molecule binding domain, e.g., an anti-CD2 Fab or an anti-CD28 Fab; or

(ii) the anti-CD3 binding domain, e.g., an anti-CD3 scFv, is situated C-terminal of the costimulatory molecule binding domain, e.g., an anti-CD2 Fab or an anti-CD28 Fab, optionally wherein:

an Fc region is situated between the anti-CD3 binding domain and the costimulatory molecule binding domain; or

the multispecific binding molecule comprises a CH2, and the anti-CD3 binding domain is situated N-terminal of the CH2.

31. The plurality of compositions, the method, or the second composition of claim 29 or 30, wherein the multispecific binding molecule comprises:

(i) a first polypeptide comprising from N-terminal to C-terminal: VH of the anti-CD3 binding domain, VL of the anti-CD3 binding domain, VH of the costimulatory molecule binding domain, CH1, CH2, and CH3; and

(ii) a second polypeptide comprising from N-terminal to C-terminal: VL of the costimulatory molecule binding domain and CL.

32. The plurality of compositions, the method, or the second composition of claim 29 or 30, wherein the multispecific binding molecule comprises:

(i) a first polypeptide comprising from N-terminal to C-terminal: VH of the costimulatory molecule binding domain, CH1, CH2, CH3, VH of the anti-CD3 binding domain, and VL of the anti-CD3 binding domain; and

(ii) a second polypeptide comprising from N-terminal to C-terminal: VL of the costimulatory molecule binding domain and CL.

33. The plurality of compositions, the method, or the second composition of claim 29 or 30, wherein the multispecific binding molecule comprises:

(i) a first polypeptide comprising from N-terminal to C-terminal: VH of the costimulatory molecule binding domain, CH1, VH of the anti-CD3 binding domain, VL of the anti-CD3 binding domain, CH2, and CH3; and

(ii) a second polypeptide comprising from N-terminal to C-terminal: VL of the costimulatory molecule binding domain and CL.

34. The plurality of compositions, the method, or the second composition of claim 29 or 30, wherein the multispecific binding molecule comprises an Fc region comprising:

(i) a L234A, L235A, S267K, and P329A mutation (LALASKPA), numbered according to the Eu numbering system;

(ii) a L234A, L235A, and P329G mutation (LALAPG), numbered according to the Eu numbering system;

(iii) a G237A, D265A, P329A, and S267K mutation (GADAPASK), numbered according to the Eu numbering system;

(iv) a L234A, L235A, and G237A mutation (LALAGA), numbered according to the Eu numbering system;

(v) a D265A, P329A, and S267K mutation (DAPASK), numbered according to the Eu numbering system;

(vi) a G237A, D265A, and P329A mutation (GADAPA), numbered according to the Eu numbering system;

(vii) a L234A, L235A, and P329A mutation (LALAPA), numbered according to the Eu numbering system; or

(viii) an amino acid sequence of any of the Fc regions in Table 20 or an amino acid sequence having at least 95% identity thereto.

35. The plurality of compositions, the method, or the second composition of claim 29, 30, or 34, wherein the multispecific binding molecule comprises:

(i) a heavy chain comprising the amino acid sequence of any of SEQ ID NOs: 726, 893, or 895, or an amino acid sequence having at least 95% sequence identity thereto; and/or

(ii) a light chain comprising the amino acid sequence of any of SEQ ID NOs: 728, 730, 892, or 894, or an amino acid sequence having at least 95% sequence identity thereto.

36. The plurality of compositions, the method, or the second composition of any one of claims 29, 30, or 34-35, wherein the multispecific binding molecule comprises:

(i) a heavy chain comprising the amino acid sequence of SEQ ID NO: 726 or an amino acid sequence having at least 95% sequence identity thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 728, or an amino acid sequence having at least 95% sequence identity thereto;

(ii) a heavy chain comprising the amino acid sequence of SEQ ID NO: 726 or an amino acid sequence having at least 95% sequence identity thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 730, or an amino acid sequence having at least 95% sequence identity thereto;

(iii) a heavy chain comprising the amino acid sequence of SEQ ID NO: 1416 or an amino acid sequence having at least 95% sequence identity thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 728, or an amino acid sequence having at least 95% sequence identity thereto;

(iv) a heavy chain comprising the amino acid sequence of SEQ ID NO: 1416 or an amino acid sequence having at least 95% sequence identity thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 730, or an amino acid sequence having at least 95% sequence identity thereto;

(v) a heavy chain comprising the amino acid sequence of SEQ ID NO: 893 or an amino acid sequence having at least 95% sequence identity thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 892, or an amino acid sequence having at least 95% sequence identity thereto;

(vi) a heavy chain comprising the amino acid sequence of SEQ ID NO: 1417 or an amino acid sequence having at least 95% sequence identity thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 892, or an amino acid sequence having at least 95% sequence identity thereto; or

(vii) a heavy chain comprising the amino acid sequence of SEQ ID NO: 895 or an amino acid sequence having at least 95% sequence identity thereto, and a light chain comprising the amino acid sequence of SEQ ID NO: 894, or an amino acid sequence having at least 95% sequence identity thereto.

37. The plurality of compositions of any one of claims 1, 5-18, 20-21, or 24-36, or the method of any one of claims 4-18 or 20-36, wherein the second composition further comprises a first population of particles and a second population of particles, e.g., a first population of mesoporous silica particles and a second population of mesoporous silica particles, wherein the first population comprises the viral vector and the second population comprises a cell activation agent, e.g., wherein the viral vector is noncovalently associated with a particle of the first population and the cell activation agent is noncovalently associated with a particle of the second population.

38. The plurality of compositions of any one of claims 1, 5-18, 20-21, or 24-37, the first composition of any one of claims 2, or 6-11, or the second composition of any one of claims 19-21, 24-27, or 29-36, wherein the first or second composition is suitable for injectable use.

39. The plurality of compositions of any one of claims 1, 5-18, 20-21, or 24-38, the first composition of any one of claims 2, 6-11, or 38, or the second composition of any one of claims 19-21, 24-27, 29-36, or 38, which further comprises:

(i) a Tet2 inhibitor, optionally wherein the Tet2 inhibitor comprises: (1) a gene editing system targeted to one or more sites within the gene encoding Tet2, or its corresponding regulatory elements; (2) a nucleic acid (e.g., an siRNA or shRNA) that inhibits expression of Tet2; (3) a protein (e.g., a dominant negative, e.g., catalytically inactive) Tet2, or a binding partner of Tet2 (e.g., a dominant negative binding partner of Tet2); (4) a small molecule that inhibits expression and/or function of Tet2; (5) a nucleic acid encoding any of (1)-(3); or (6) any combination of (1) –(5); and/or

(ii) a ZBTB32 inhibitor, optionally wherein the ZBTB32 inhibitor comprises: (1) a gene editing system targeting the ZBTB32 gene or one or more components thereof; (2) a nucleic acid encoding one or more components of the gene editing system; or (3) a combination of (1) and (2). In an embodiment, the ZBTB32 inhibitor comprises: (1) a gene editing system targeting the ZBTB32 gene or one or more components thereof. In an embodiment, the ZBTB32 inhibitor comprises (2) a nucleic acid encoding one or more components of the gene editing system. In an embodiment, the ZBTB32 inhibitor comprises a combination of (1) and (2).

40. The method of any one of claims 3-18 or 20-37, which further comprises administering to the subject:

(i) a Tet2 inhibitor, optionally wherein the Tet2 inhibitor comprises: (1) a gene editing system targeted to one or more sites within the gene encoding Tet2, or its corresponding regulatory elements; (2) a nucleic acid (e.g., an siRNA or shRNA) that inhibits expression of Tet2; (3) a protein (e.g., a dominant negative, e.g., catalytically inactive) Tet2, or a binding partner of Tet2 (e.g., a dominant negative binding partner of Tet2); (4) a small molecule that inhibits expression and/or function of Tet2; (5) a nucleic acid encoding any of (1)-(3); or (6) any combination of (1) –(5); and/or

(ii) a ZBTB32 inhibitor, optionally wherein the ZBTB32 inhibitor comprises: (1) a gene editing system targeting the ZBTB32 gene or one or more components thereof; (2) a nucleic acid encoding one or more components of the gene editing system; or (3) a combination of (1) and (2). In an embodiment, the ZBTB32 inhibitor comprises: (1) a gene editing system targeting the ZBTB32 gene or one or more components thereof. In an embodiment, the ZBTB32 inhibitor comprises (2) a nucleic acid encoding one or more components of the gene editing system. In an embodiment, the ZBTB32 inhibitor comprises a combination of (1) and (2).

41. A method of transducing cells of a subject *in vivo* or treating a disease, disorder, or condition in a subject, comprising administering the first composition and the second composition of the plurality of compositions of any one of claims 1, 5-18, 20-21, or 24-39.

42. A method of transducing cells of a subject *in vivo* or treating a disease, disorder, or condition in a subject, comprising administering the first composition of any one of claims 2, 6-11, 38, or 39, and the second composition of any one of claims 19-21, 24-27, 29-36, or 38.

43. The method of any one of claims 3-18, 20-21, 24-37, or 40-42, wherein the first composition and the second composition are administered sequentially.

44. The method of any one of claims 3-18, 20-21, 24-37, or 40-43, wherein the first composition is administered prior to the administration of the second composition, optionally wherein:

(i) the first composition is administered about 1-4 weeks, e.g., about 2 weeks, prior to the administration of the second composition; or

(ii) the first composition is administered at least two weeks prior to the administration of the second composition.

45. The method of any one of claims 3-18, 20-21, 24-37, or 40-44, further comprising evaluating, e.g., measuring, lymphangiogenesis in a sample from the subject (e.g., a sample from or close to the site of administration), wherein lymphangiogenesis is measured after the administration of the first composition and/or prior to the administration of the second composition,

optionally wherein measuring lymphangiogenesis comprises acquiring a value for the level and/or activity of lymphatic endothelial cells (LECs) (e.g., CD45-CD31+PDPN+ cells) in the sample.

46. The method of any one of claims 3-18, 20-21, 24-37, or 40-45, further comprising evaluating, e.g., measuring, the recruitment of T cells in a sample from the subject (e.g., a sample from or close to the site of administration), wherein the recruitment of T cells is measured after the administration of the first composition and/or prior to the administration of the second composition,

optionally wherein measuring the recruitment of T cells comprises acquiring a value for the level and/or activity of T cells (e.g., naïve T cells, e.g., CD45RA+CD62L+ T cells and/or CD45RA+CD62L+CCR7+CD27+CD95+ T cells) in the sample.

47. The plurality of compositions of any one of claims 1, 5-18, 20-21, or 24-39 for use in a method of transducing cells of a subject *in vivo* or treating a disease, disorder, or condition in a subject.

48. The first composition of any one of claims 2, 6-11, 38, or 39, in combination with the second composition of any one of claims 19-21, 24-27, 29-36, or 38 for use in a method of transducing cells of a subject *in vivo* or treating a disease, disorder, or condition in a subject.

49. The second composition of any one of claims 19-21, 24-27, 29-36, or 38, in combination with the first composition of any one of claims 2, 6-11, 38, or 39, for use in a method of transducing cells of a subject *in vivo* or treating a disease, disorder, or condition in a subject.

50. The method of any one of claims 3-18, 20-37, or 40-46, wherein:

(i) the subject has or has been diagnosed with having a disease, disorder, or condition; and/or

(ii) the subject is a human.

51. The method of any one of claims 3-18, 20-37, 40-46, or 50, wherein the disease, disorder, or condition comprises:

(i) a cancer;

(ii) a hematological cancer, optionally wherein the hematological cancer comprises a leukemia or lymphoma;

(iii) a hematological cancer chosen from chronic lymphocytic leukemia (CLL), mantle cell lymphoma (MCL), multiple myeloma, acute lymphoid leukemia (ALL), Hodgkin lymphoma, B-cell acute lymphoid leukemia (BALL), T-cell acute lymphoid leukemia (TALL), small lymphocytic leukemia (SLL), B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt lymphoma, diffuse large B cell lymphoma (DLBCL), DLBCL associated with chronic inflammation, chronic myeloid leukemia, myeloproliferative neoplasms, follicular lymphoma, pediatric follicular lymphoma, hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma (extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue), Marginal zone lymphoma, myelodysplasia, myelodysplastic syndrome, non-Hodgkin lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, splenic marginal zone lymphoma, splenic lymphoma/leukemia, splenic diffuse red pulp small B-cell lymphoma, hairy cell leukemia-variant, lymphoplasmacytic lymphoma, a heavy chain disease, plasma cell myeloma, solitary plasmocytoma of bone, extraosseous plasmocytoma, nodal marginal zone lymphoma, pediatric nodal marginal zone lymphoma, primary cutaneous follicle center lymphoma, lymphomatoid granulomatosis, primary mediastinal (thymic) large B-cell lymphoma, intravascular large B-cell lymphoma, ALK+ large B-cell lymphoma, large B-cell

lymphoma arising in HHV8-associated multicentric Castleman disease, primary effusion lymphoma, B-cell lymphoma, acute myeloid leukemia (AML), or unclassifiable lymphoma;

(iv) a solid cancer; or

(v) a solid cancer chosen from: one or more of mesothelioma, malignant pleural mesothelioma, non-small cell lung cancer, small cell lung cancer, squamous cell lung cancer, large cell lung cancer, pancreatic cancer, pancreatic ductal adenocarcinoma, esophageal adenocarcinoma , breast cancer, glioblastoma, ovarian cancer, colorectal cancer, prostate cancer, cervical cancer, skin cancer, melanoma, renal cancer, liver cancer, brain cancer, thymoma, sarcoma, carcinoma, uterine cancer, kidney cancer, gastrointestinal cancer, urothelial cancer, pharynx cancer, head and neck cancer, rectal cancer, esophagus cancer, or bladder cancer, or a metastasis thereof;

(vi) an autoimmune disease, optionally wherein the viral vector or nucleic acid encodes a CAR that binds to a B cell antigen, e.g., CD 19, CD20, CD22, CD123, FcRn5, FcRn2, BCMA, CS-1 and CD138.

52. A kit comprising the first composition and the second composition of the plurality of compositions of any one of claims 1, 5-18, 20-21, or 24-39.

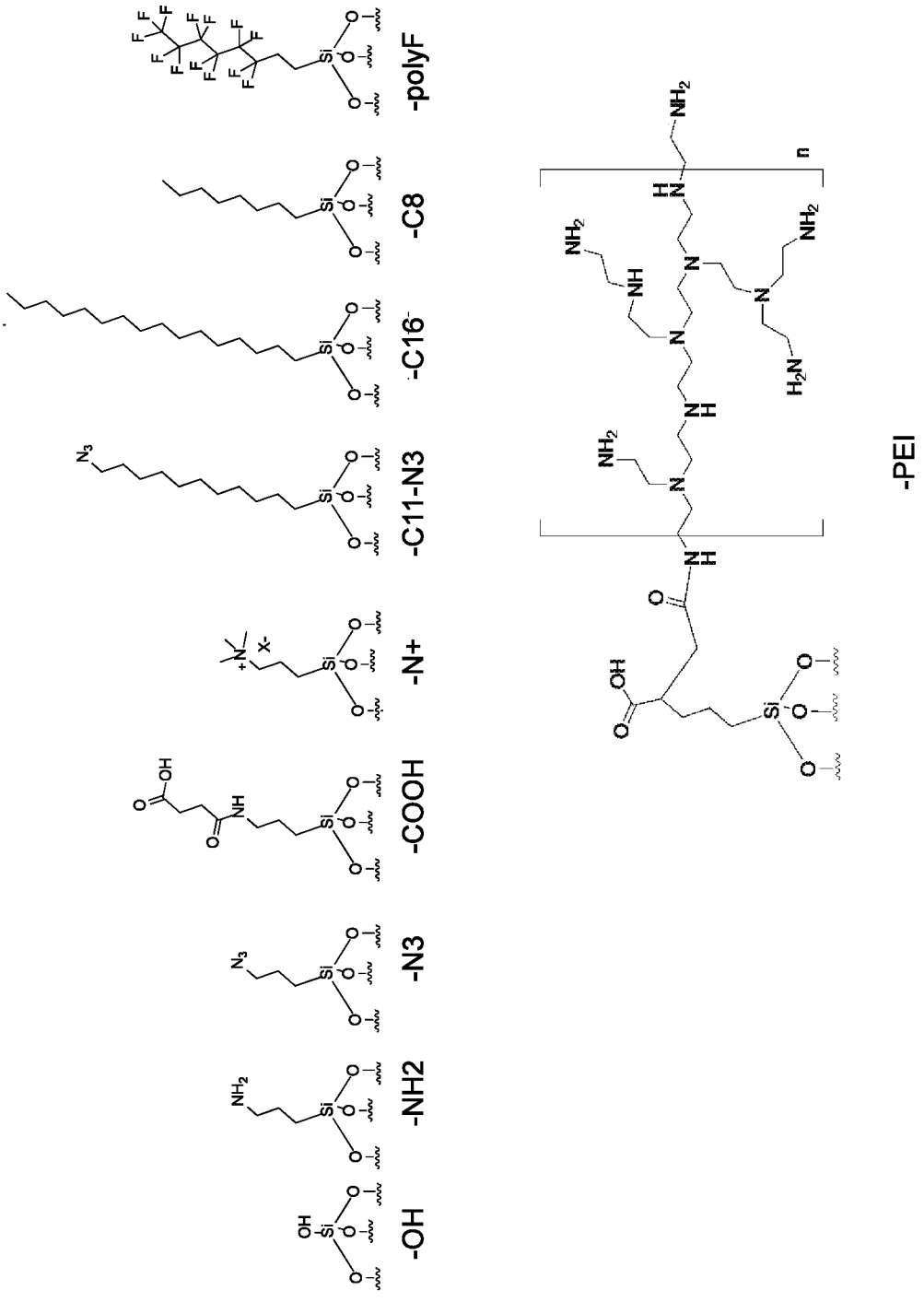
53. The plurality of compositions of any one of claims 1, 5-18, 20-21, or 24-39, the method of any one of claims 3-18, 20-37, 40-46, or 50-51, or the second composition of any one of claims 19-21, 24-27, 29-36, or 38, wherein the viral vector or the nucleic acid encodes:

(i) a first CAR that binds to a B cell antigen and a second CAR that binds to (a) a solid tumor antigen, (b) a myeloid tumor antigen, or (c) an antigen of a hematological tumor not of B-cell lineage; or

(2) a CAR that comprises a first binding domain that binds to a B cell antigen and a second binding domain that binds to (a) a solid tumor antigen, (b) a myeloid tumor antigen, or (c) an antigen of a hematological tumor not of B-cell lineage.

54. The method of claim 53, wherein the disease, disorder, or condition is a solid tumor.

FIG. 1



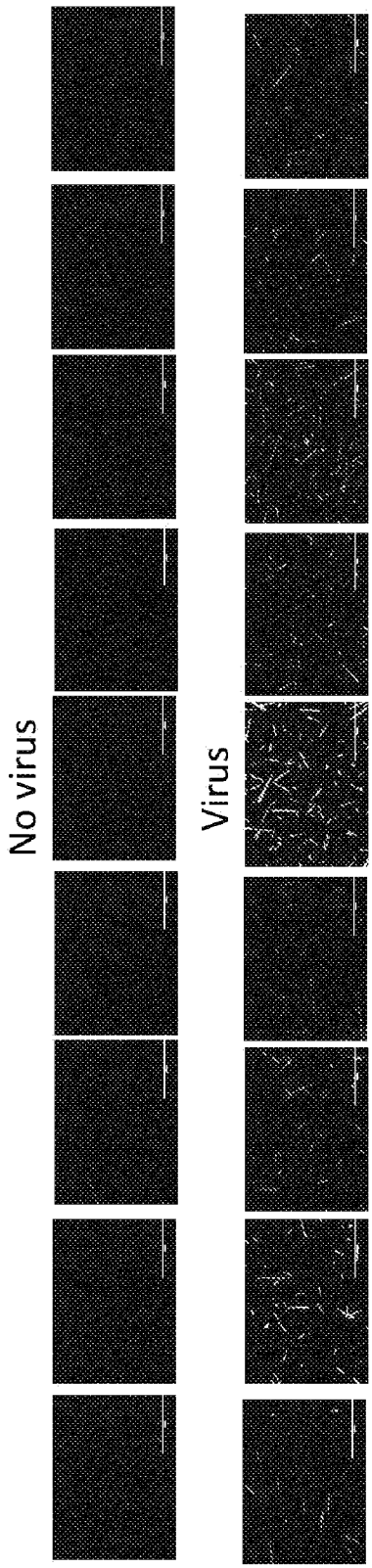


FIG. 2

FIG. 3

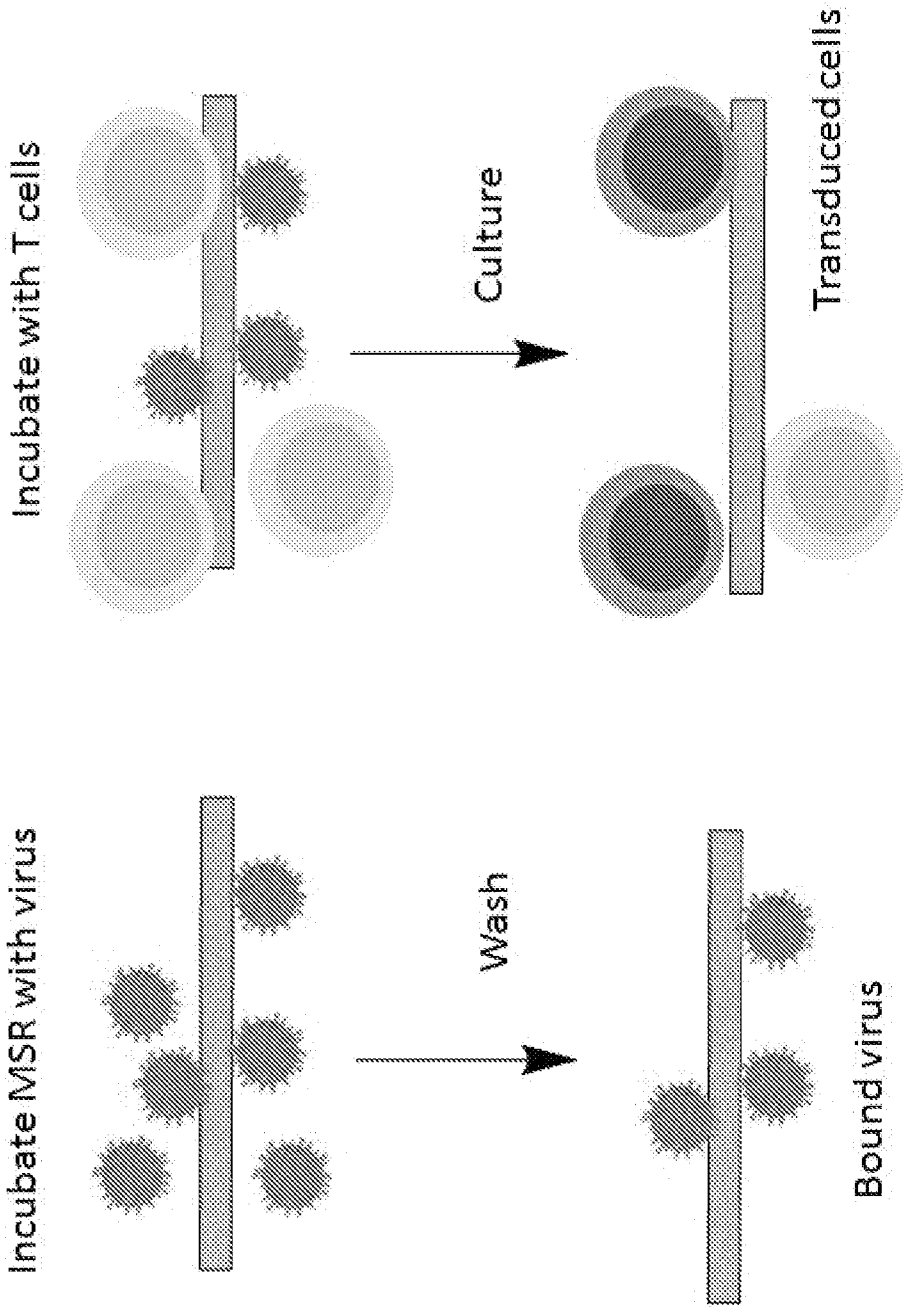

Incubate MSR with virus
Wash
Bound virus
Incubate with T cells
Culture
Transduced cells

FIG. 4

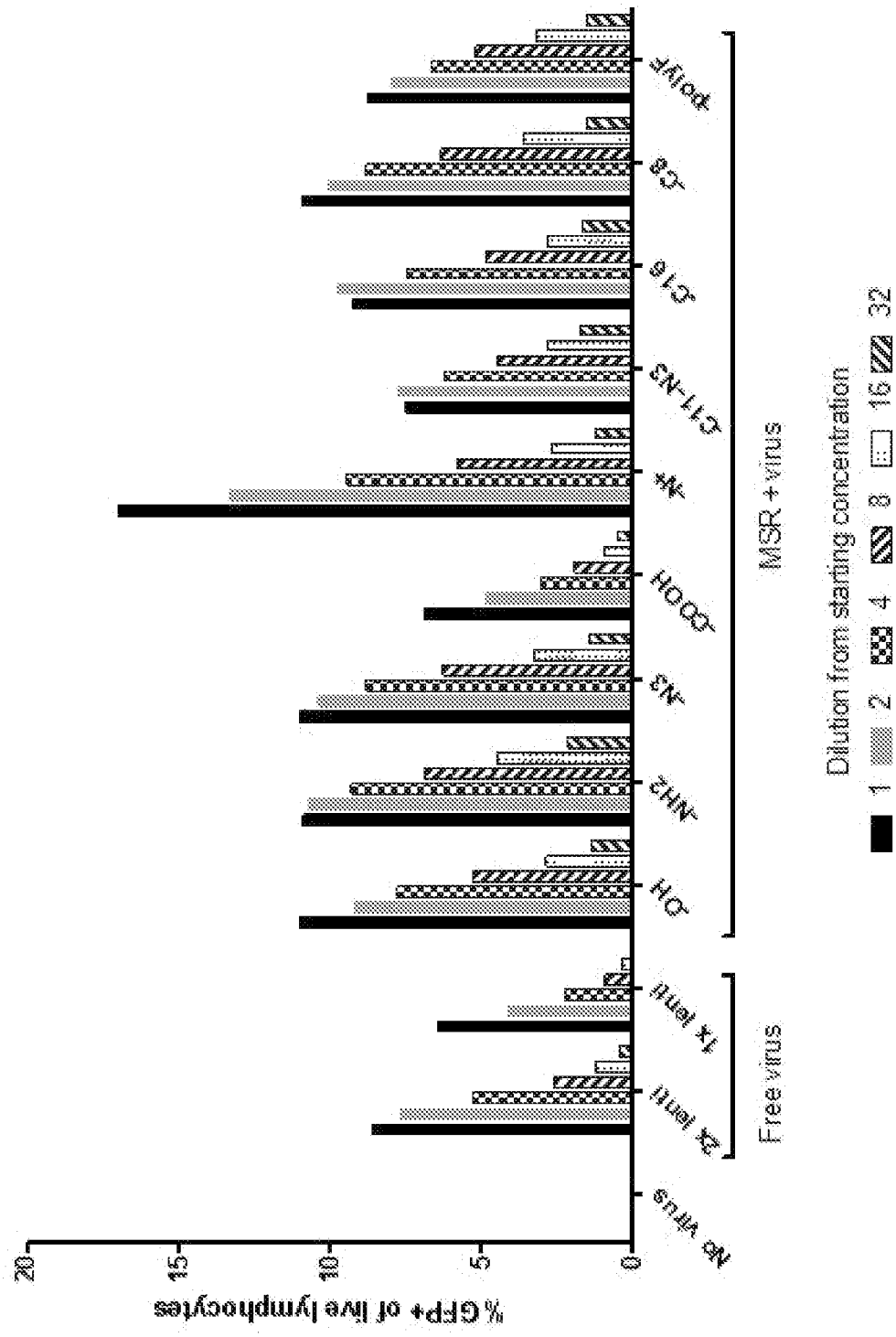
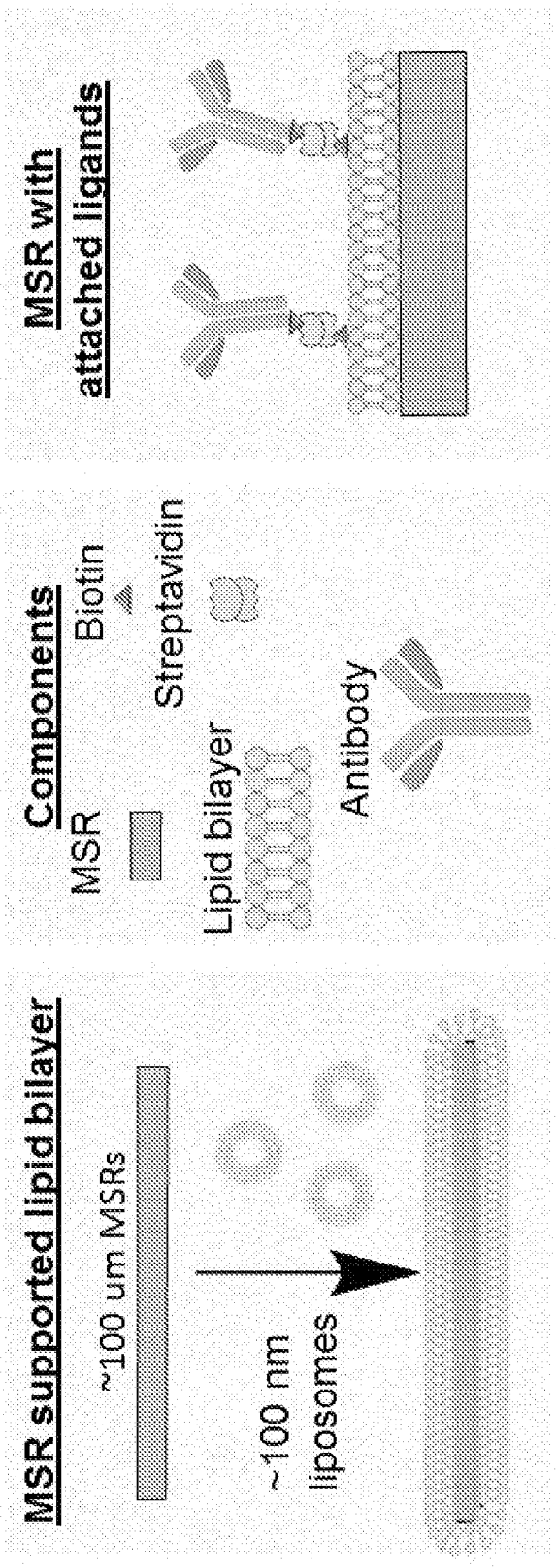

% GFP+ of live lymphocyte
% GFP+ of live lymphocytes
20
15
10
5
0
No virus
2x lentiviral
1x lentiviral
OH
NH2
N3
COOH
NH
C11-N3
C16
C8
polyF
Free virus
MSR + virus
Dilution from starting concentration
1
2
4
8
16
32

FIG. 5


MSR supported lipid bilayer
~100 um MSRs
~100 nm liposomes
Components
MSR
Biotin
Streptavidin
Lipid bilayer
Antibody
MSR with attached ligands

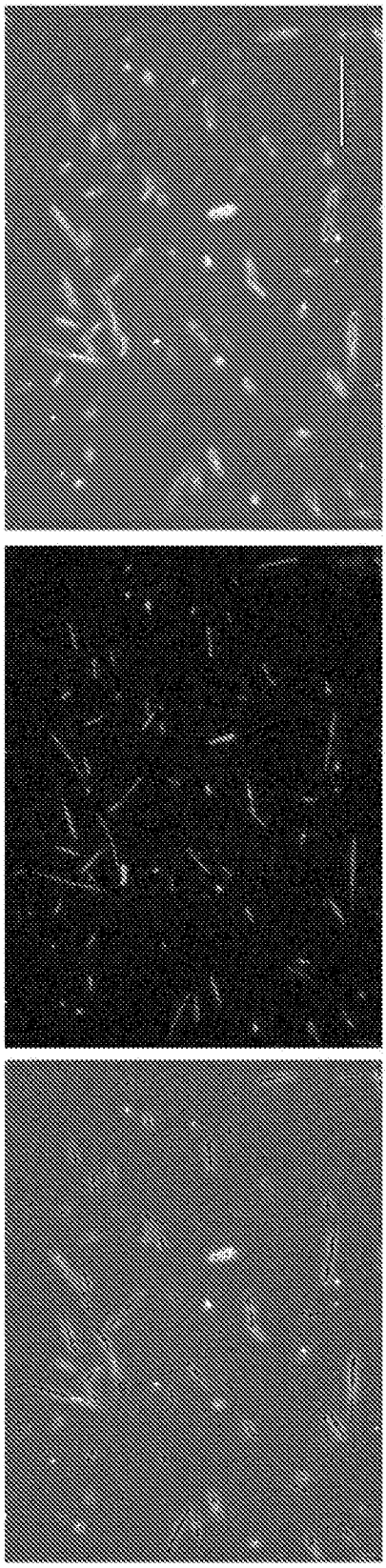


FIG. 6

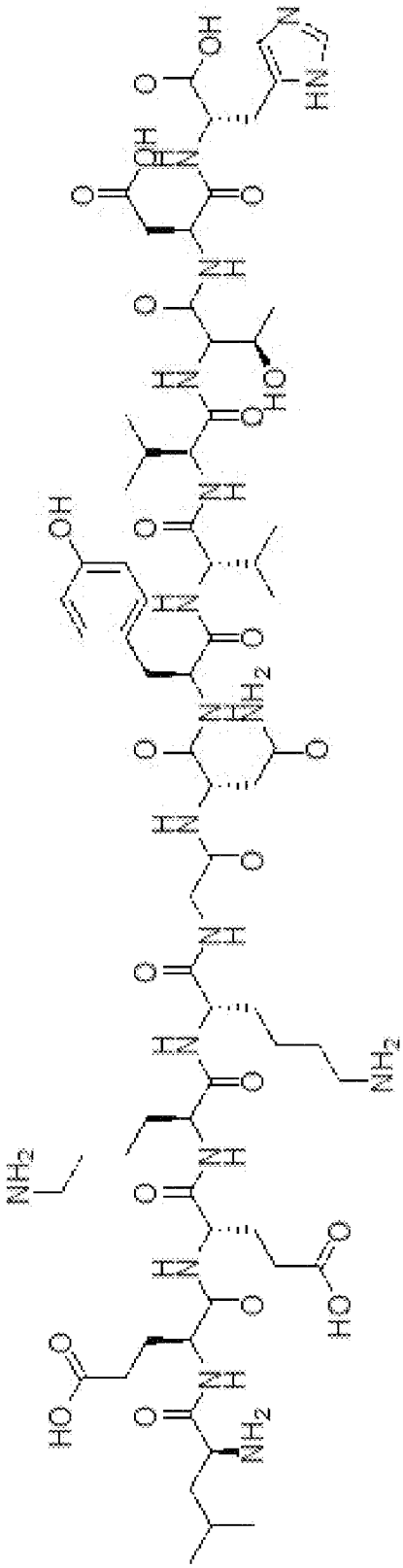


FIG. 7

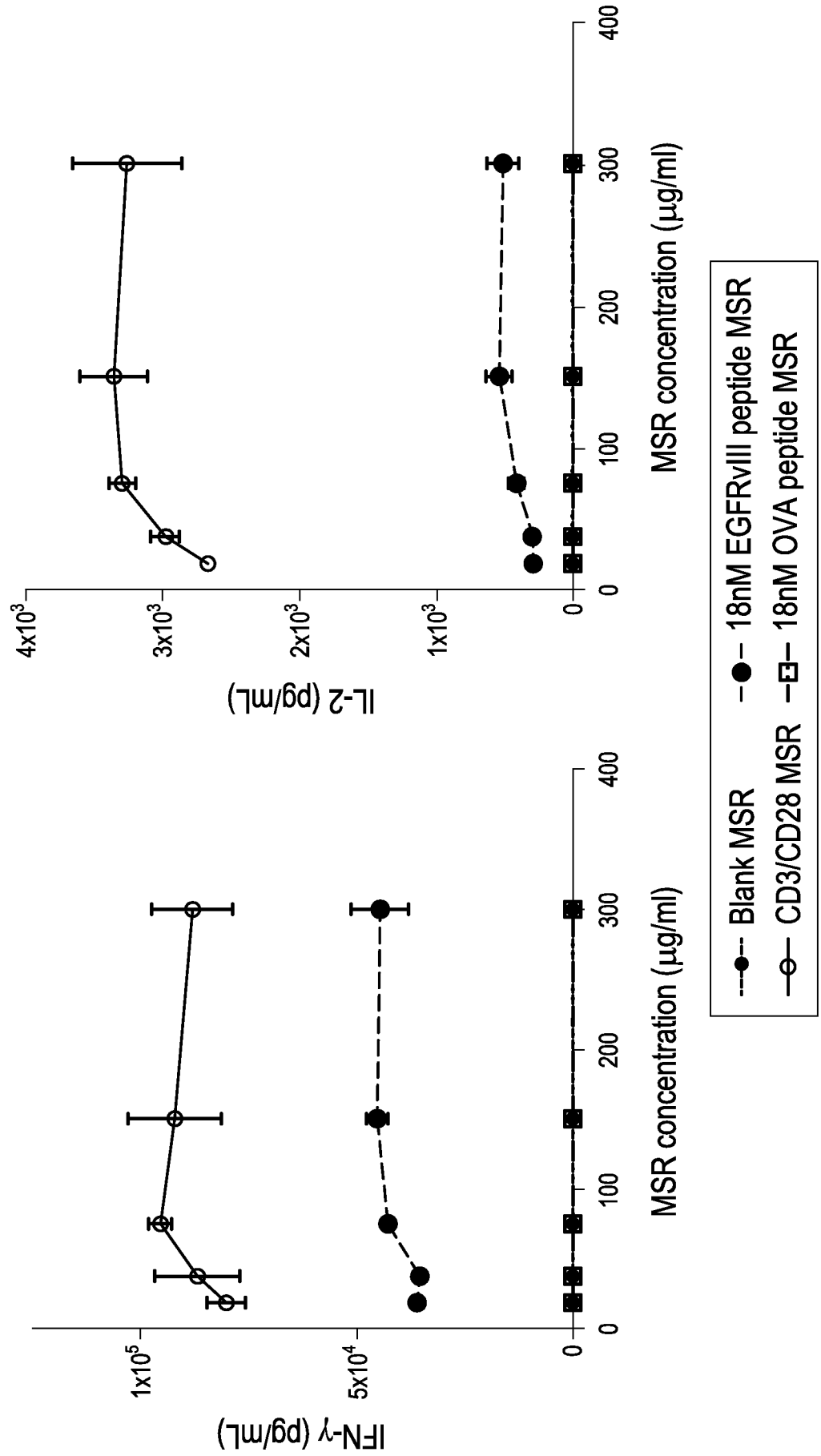

IL-2 (pg/mL)
4x10^3
3x10^3
2x10^3
1x10^3
0
100
200
300
400
MSR concentration (µg/ml)
IFN-γ (pg/mL)
1x10^5
5x10^4
0
100
200
300
400
MSR concentration (µg/ml)
Blank MSR
18nM EGFRvIII peptide MSR
CD3/CD28 MSR
18nM OVA peptide MSR

FIG. 8

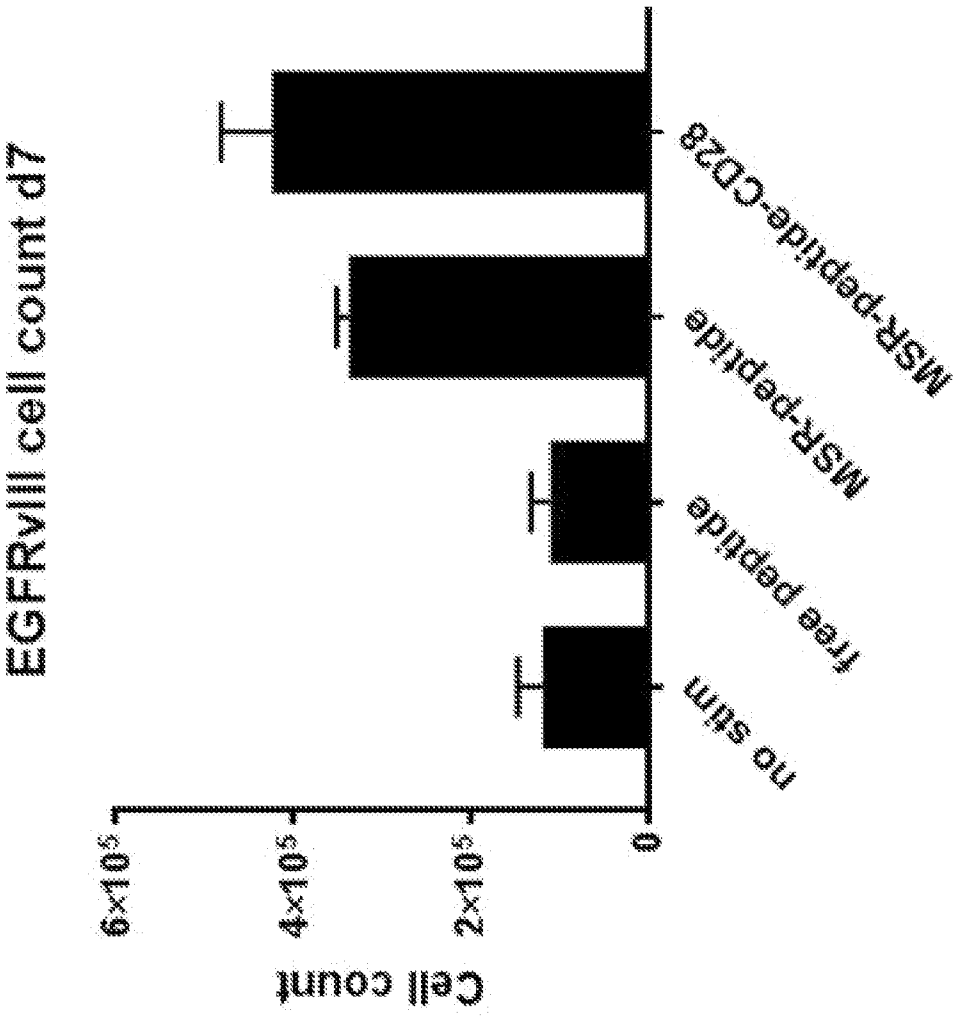
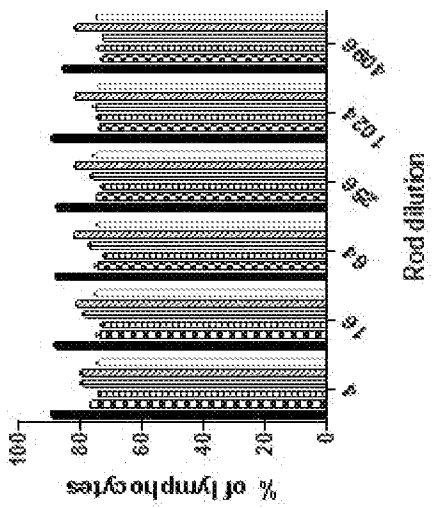

EGFRvIII cell count d7
Cell count
6x10^5
4x10^5
2x10^5
0
no stim
free peptide
MSR-peptide
MSR-peptide-CD28

FIG. 9

FIG. 10A



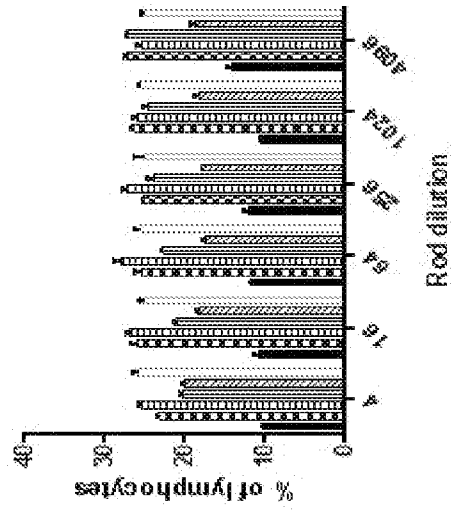
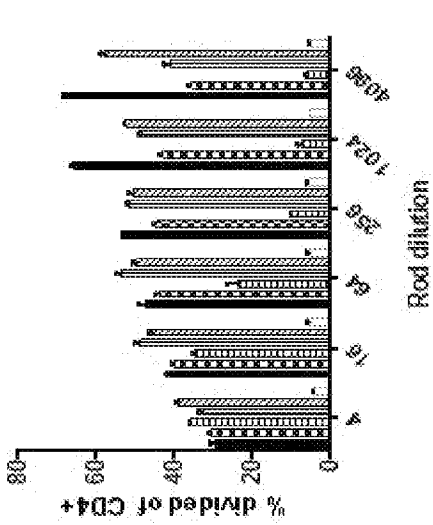
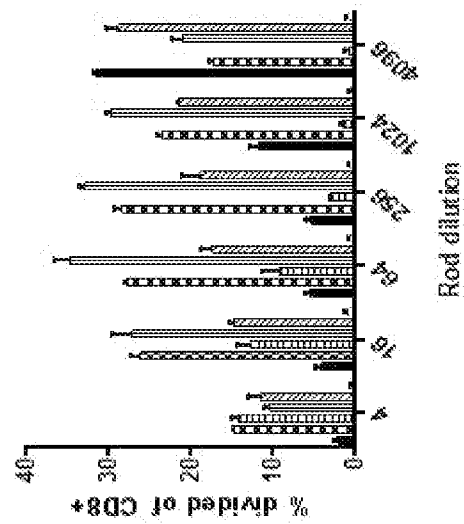


FIG. 10B





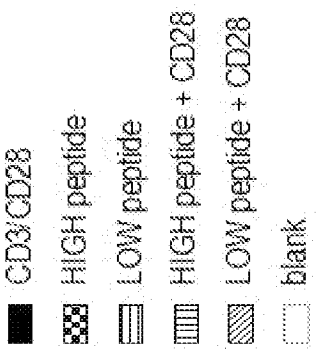
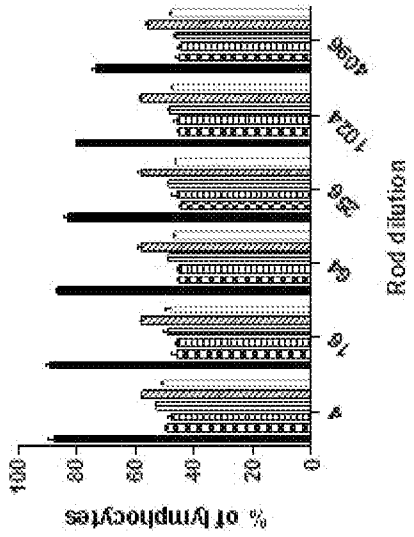


FIG. 11A



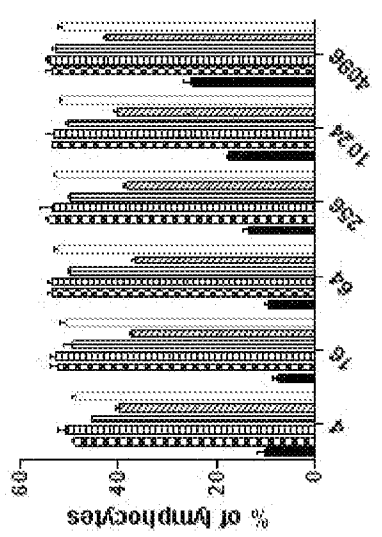
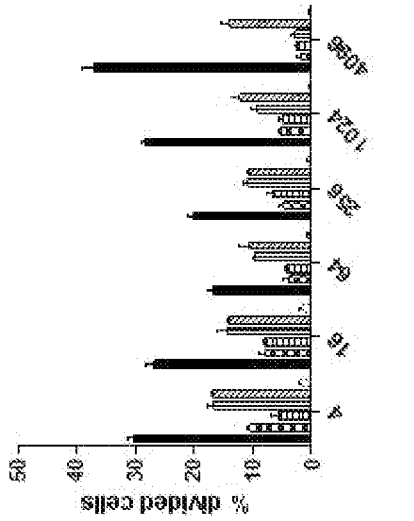
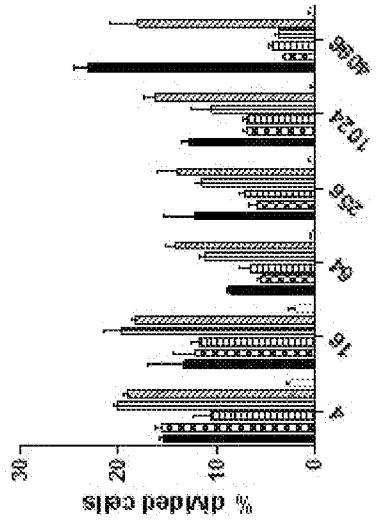
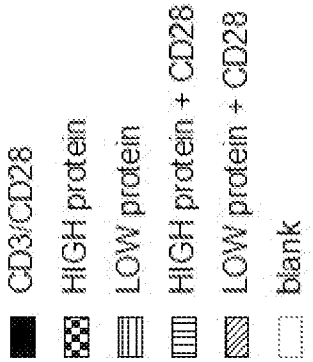


FIG. 11B







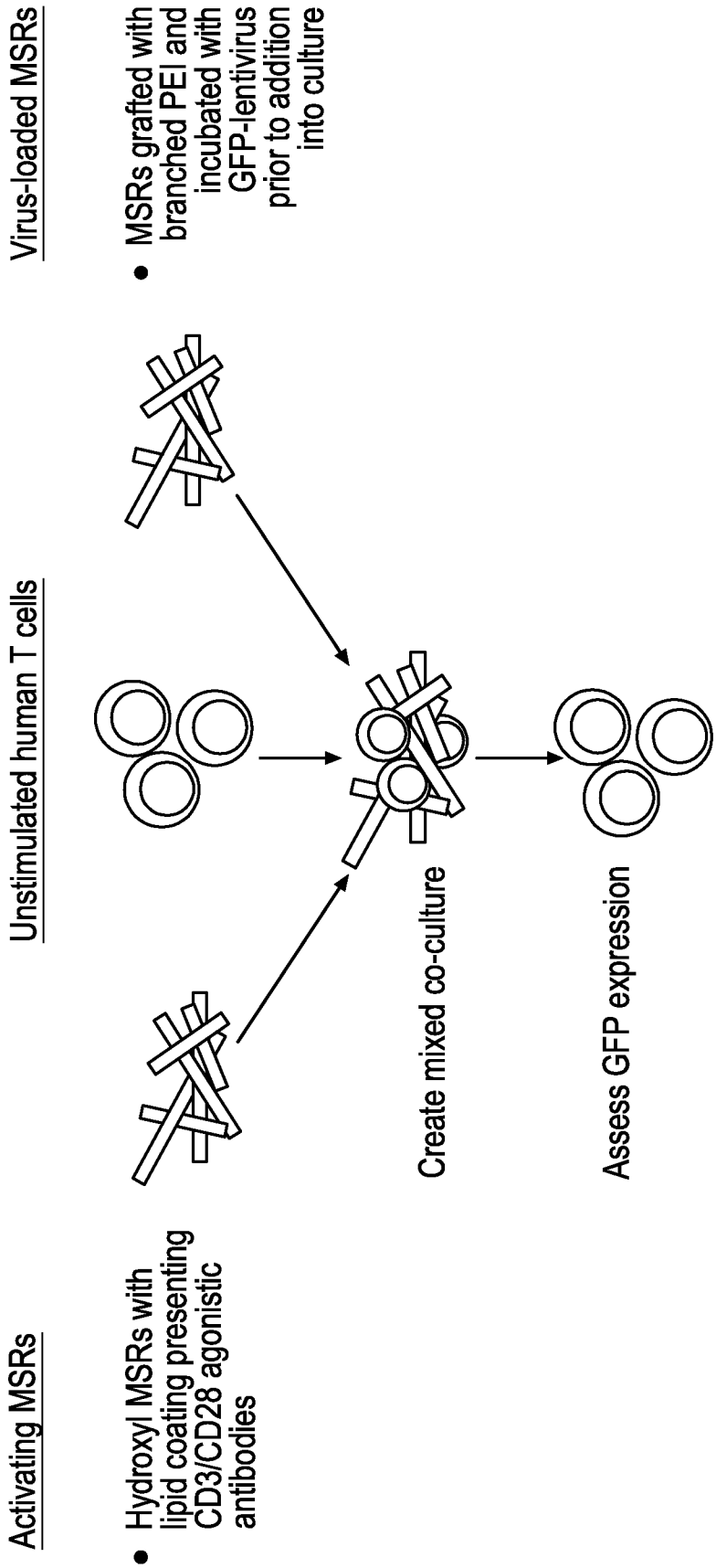

Activating MSRs
• Hydroxyl MSRs with lipid coating presenting CD3/CD28 agonistic antibodies
Unstimulated human T cells
Virus-loaded MSRs
• MSRs grafted with branched PEI and incubated with GFP-lentivirus prior to addition into culture
Create mixed co-culture
Assess GFP expression

FIG. 12

FIG. 13

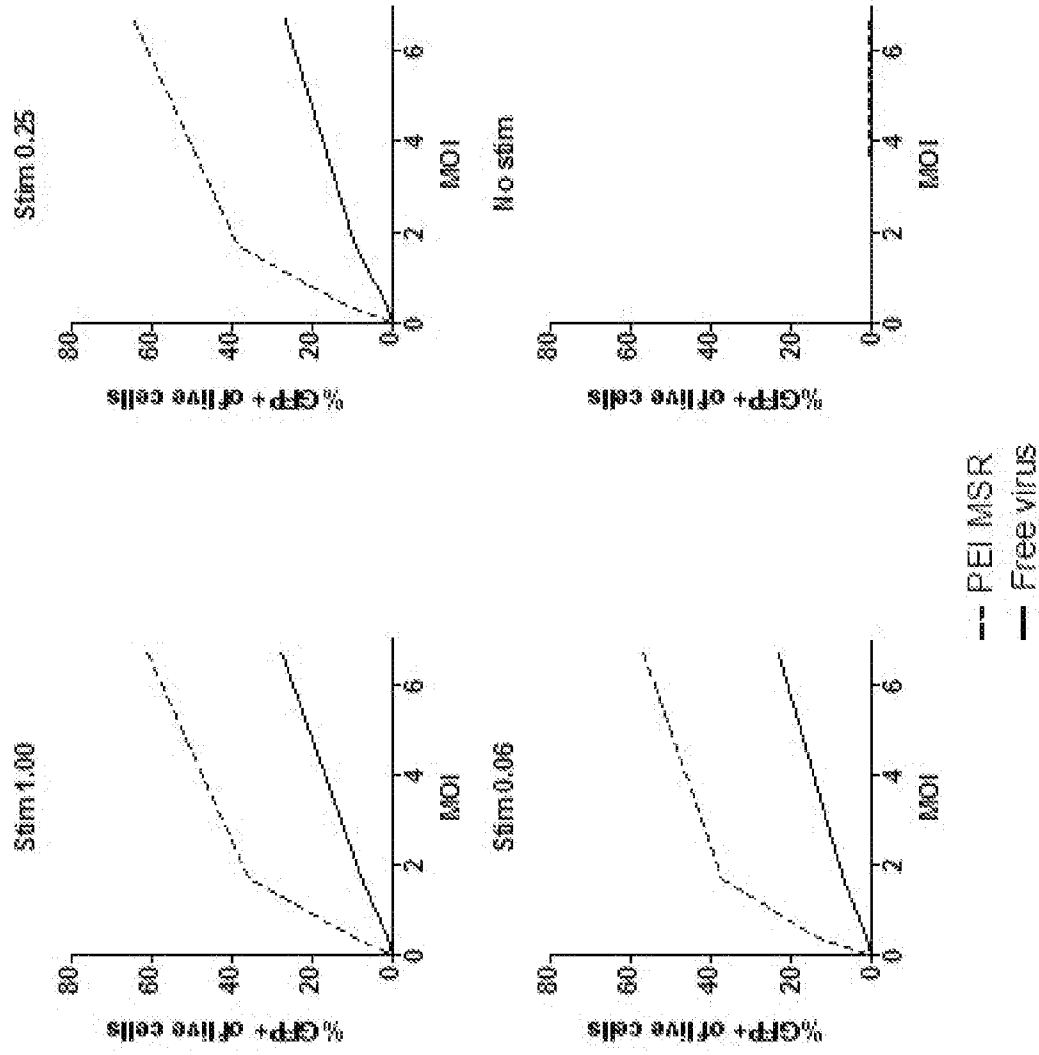
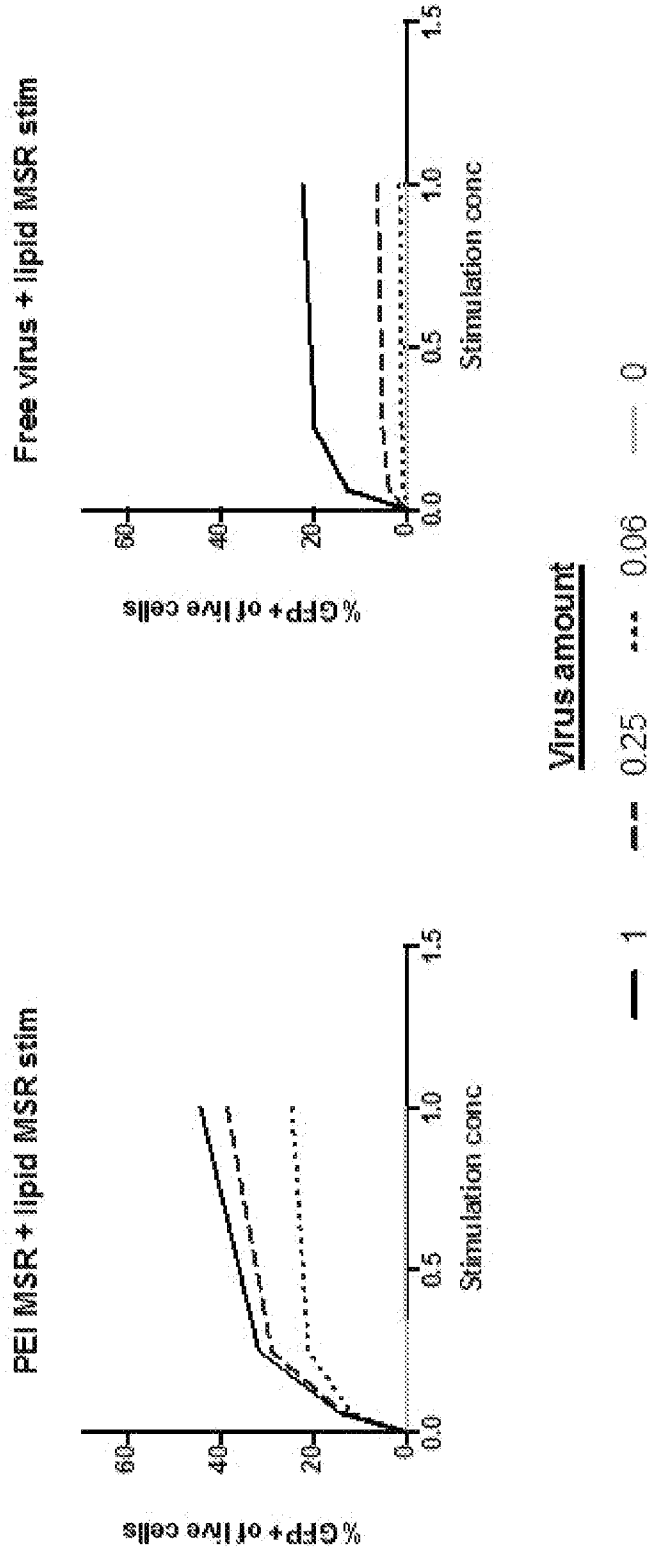

Stim 0.25
No stim
Stim 1.00
Stim 0.06
% GFP+ of live cells
MOI
0
20
40
60
80
0
2
4
6
PEI MSR
Free virus

FIG. 14


PEI MSR + lipid MSR stim
Free virus + lipid MSR stim
% GFP+ of live cells
Stimulation conc
0
20
40
60
0.0
0.5
1.0
1.5
Virus amount
1
0.25
0.06
0

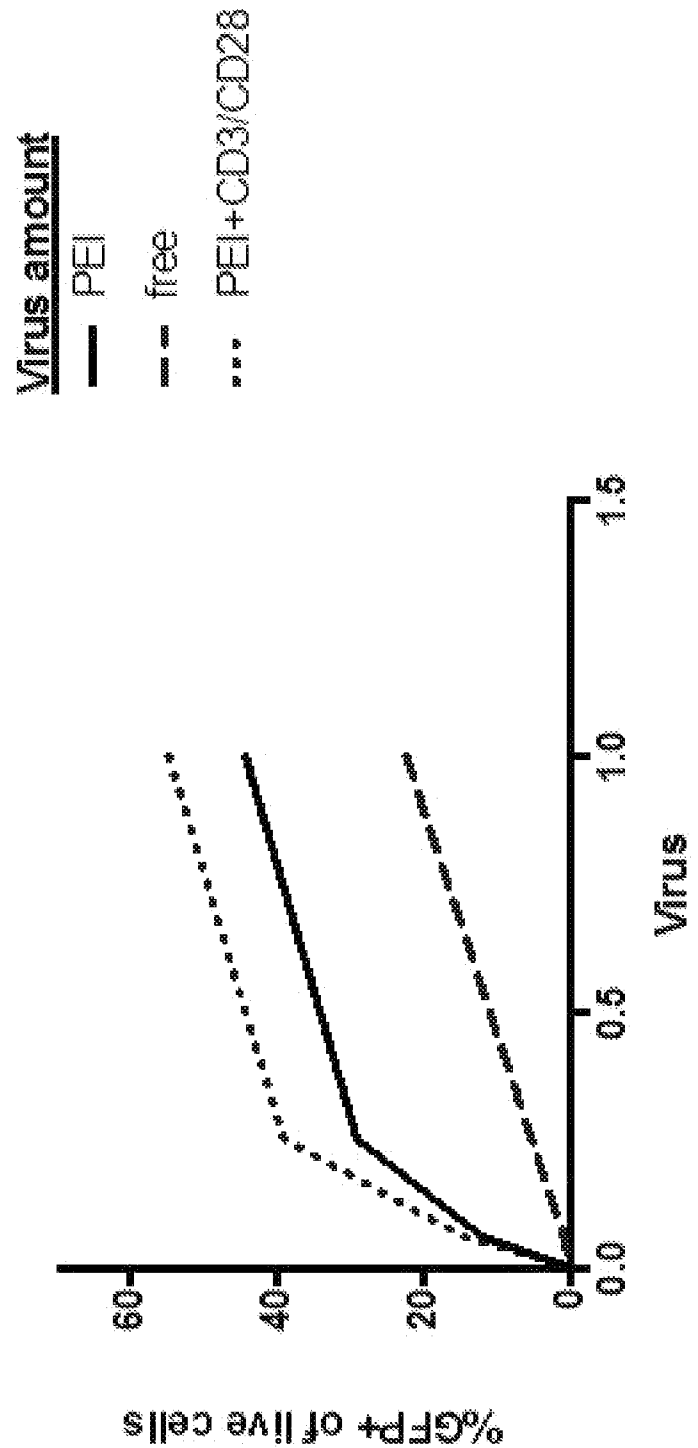

Virus amount
PEI
free
PEI+CD3/CD28
%GFP+ of live cells
0
20
40
60
0.0
0.5
1.0
1.5
Virus

FIG. 15

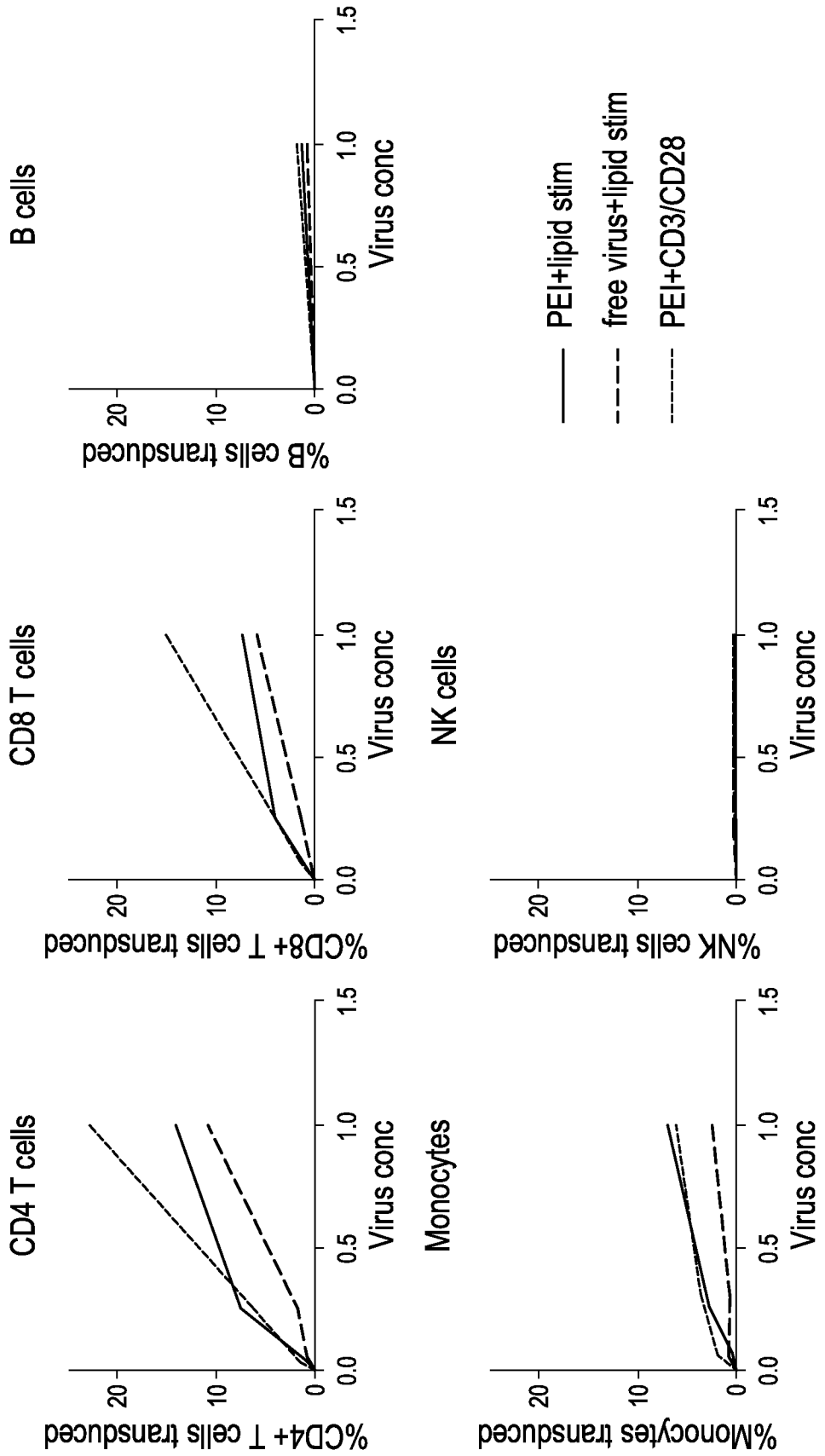

B cells
%B cells transduced
Virus conc
CD8 T cells
%CD8+ T cells transduced
Virus conc
NK cells
%NK cells transduced
Virus conc
CD4 T cells
%CD4+ T cells transduced
Virus conc
Monocytes
%Monocytes transduced
Virus conc
PEI+lipid stim
free virus+lipid stim
PEI+CD3/CD28

FIG. 16

FIG. 17

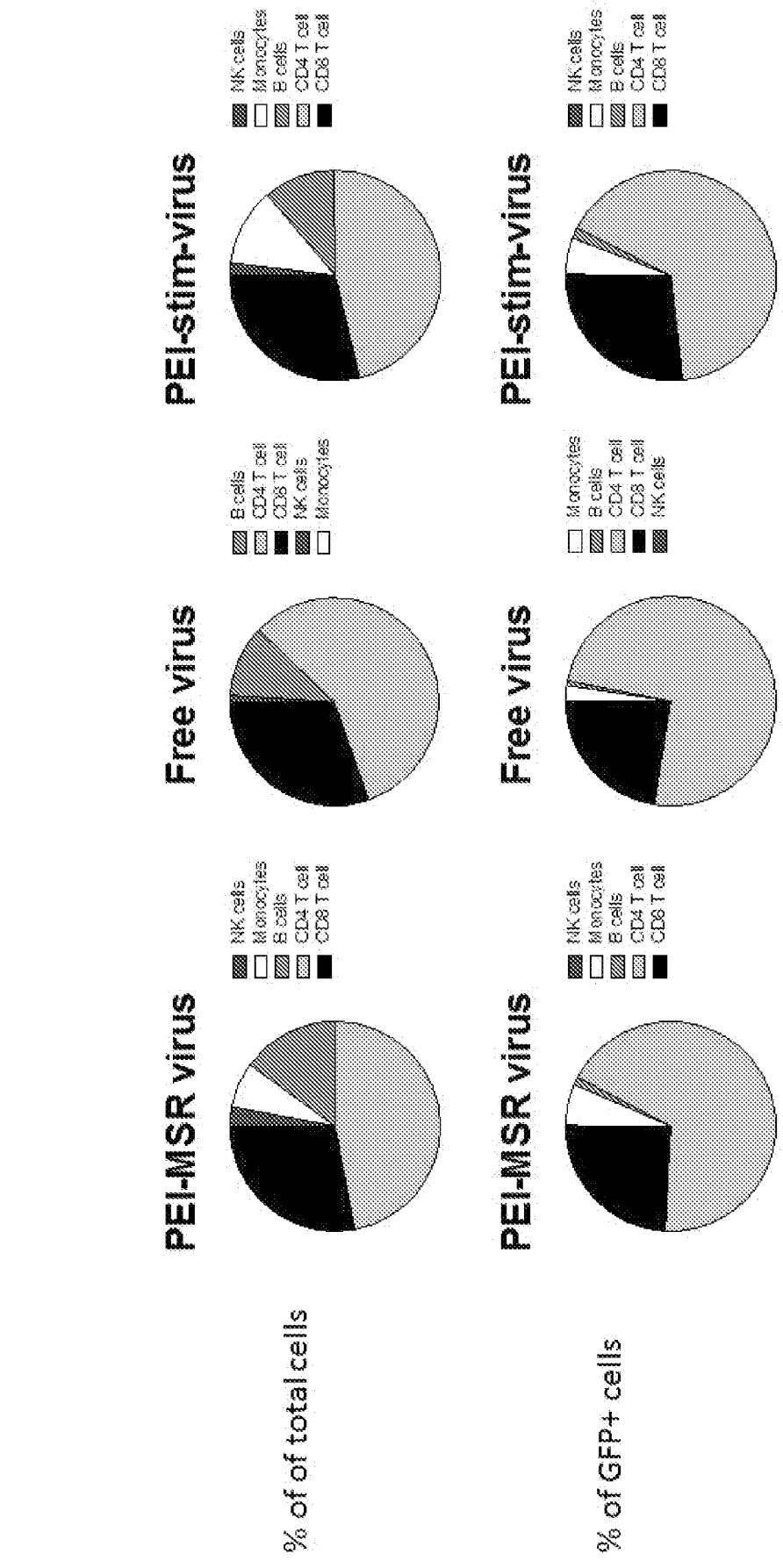

% of of total cells
% of GFP+ cells
PEI-MSR virus
Free virus
PEI-stim-virus
NK cells
Monocytes
B cells
CD4 T cell
CD8 T cell

FIG. 18

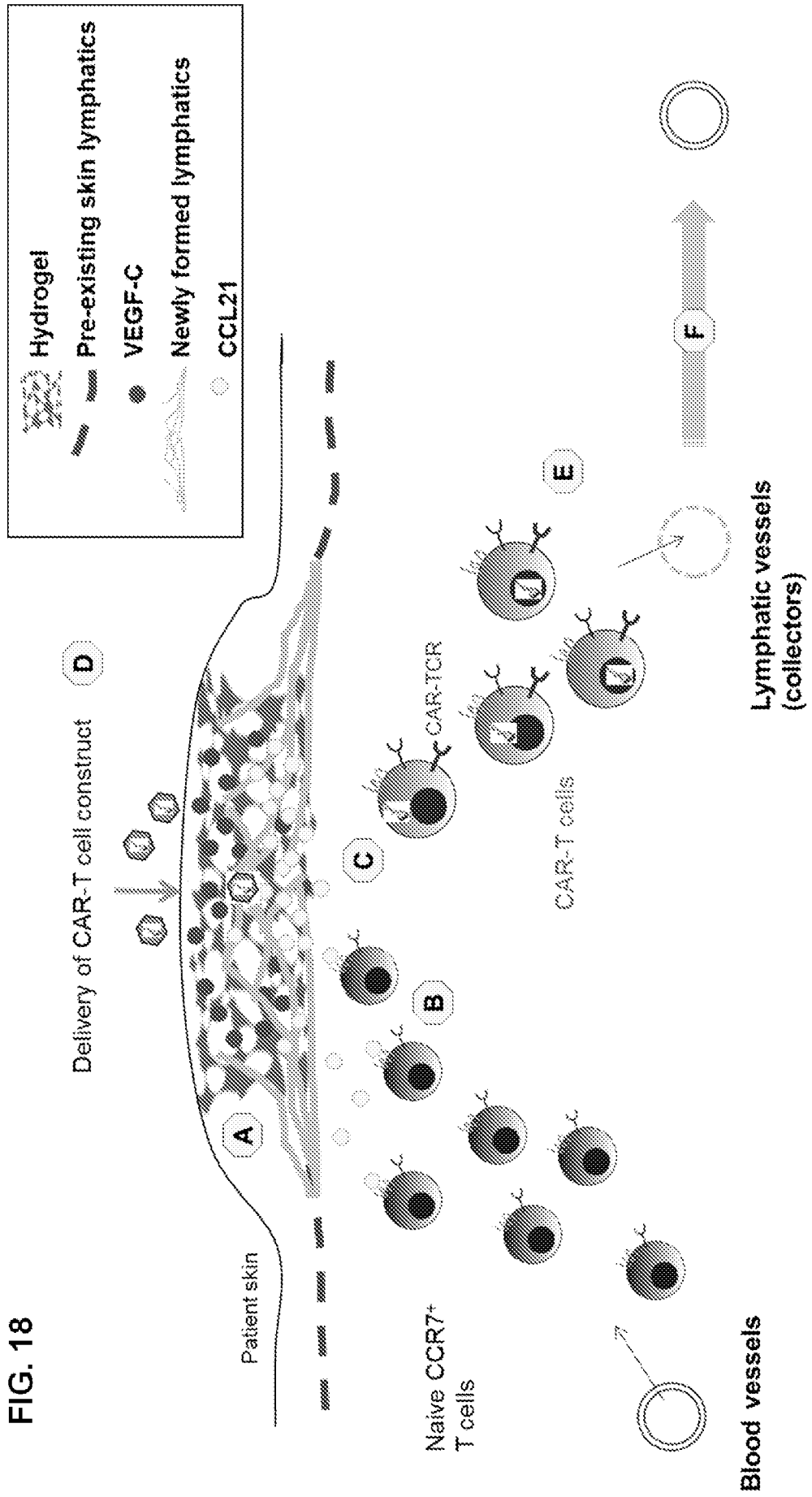

Hydrogel
Pre-existing skin lymphatics
VEGF-C
Newly formed lymphatics
CCL21
Delivery of CAR-T cell construct
D
Patient skin
A
B
C
CAR-TCR
CAR-T cells
E
F
Naive CCR7+ T cells
Blood vessels
Lymphatic vessels (collectors)

FIG. 19A

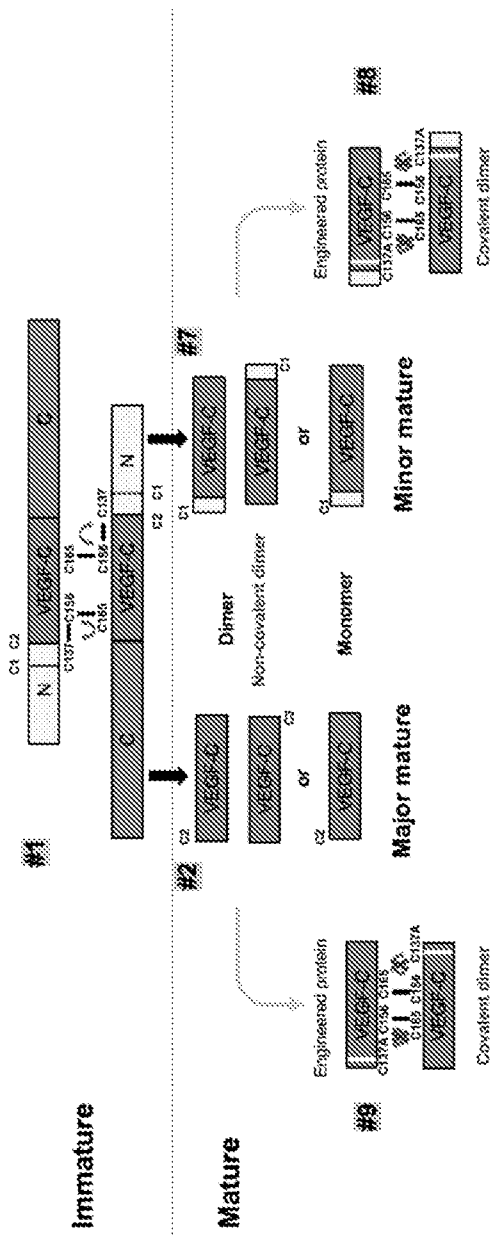

Immature
Mature
#1
#2
#7
#8
#9
Dimer
Non-covalent dimer
Monomer
Major mature
Minor mature
Engineered protein
Covalent dimer
or

FIG. 19C

Lane	Product	Lane	Product
1	Molecular weight marker	14	Molecular weight marker
2	VEGF-C 1 NR **	15	VEGF-C 7 NR *
3	VEGF-C 1 R **	16	VEGF-C 7 R *
4	Molecular weight marker	17	Molecular weight marker
5	VEGF-C 2 NR **	18	VEGF-C 8 NR **
6	VEGF-C 2 R **	19	VEGF-C 8 R **
7	Molecular weight marker	20	Molecular weight marker
8	VEGF-C 2 NR *	21	VEGF-C 9 NR **
9	VEGF-C 2 R *	22	VEGF-C 9 R **
10	Molecular weight marker	23	Molecular weight marker
11	VEGF-C 7 NR **	24	VEGF-C 9 NR *
12	VEGF-C 7 R **	25	VEGF-C 9 R *
13	Molecular weight marker	26	Molecular weight marker

FIG. 19B

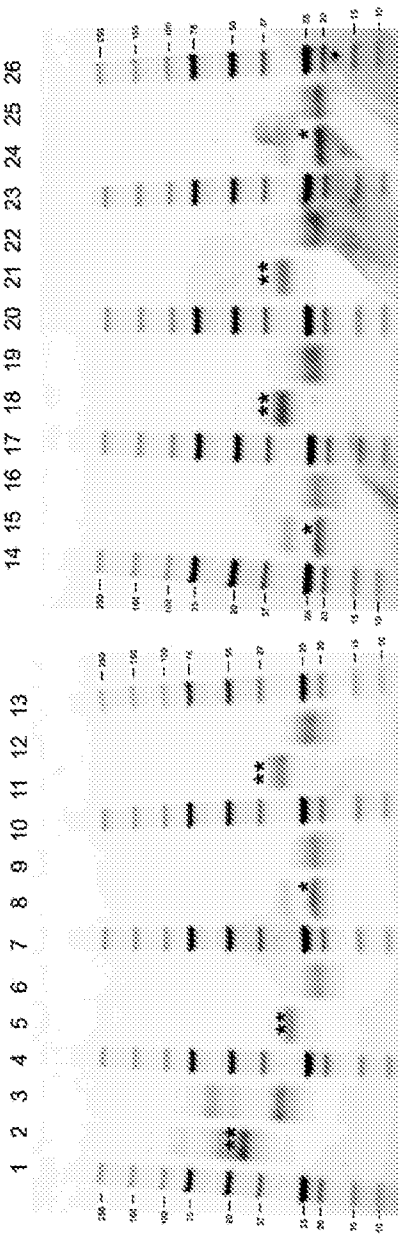


FIG. 20C

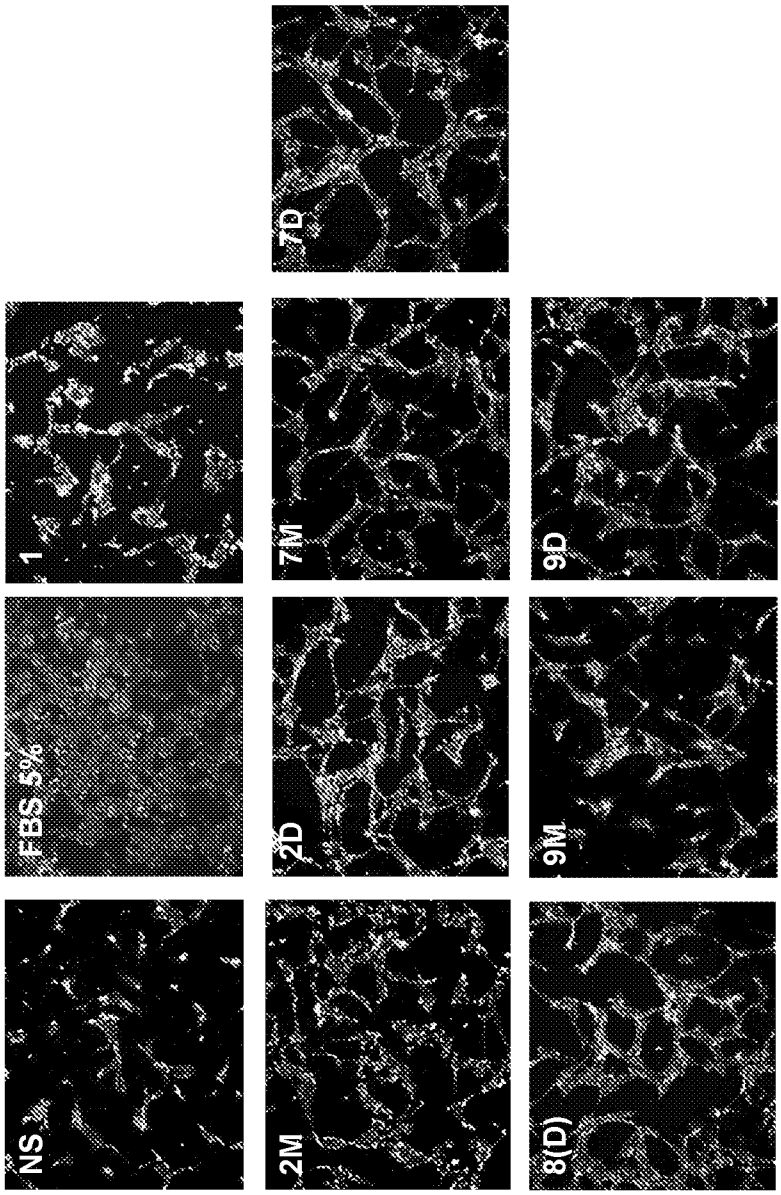


FIG. 20A

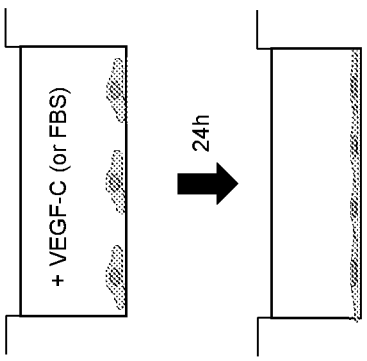


FIG. 20B

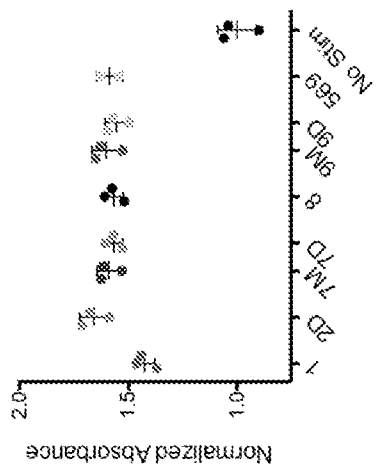


FIG. 21A

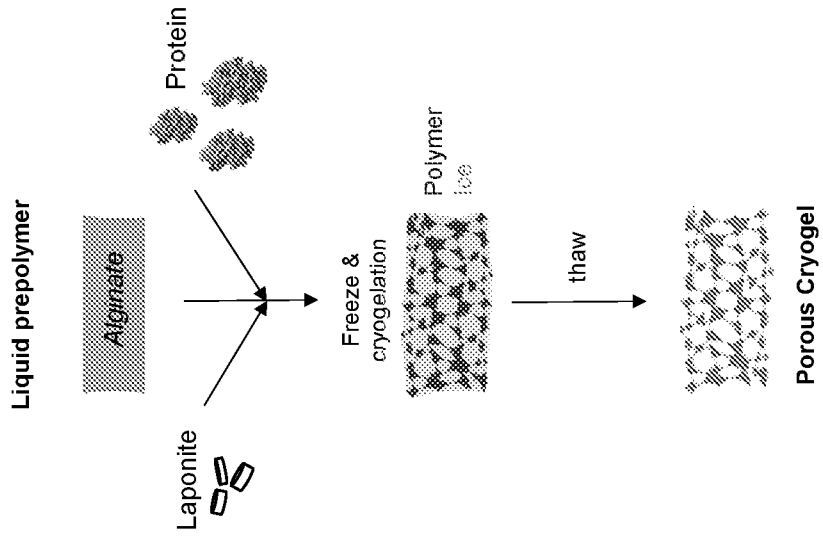


FIG. 21B

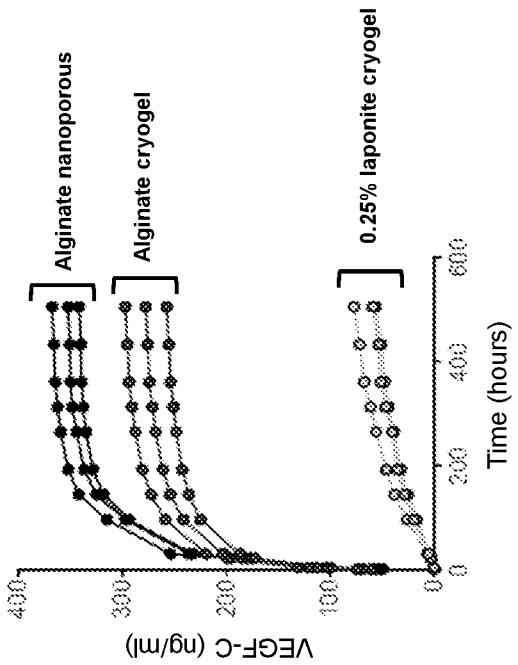


FIG. 21D

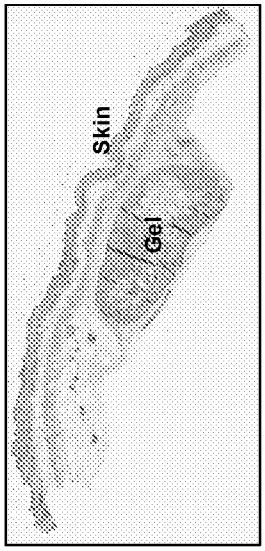


FIG. 21C

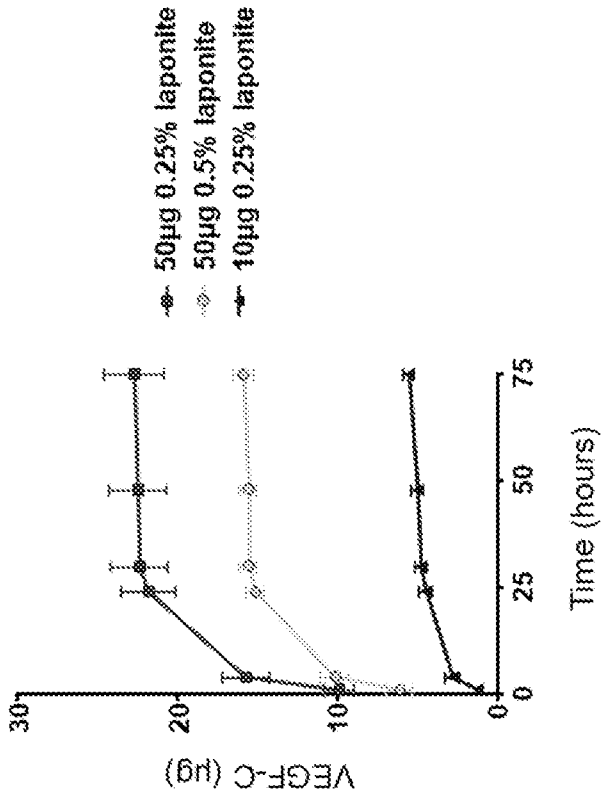


FIG. 22A

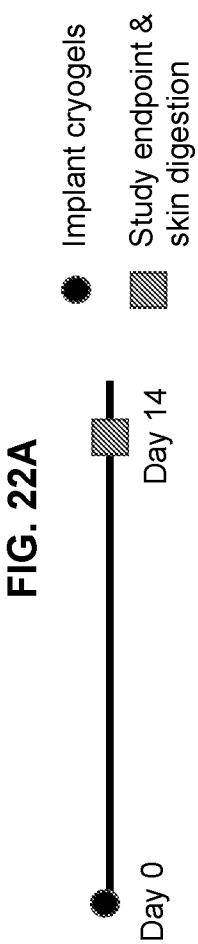


FIG. 22B

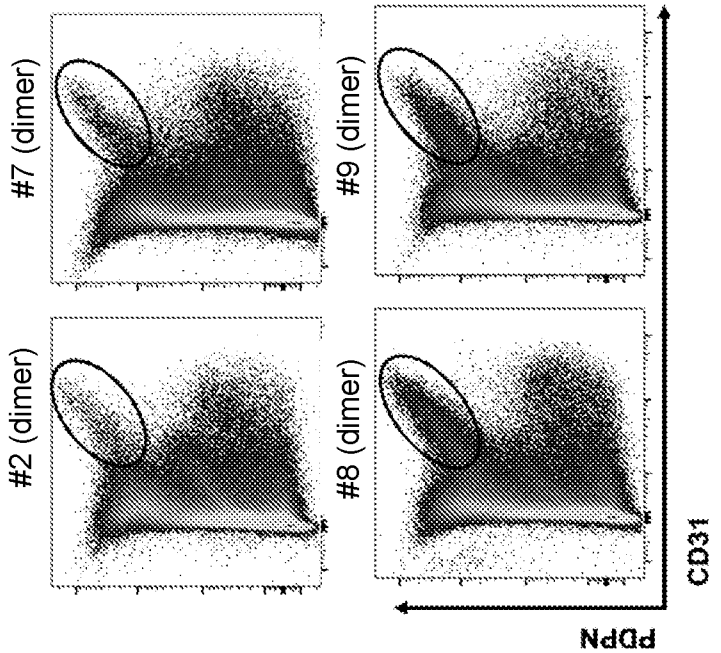


FIG. 22C

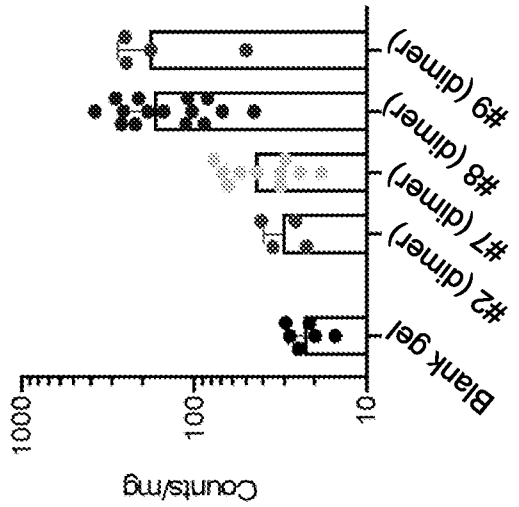


FIG. 23A

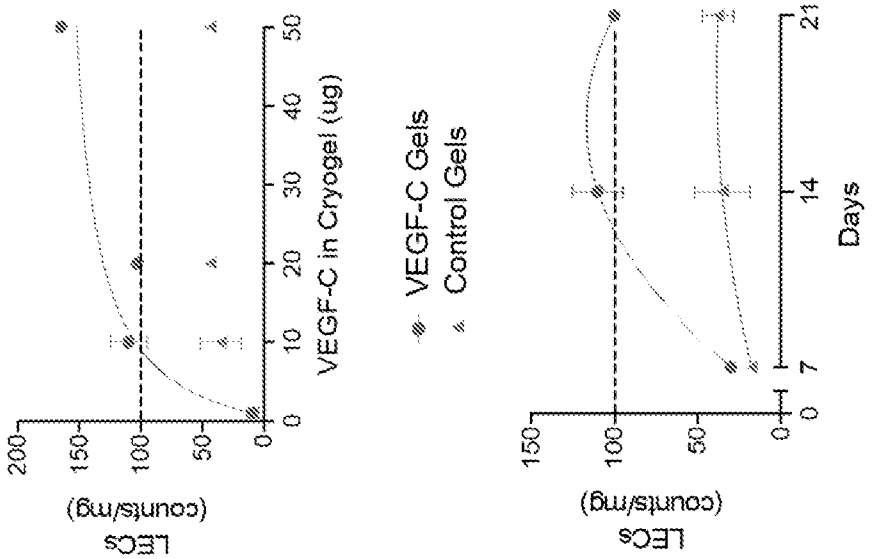


FIG. 23B

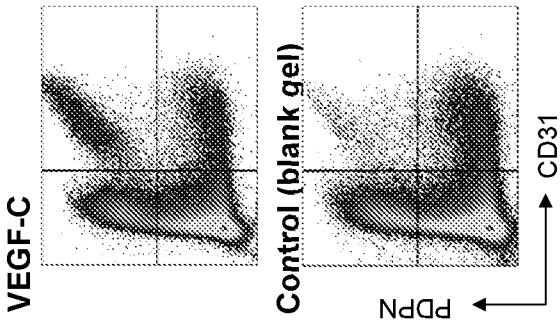


FIG. 23C

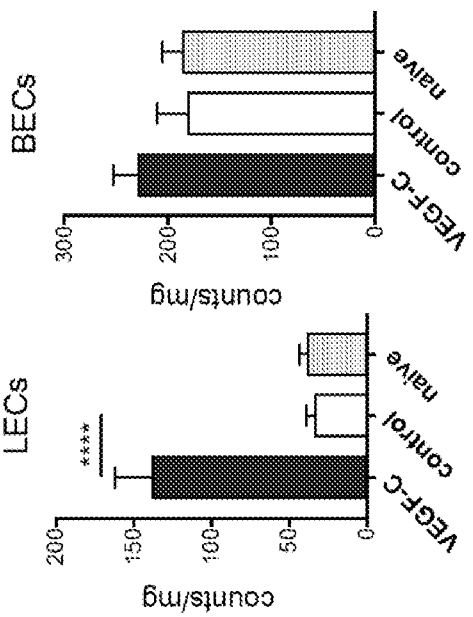


FIG. 23D

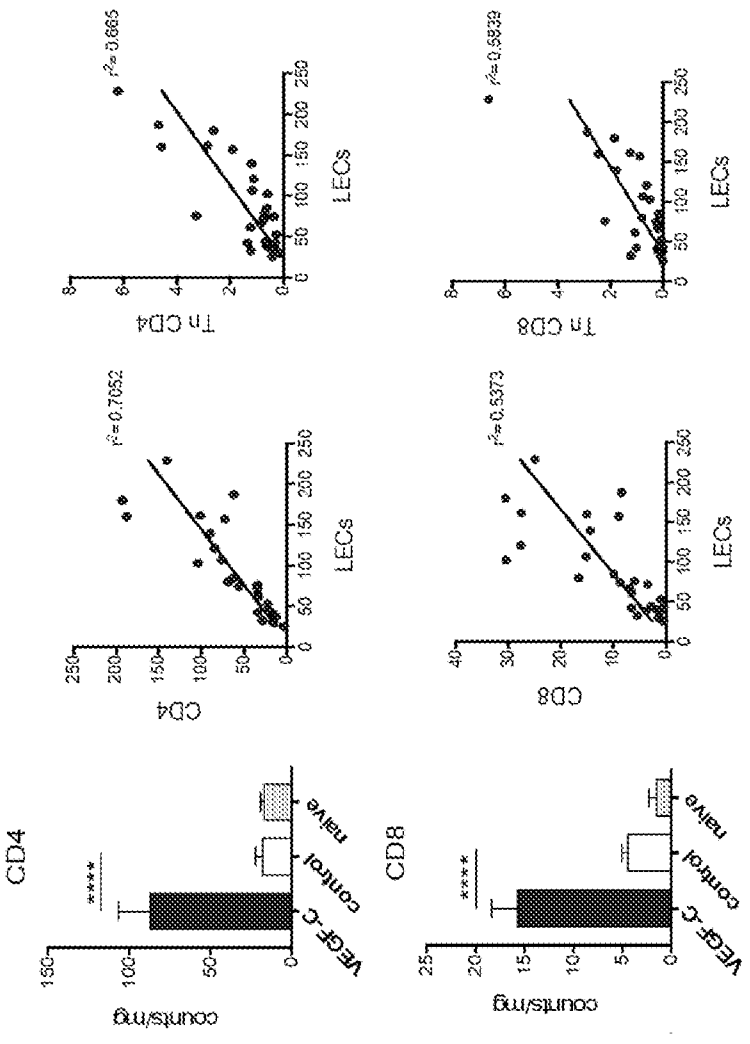
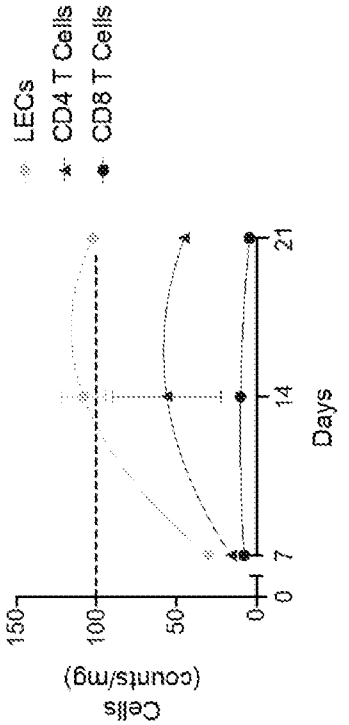


FIG. 23E



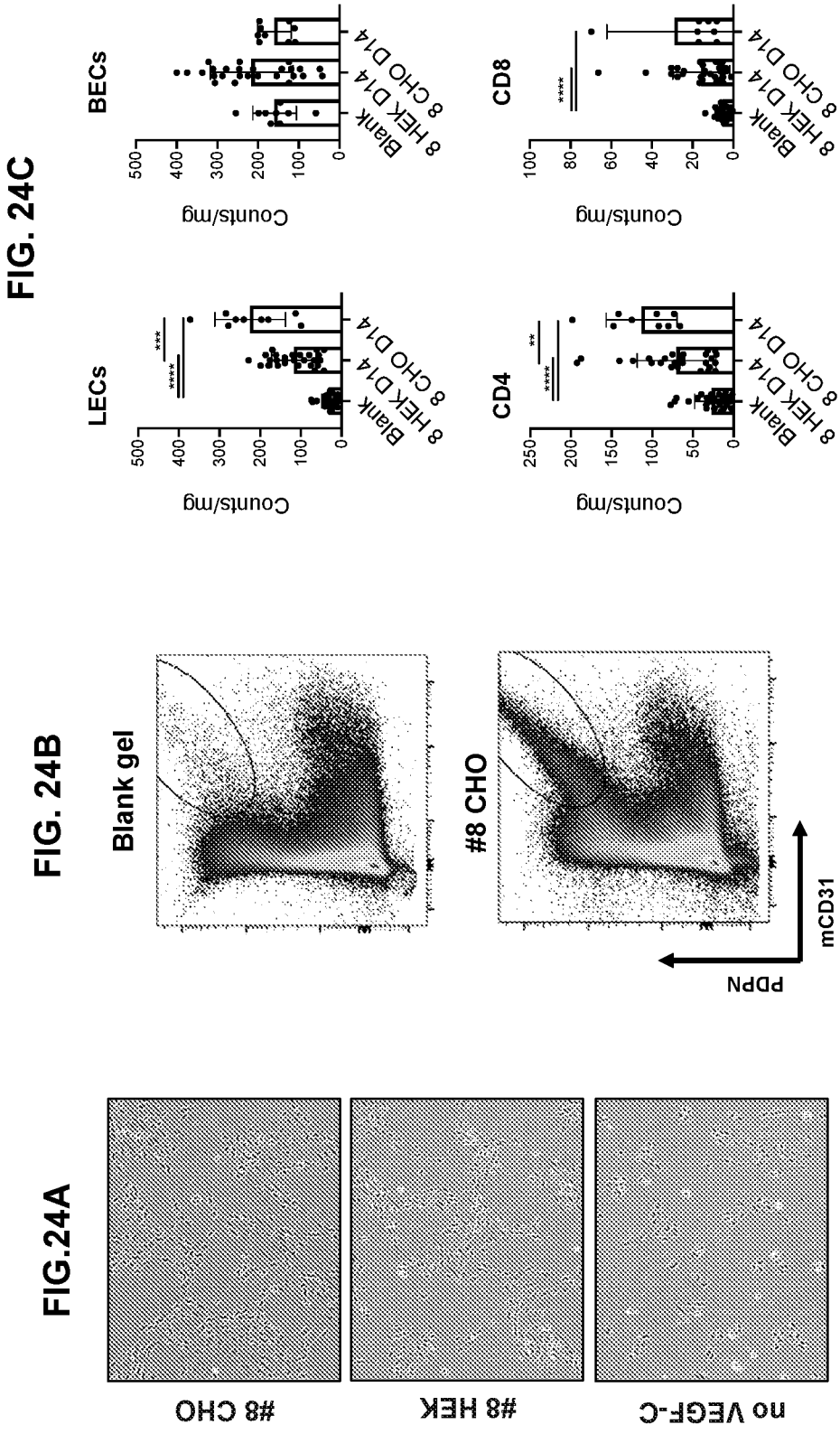

FIG.24A
no VEGF-C
#8 HEK
#8 CHO
FIG. 24B
Blank gel
#8 CHO
PDPN
mCD31
FIG. 24C
LECs
BECs
CD4
CD8
Counts/mg
Blank
8 HEK D14
8 CHO D14
***
****
**

FIG. 25B

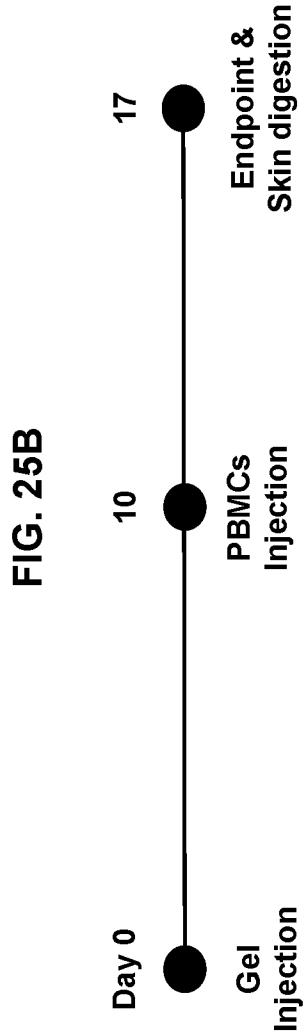


FIG. 25A

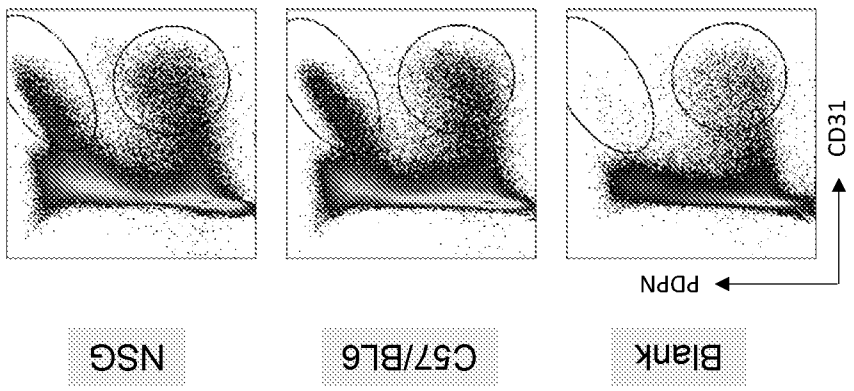


FIG. 25C

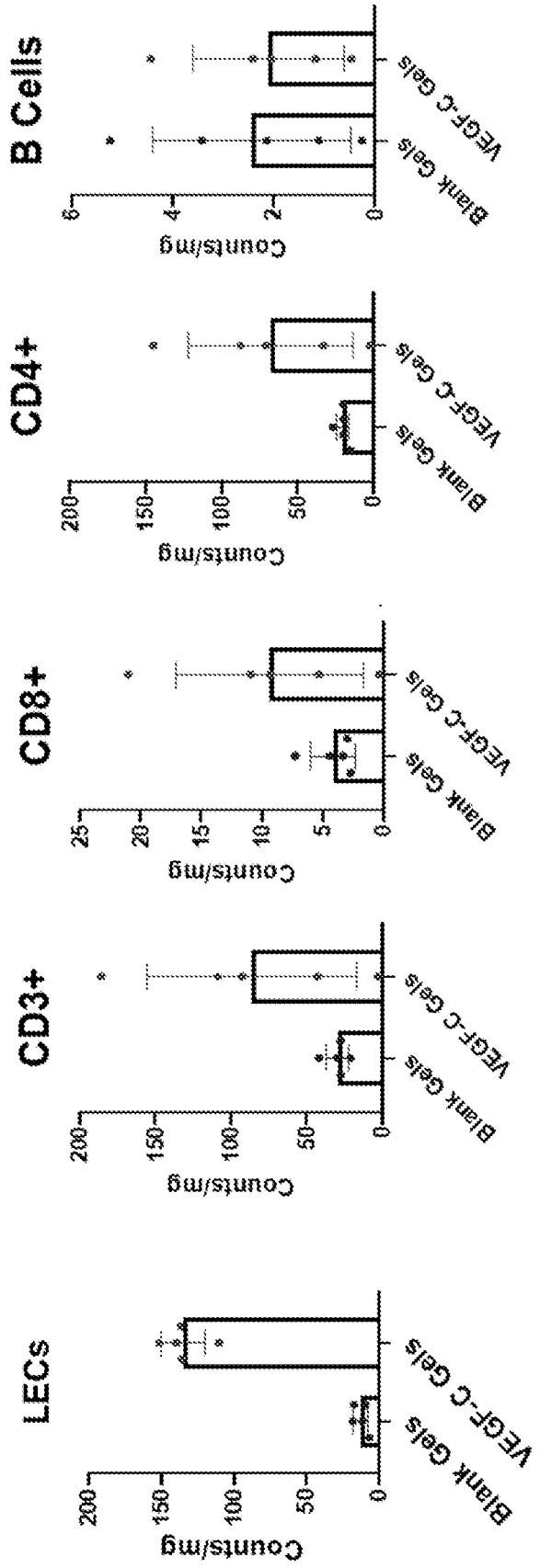


FIG. 26A

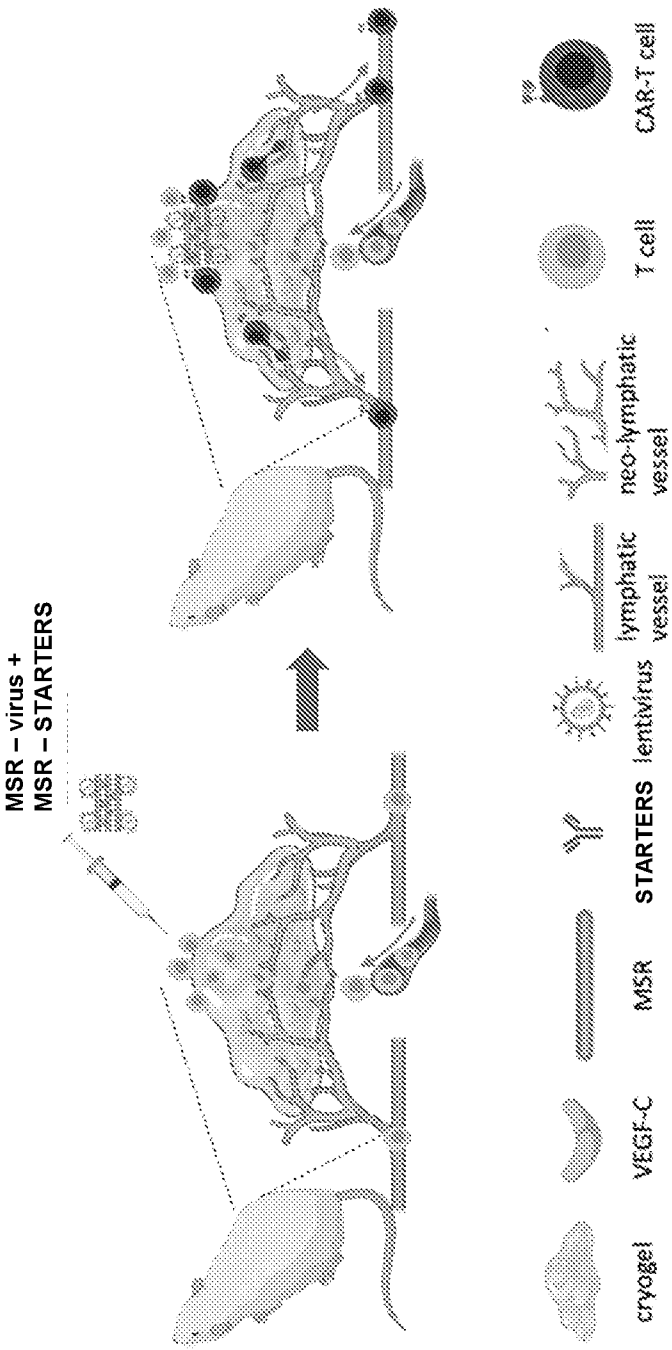

MSR – virus +
MSR – STARTERS
cryogel
VEGF-C
MSR
STARTERS
lentivirus
lymphatic vessel
neo-lymphatic vessel
T cell
CAR-T cell

FIG. 26B

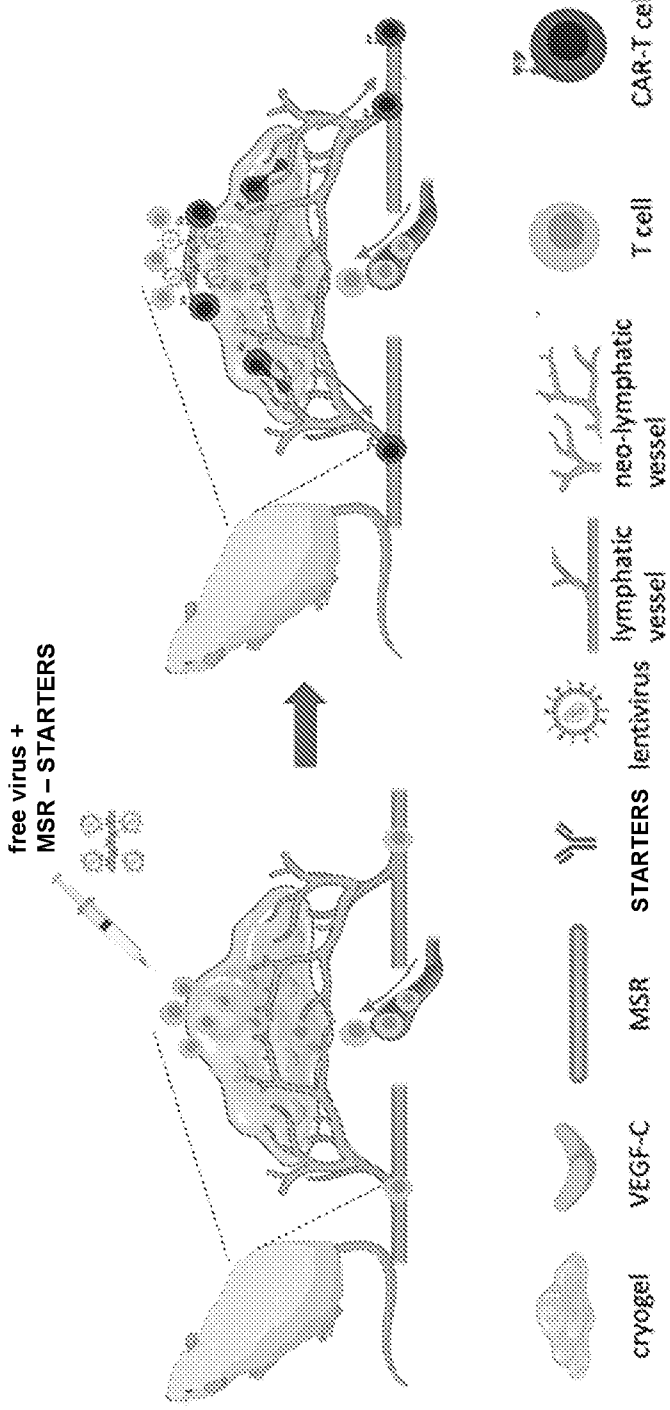

free virus +
MSR – STARTERS
cryogel
VEGF-C
MSR
STARTERS
lentivirus
lymphatic vessel
neo-lymphatic vessel
T cell
CAR-T cell

FIG. 27A

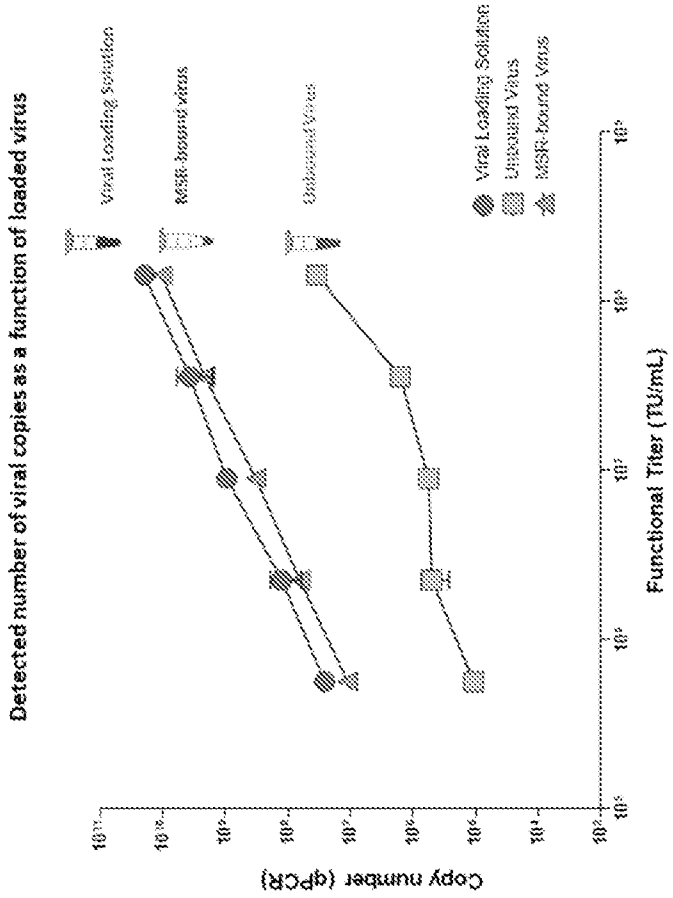


FIG. 27B

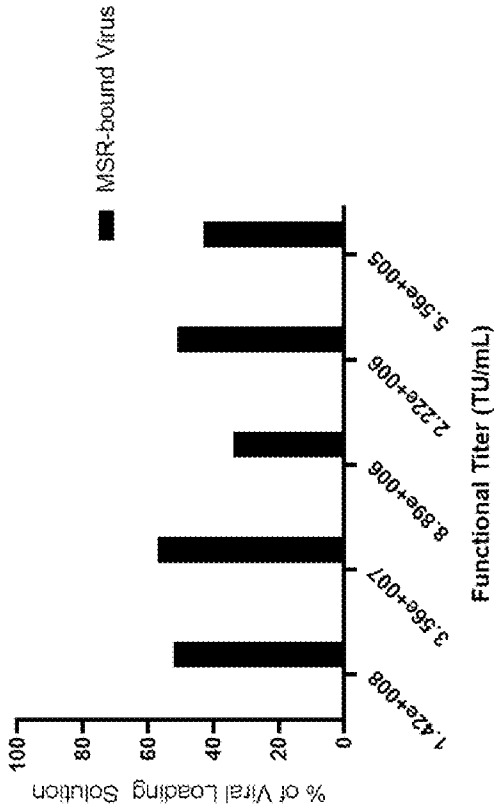


FIG. 28

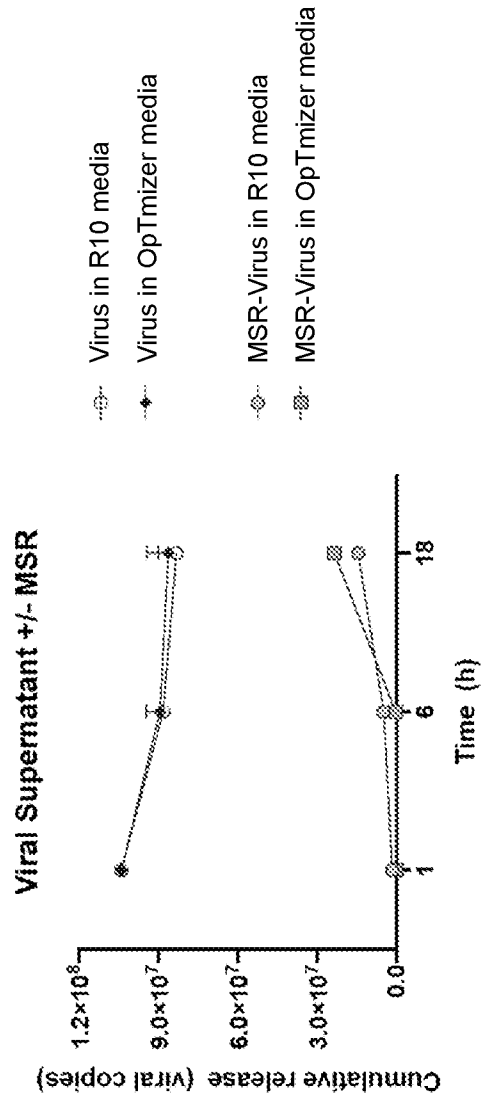

Viral Supernatant +/- MSR
Virus in R10 media
Virus in OpTmizer media
MSR-Virus in R10 media
MSR-Virus in OpTmizer media
Cumulative release (viral copies)
1.2×10^8
9.0×10^7
6.0×10^7
3.0×10^7
0.0
1
6
18
Time (h)

FIG. 29A

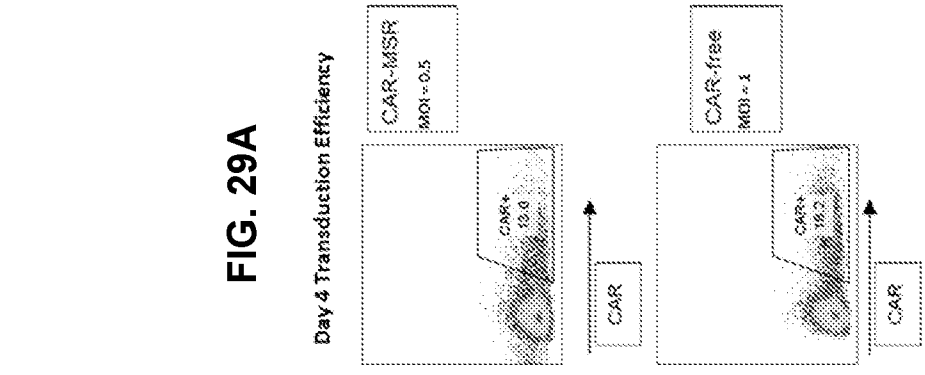


FIG. 29B

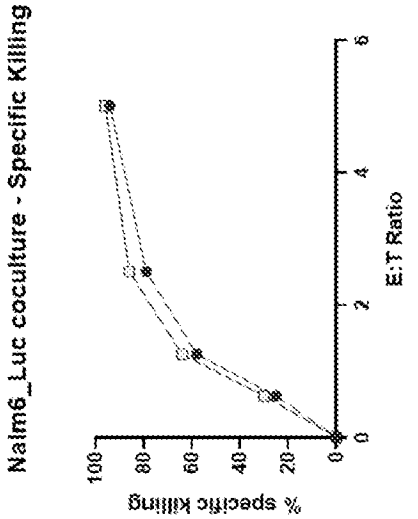


FIG. 29C

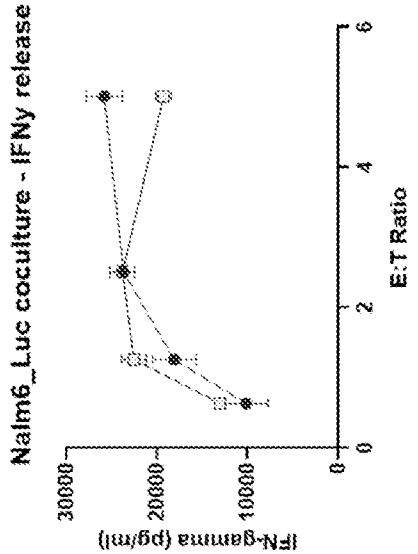


FIG. 30A

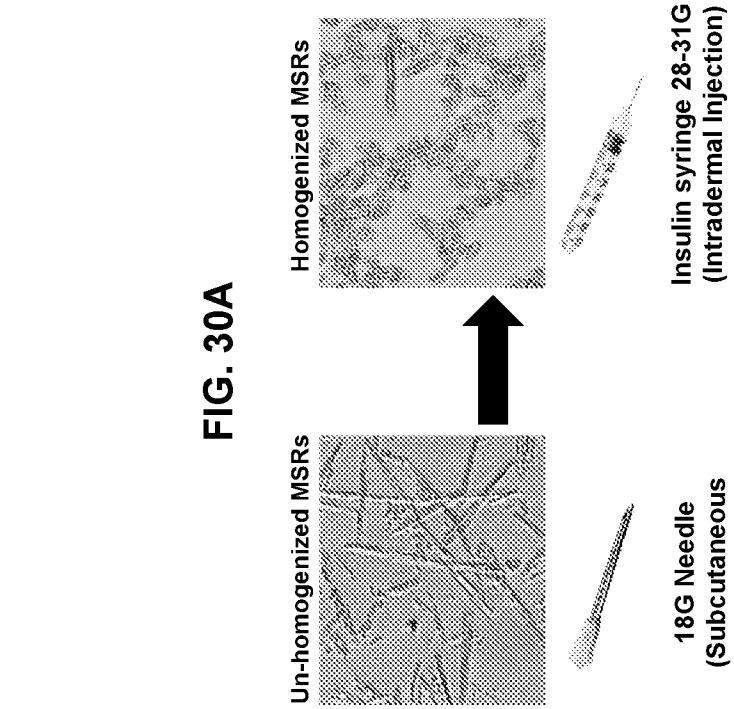


FIG. 30B

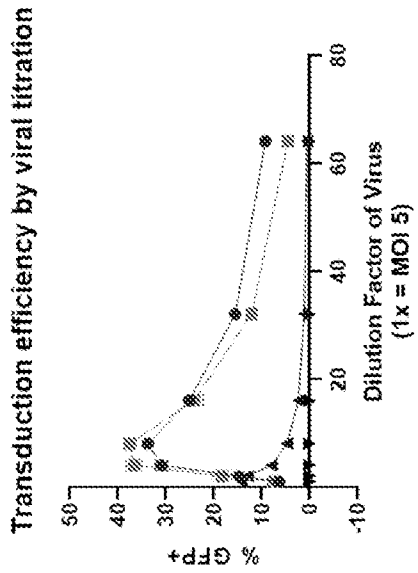


FIG. 31B

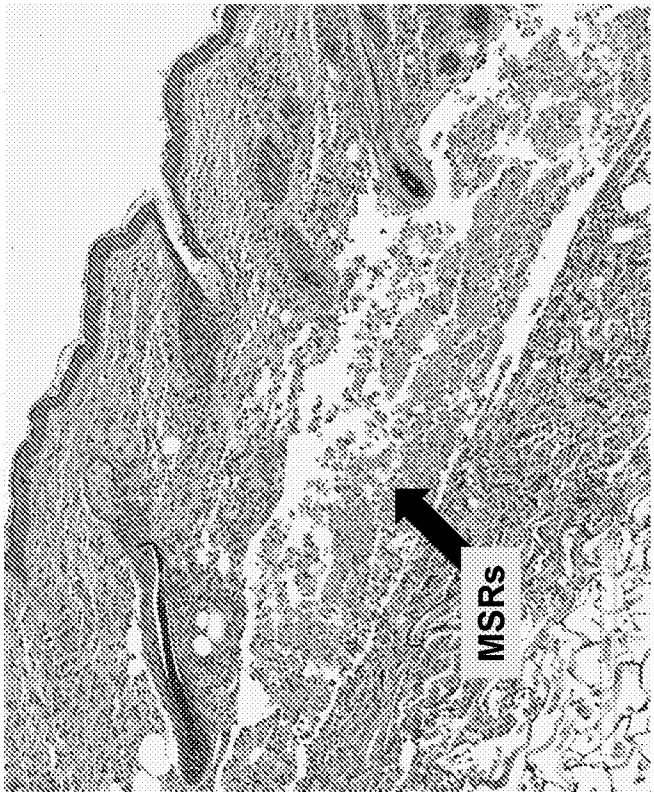


FIG. 31A

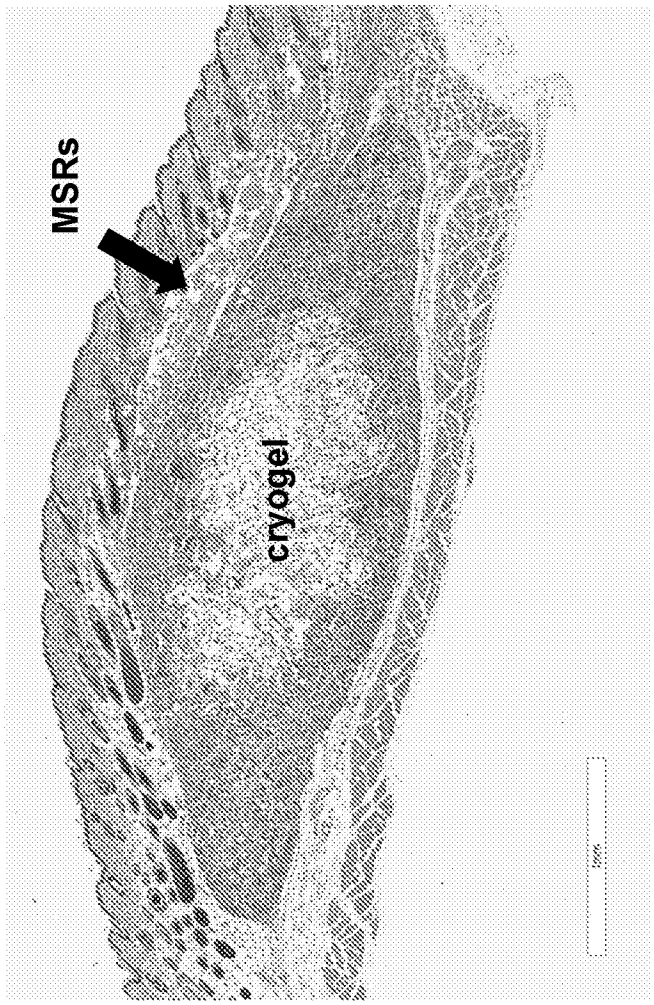


FIG. 32B

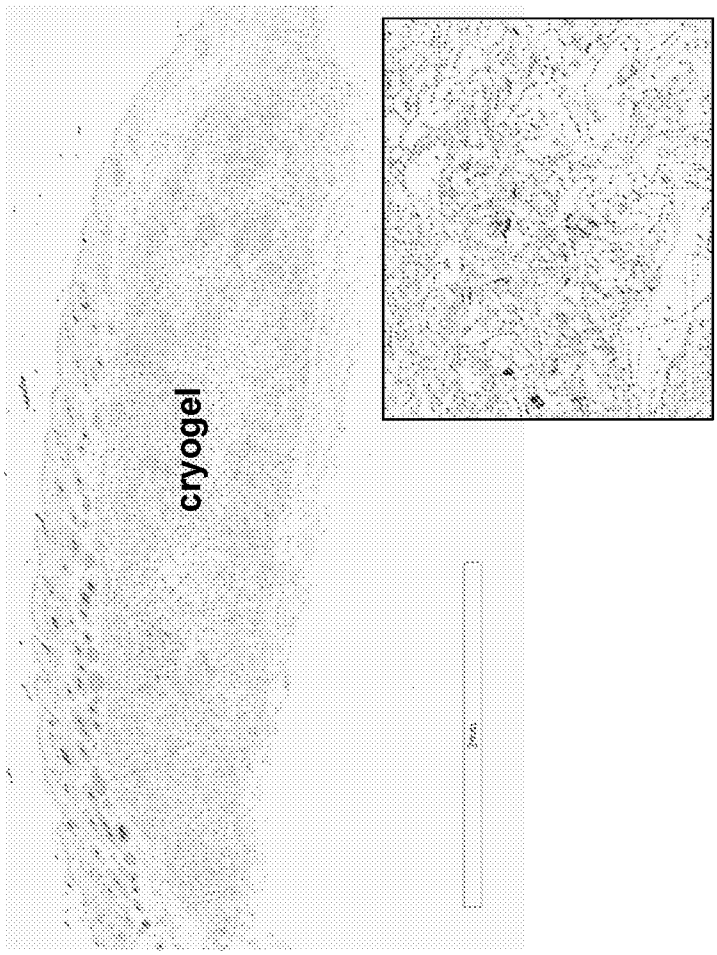


FIG. 32A

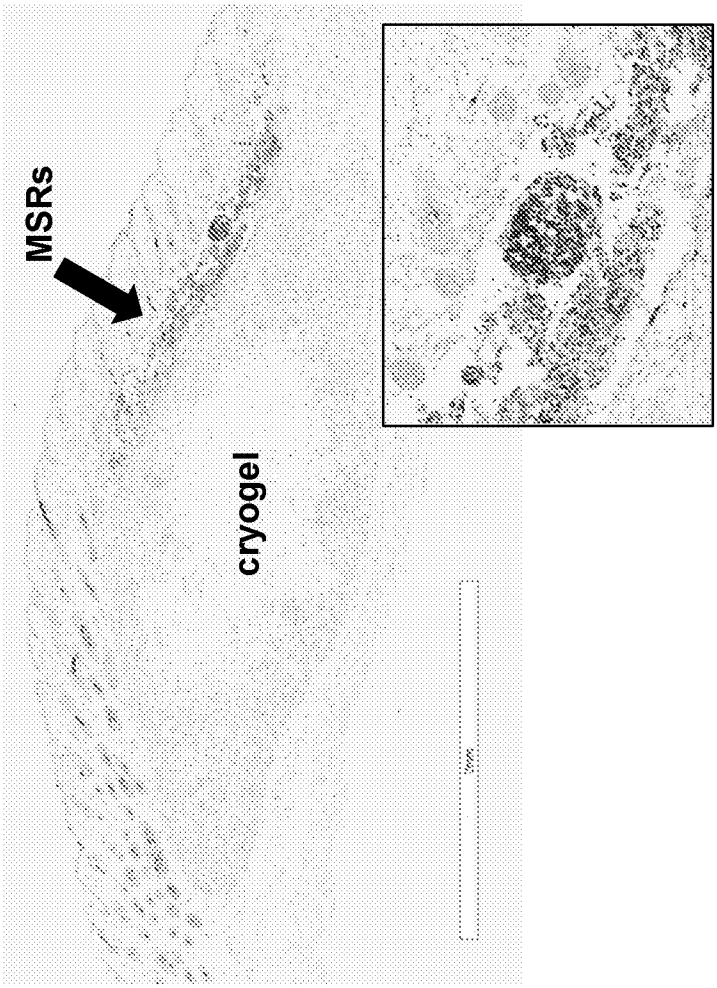


FIG. 33B

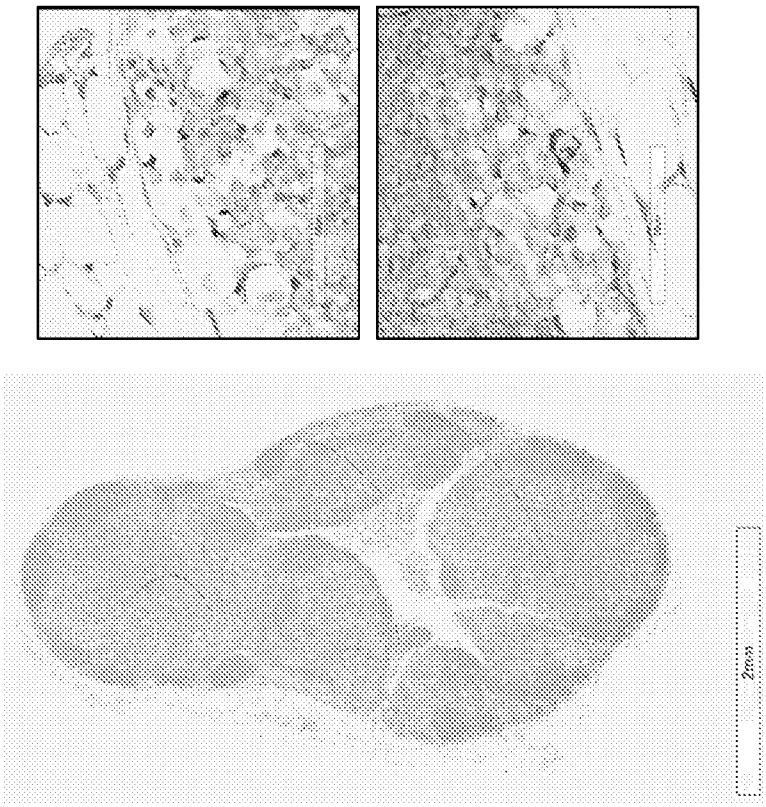


FIG. 33A

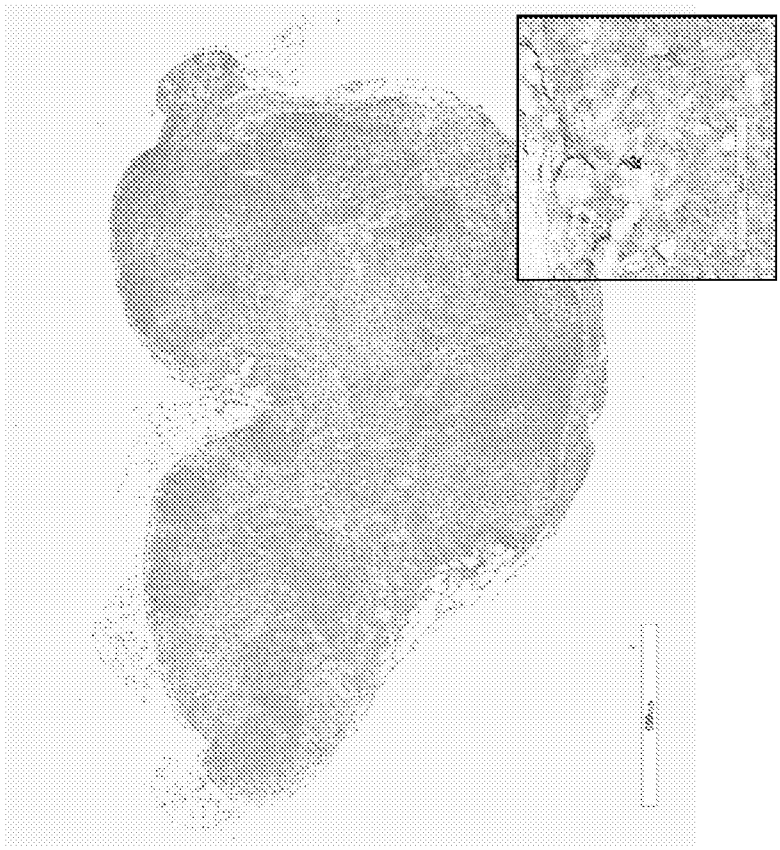


FIG. 34A

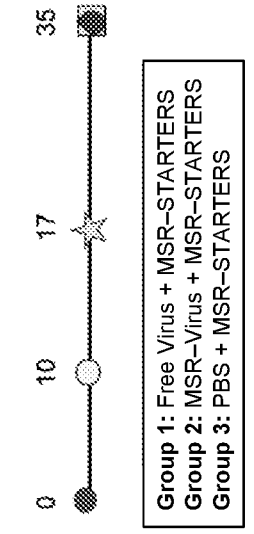


FIG. 34B

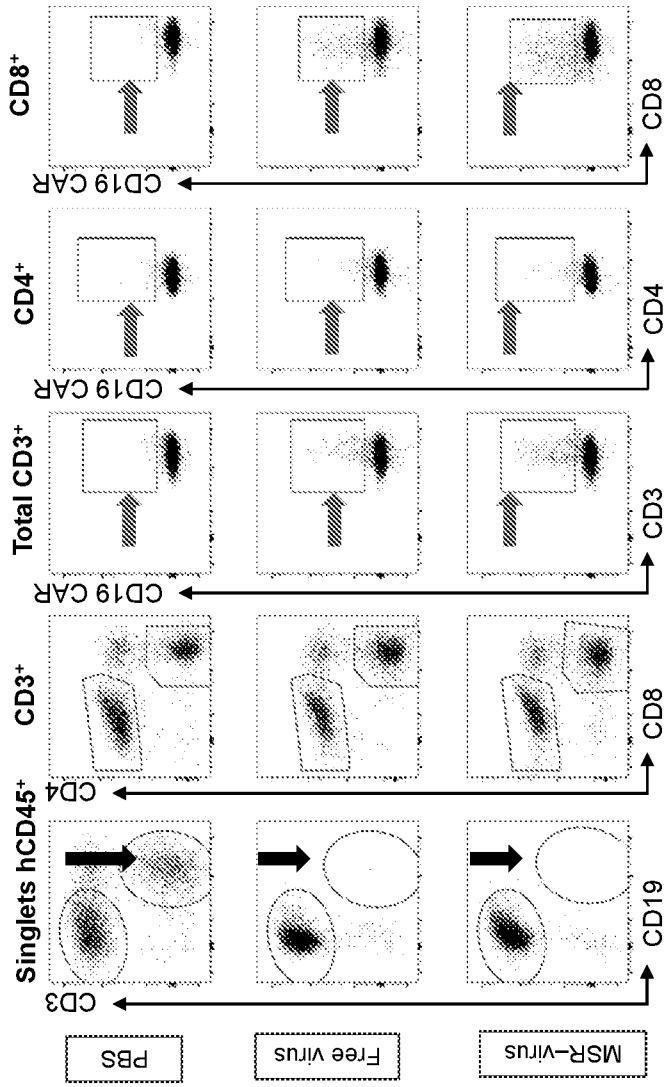
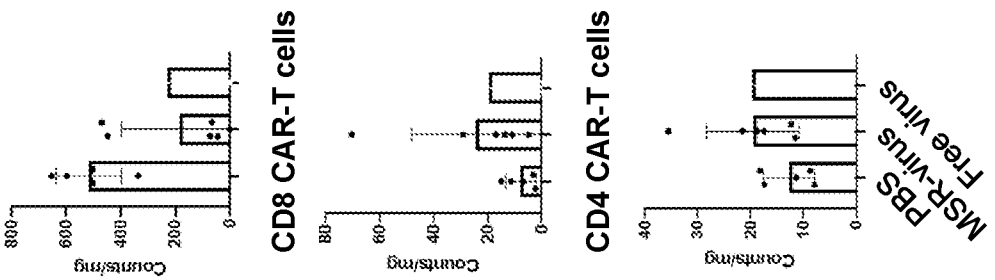


FIG. 34C



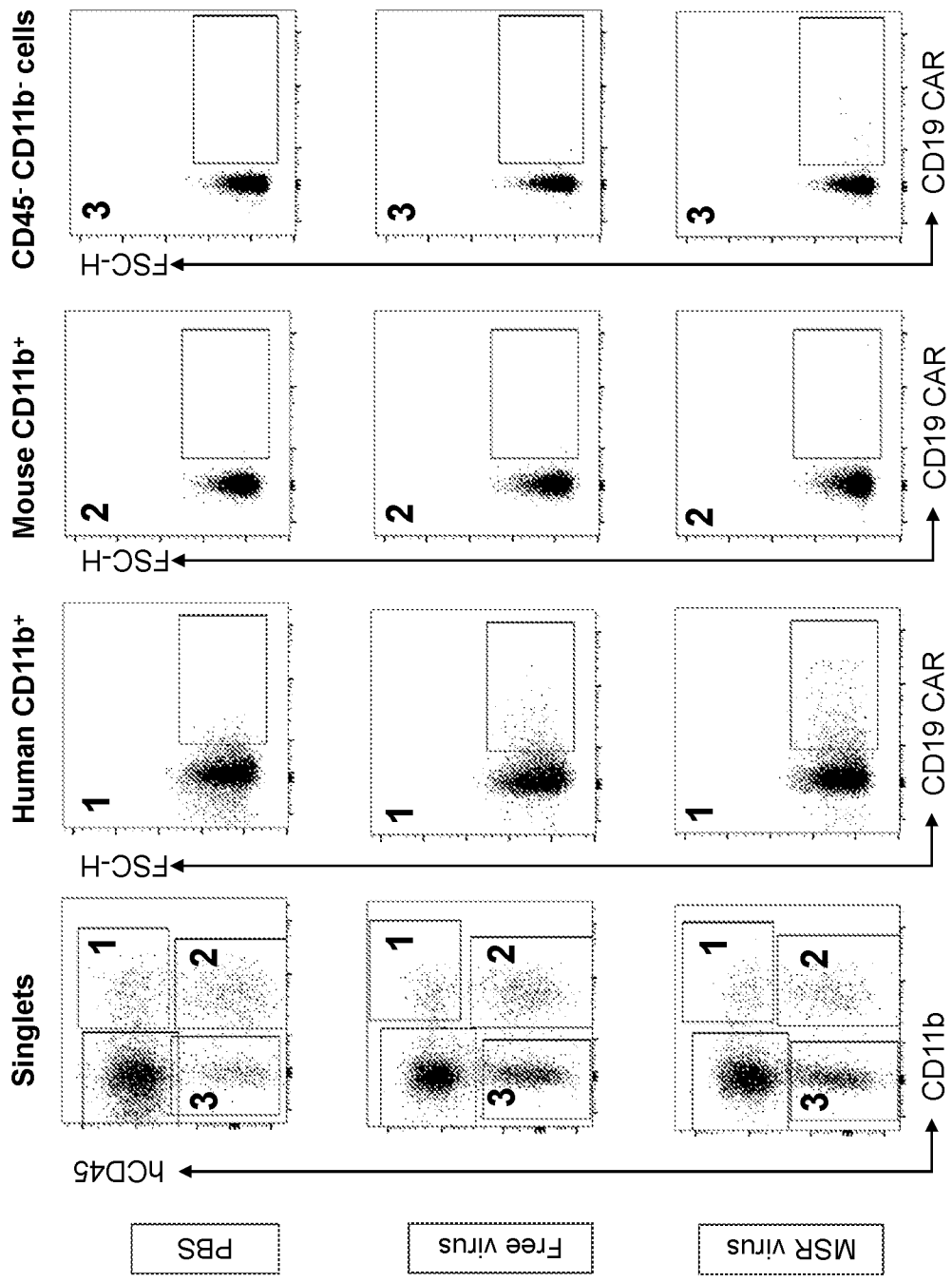

MSR virus
Free virus
PBS
hCD45
CD11b
Singlets
Human CD11b+
Mouse CD11b+
CD45- CD11b- cells
FSC-H
CD19 CAR
1
2
3

FIG. 35

FIG. 36B

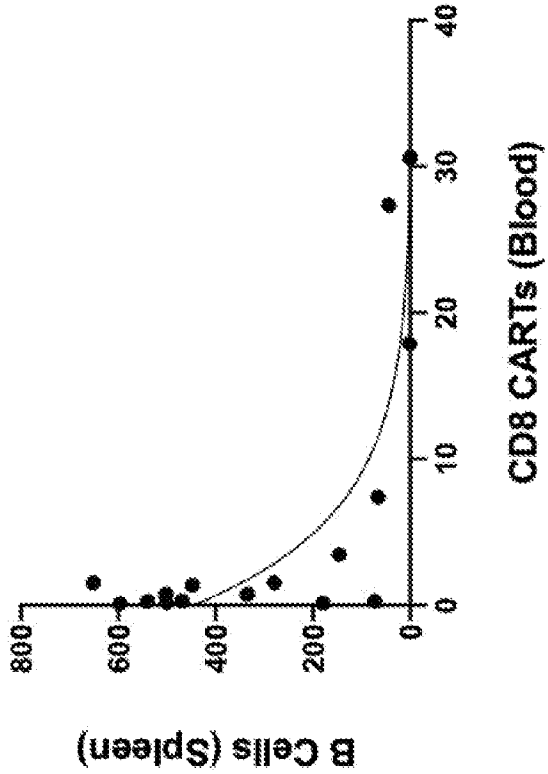
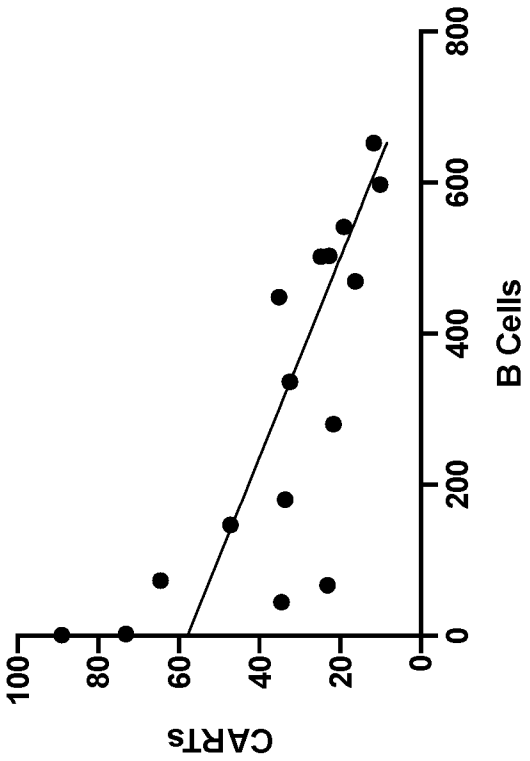


FIG. 36A



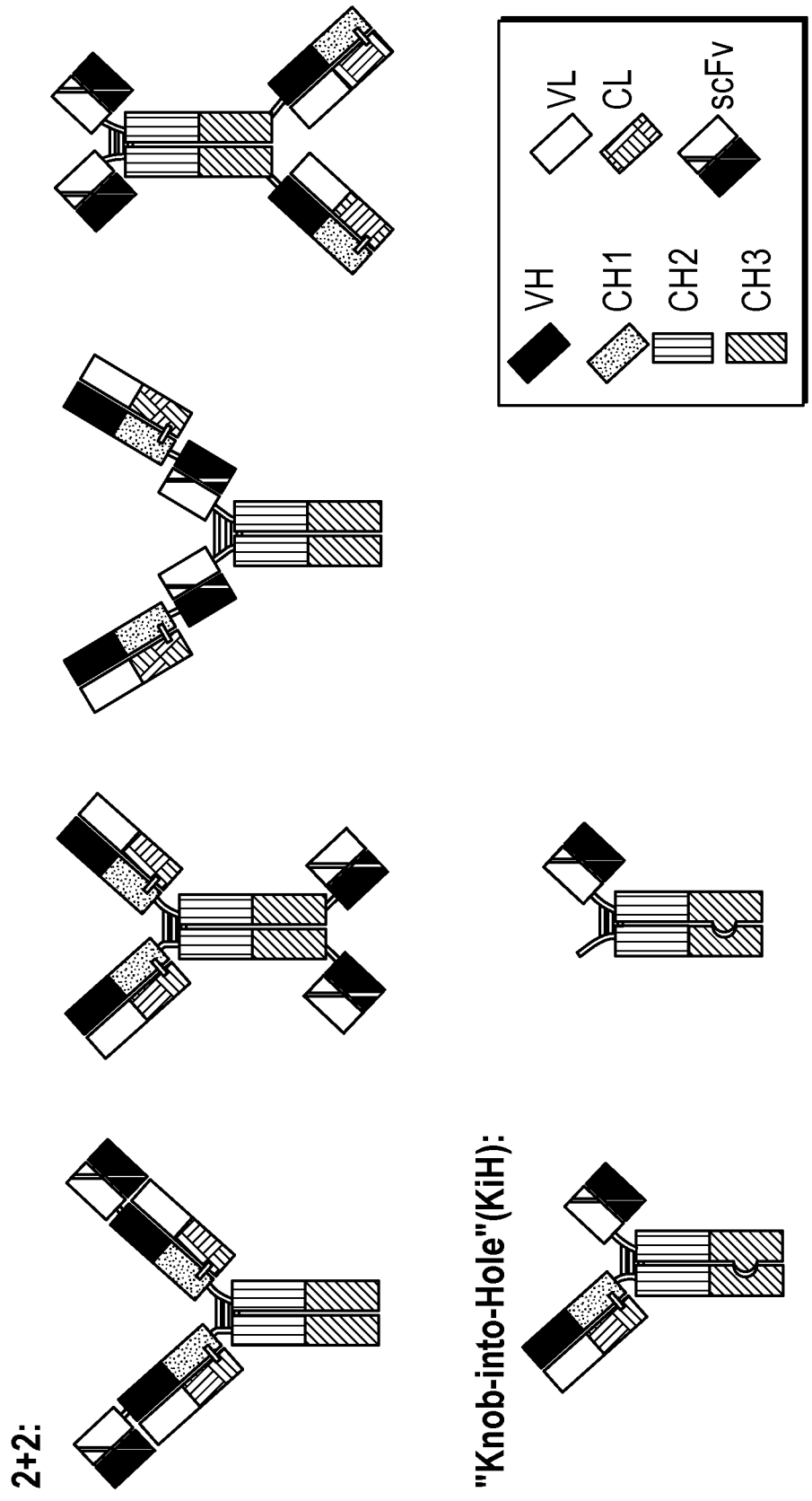


FIG. 37A

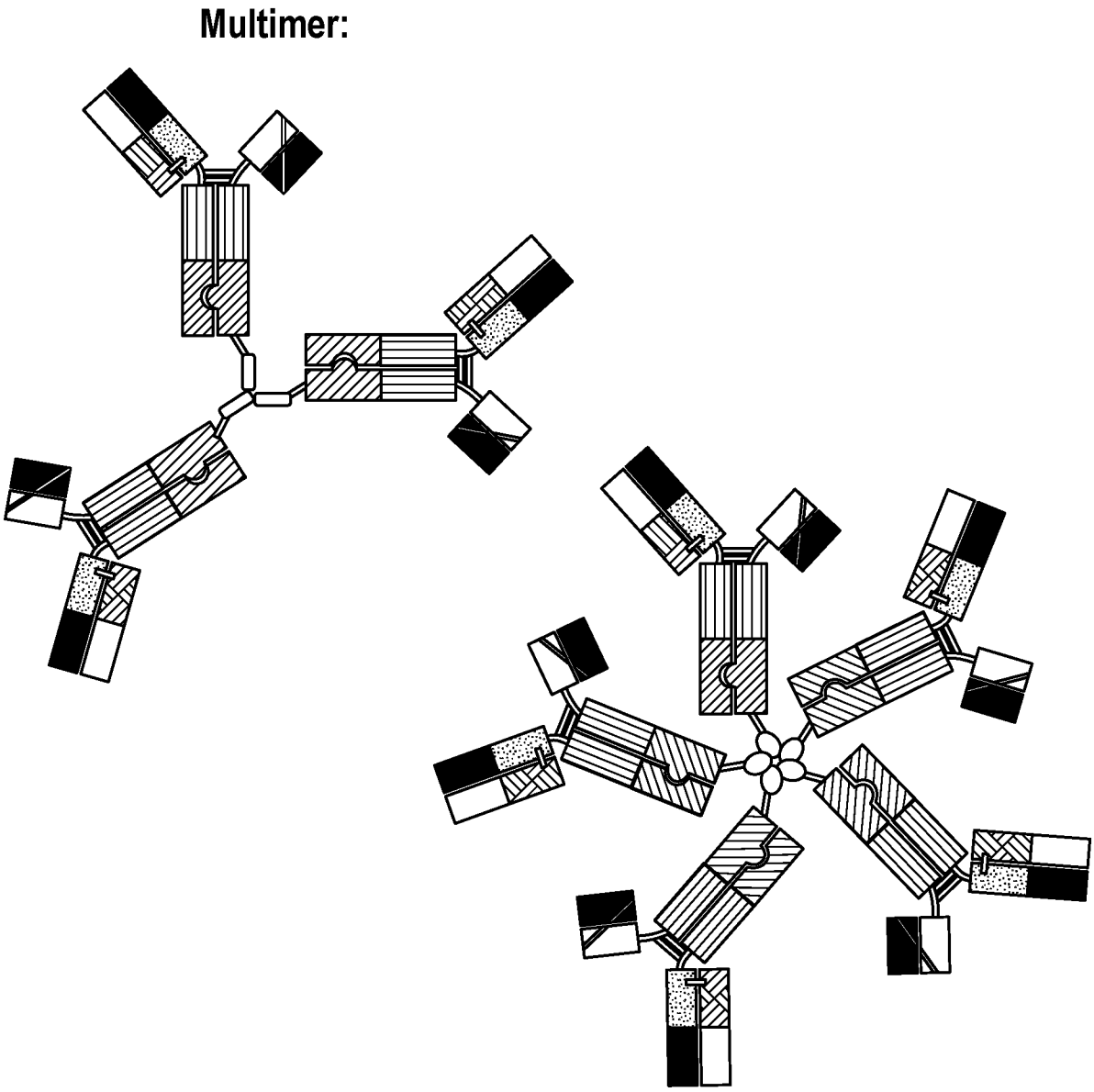


FIG. 37B

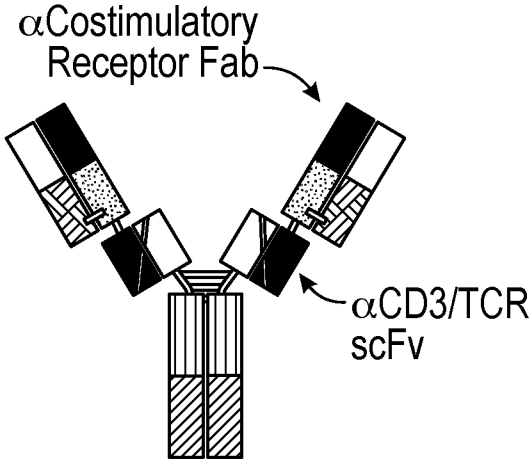


FIG. 37C

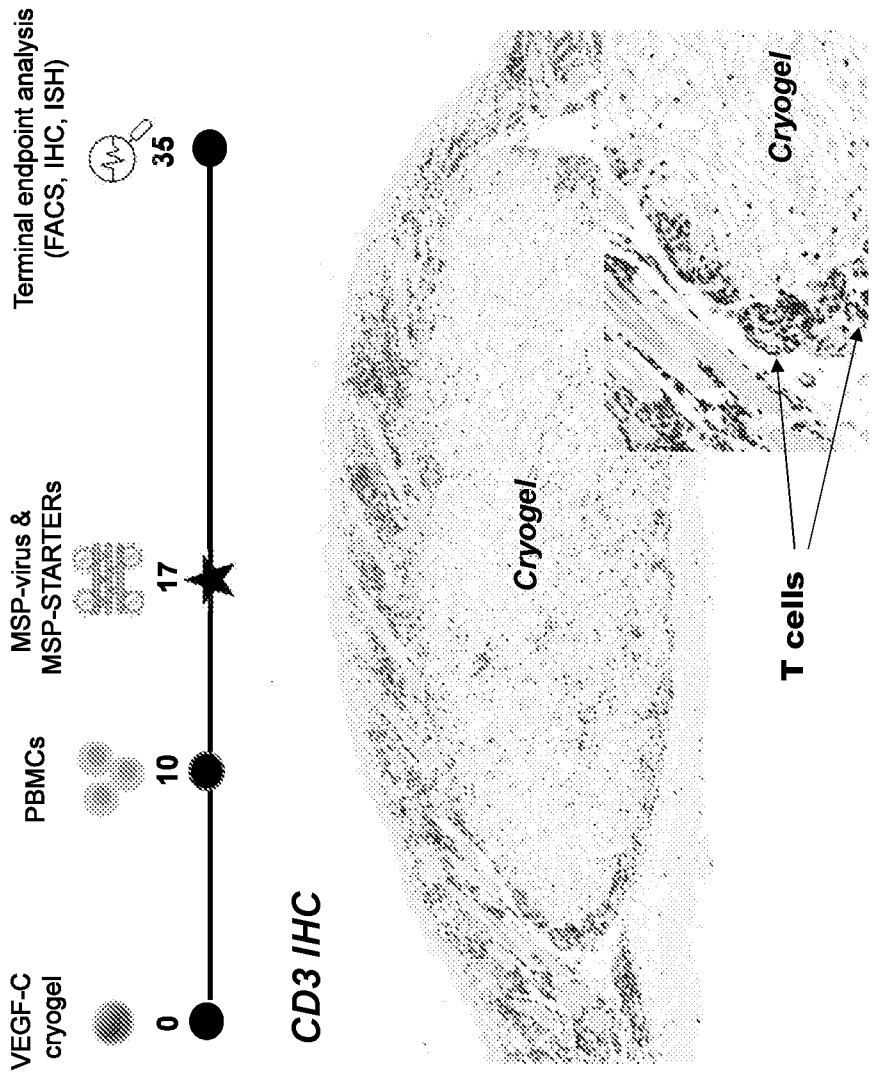
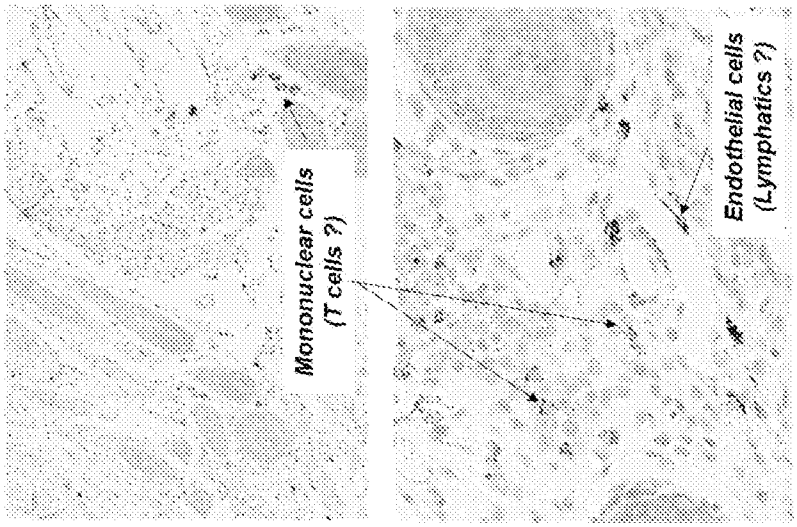

VEGF-C cryogel
PBMCs
MSP-virus & MSP-STARTERs
Terminal endpoint analysis (FACS, IHC, ISH)
0
10
17
35
CD3 IHC
Cryogel
Cryogel
T cells

FIG. 38


Mononuclear cells
(T cells ?)
Endothelial cells
(Lymphatics ?)


CAR ISH
Cryogel

FIG. 39

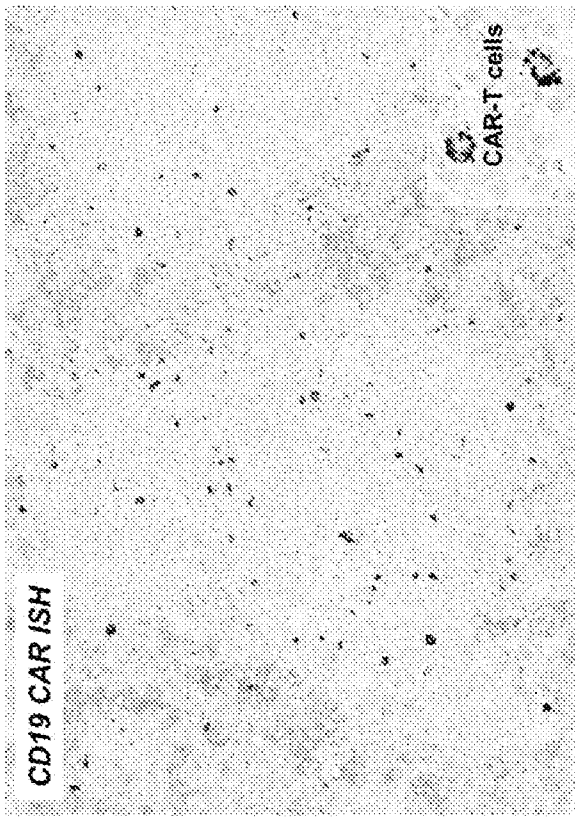


FIG. 40

FIG. 41A

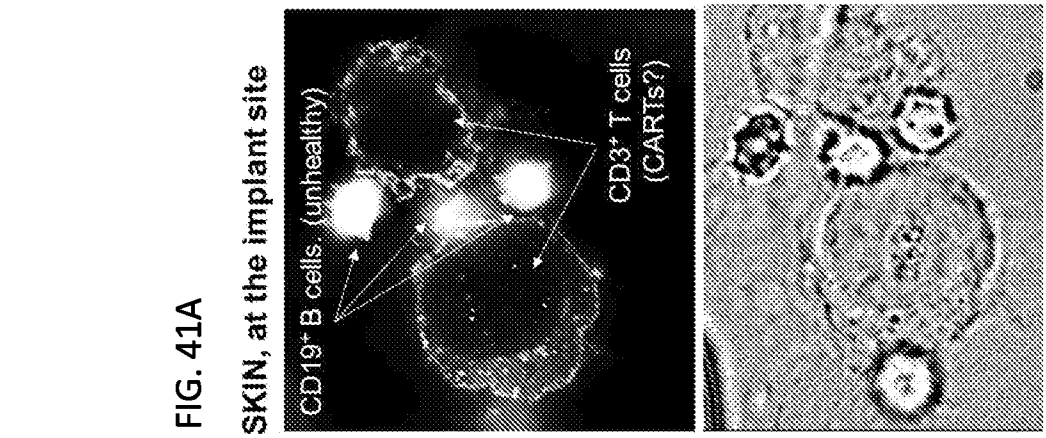


FIG. 41B

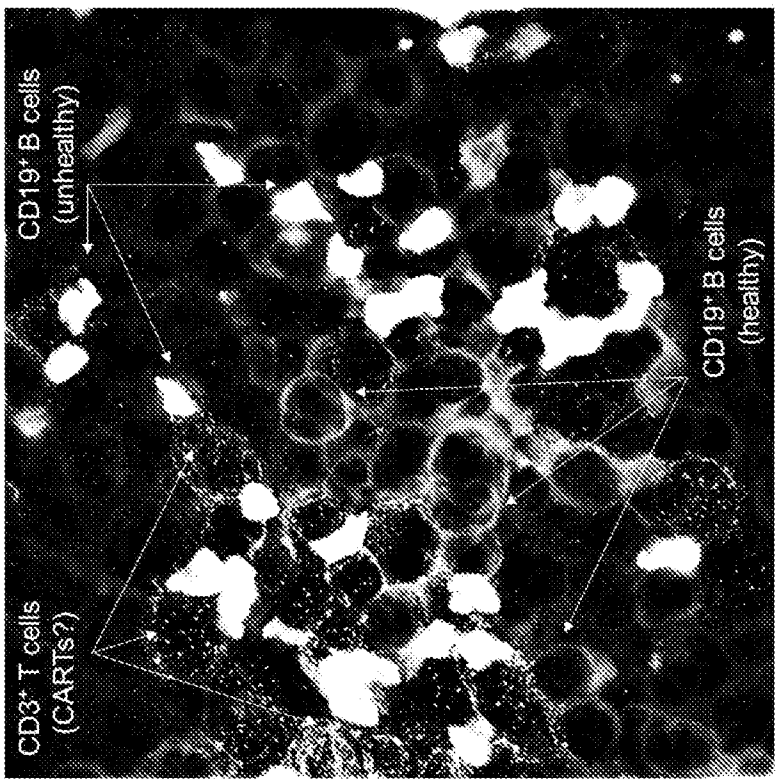
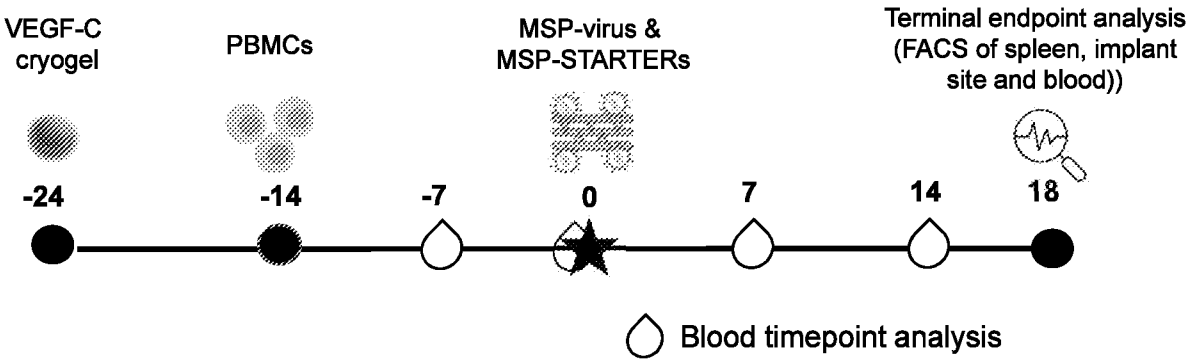
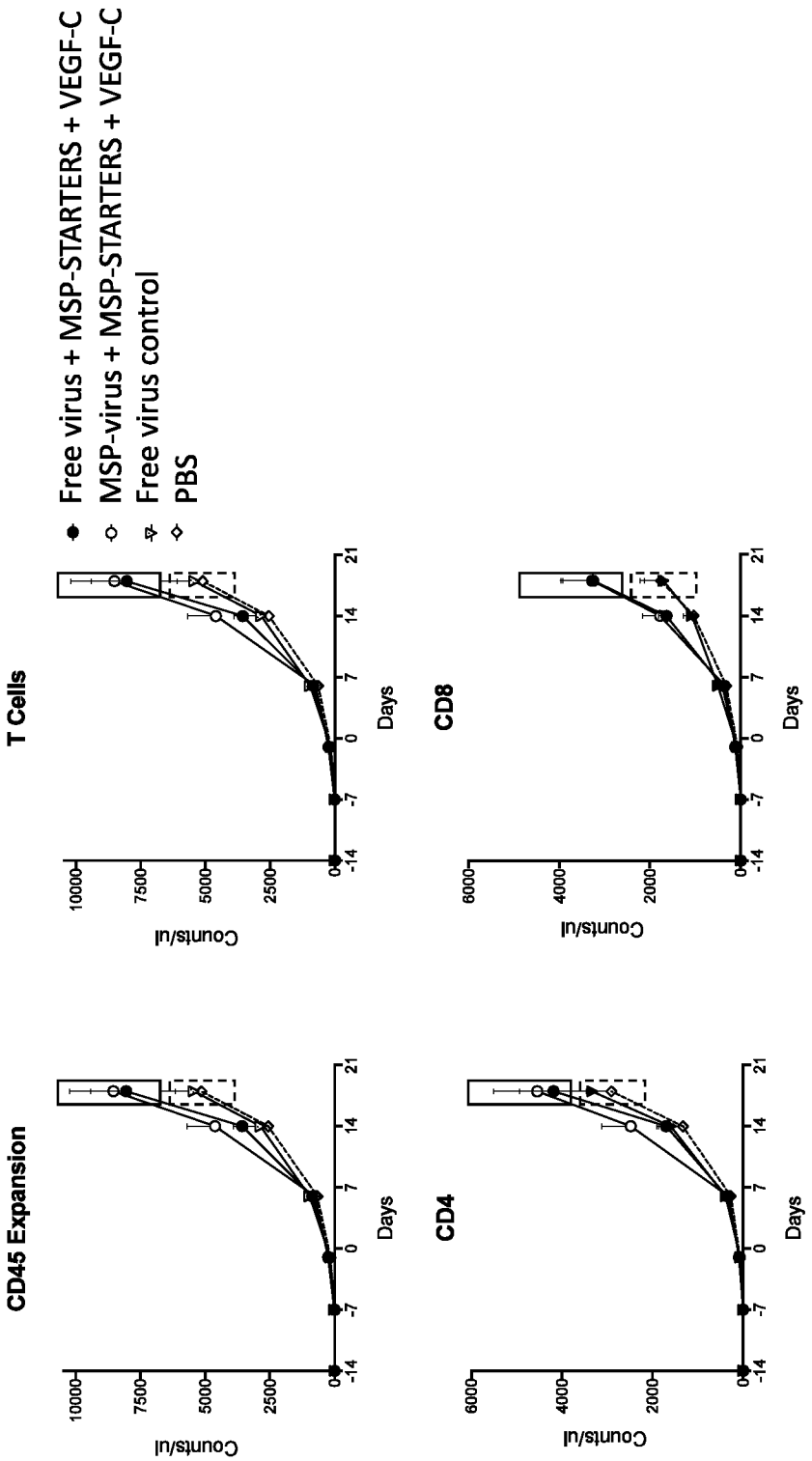


FIG. 42A



Group	Virus	MSP Injection Volume (ul)	MSP Dose (mg)	STARTERS	PBMCs
VEGF-C cryogel + Free Virus + MSP-STARTERs	1.1e^7	10	0.15	89.6	20e^6
VEGF-C cryogel + MSP-Virus + MSP-STARTERS	1.1e^7	20	0.3	89.6	20e^6
VEGF-C cryogel + PBS+ MSP-STARTERS ("PBS)	1.1e^7	10	0.15	89.6	20e^6
Blank cryogel + Free Virus + Blank MSPs ("Free virus control")	1.1e^7	10	0.15	0	20e^6
MSP Concentration: 15 mg/ml					

FIG. 42B


Free virus + MSP-STARTERS + VEGF-C
MSP-virus + MSP-STARTERS + VEGF-C
Free virus control
PBS
T Cells
CD45 Expansion
CD8
CD4
Counts/ul
Days
10000
7500
5000
2500
0
6000
4000
2000
-14
-7
0
7
14
21

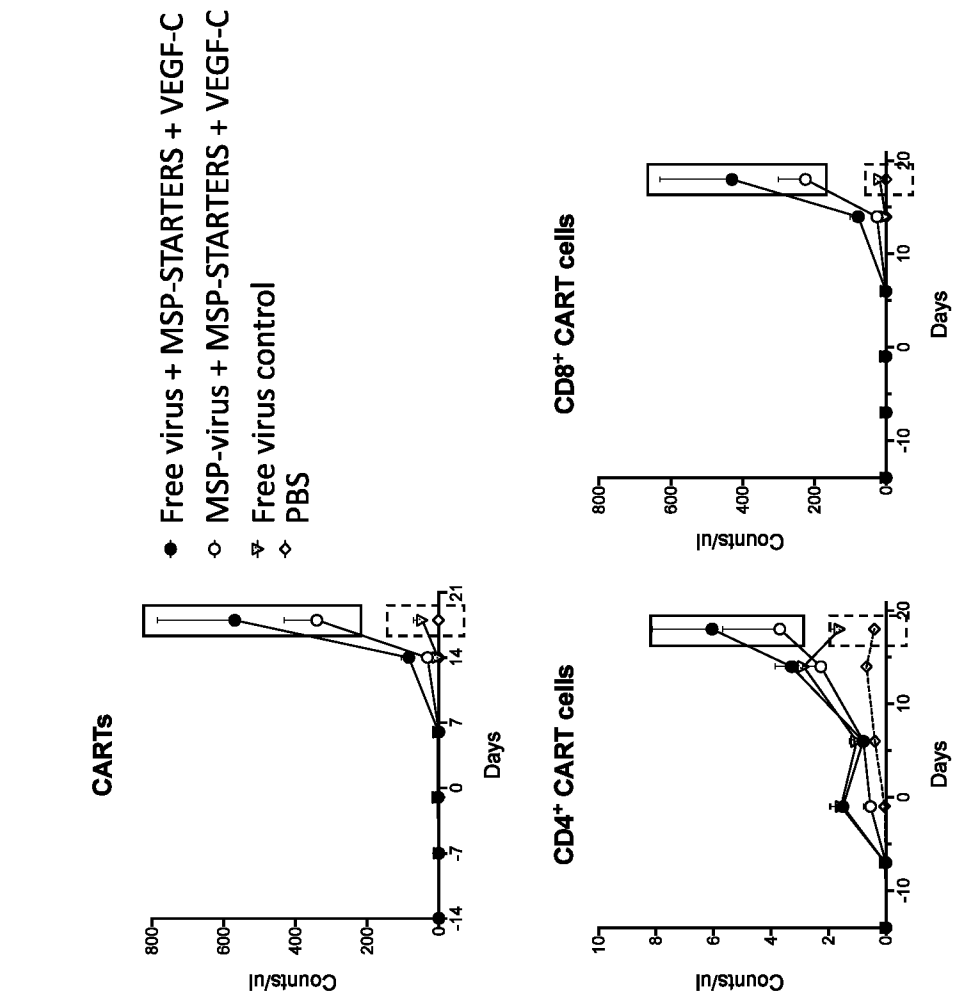

Free virus + MSP-STARTERS + VEGF-C
MSP-virus + MSP-STARTERS + VEGF-C
Free virus control
PBS
CARTs
CD8+ CART cells
CD4+ CART cells
Counts/ul
Days

FIG. 43A

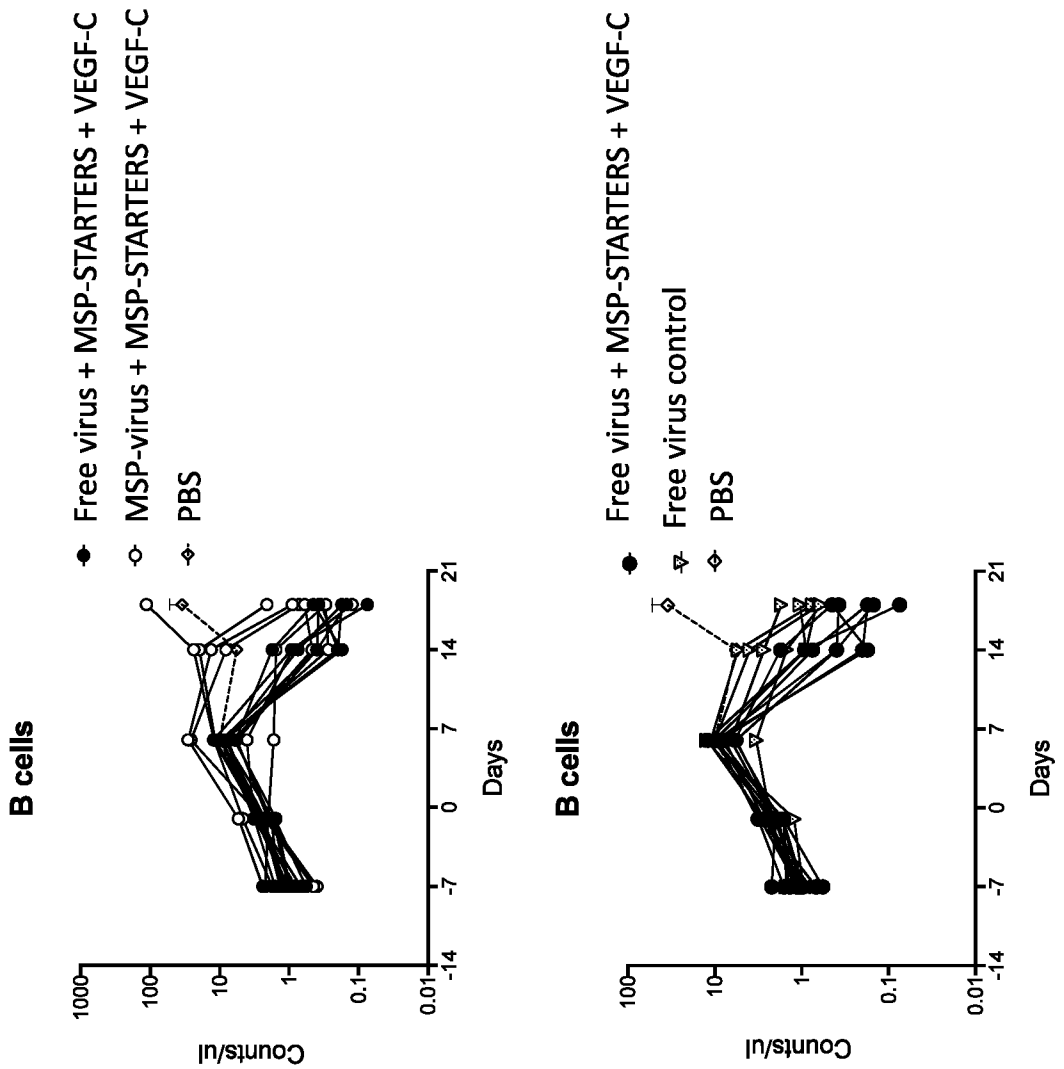

B cells
Free virus + MSP-STARTERS + VEGF-C
MSP-virus + MSP-STARTERS + VEGF-C
PBS
Counts/ul
1000
100
10
1
0.1
0.01
-14
-7
0
7
14
21
Days
B cells
Free virus + MSP-STARTERS + VEGF-C
Free virus control
PBS
Counts/ul
100
10
1
0.1
0.01
-14
-7
0
7
14
21
Days

FIG. 43B

FIG. 44A

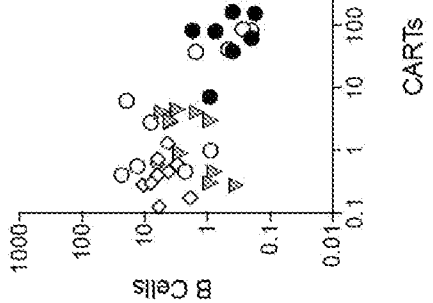


FIG. 44B

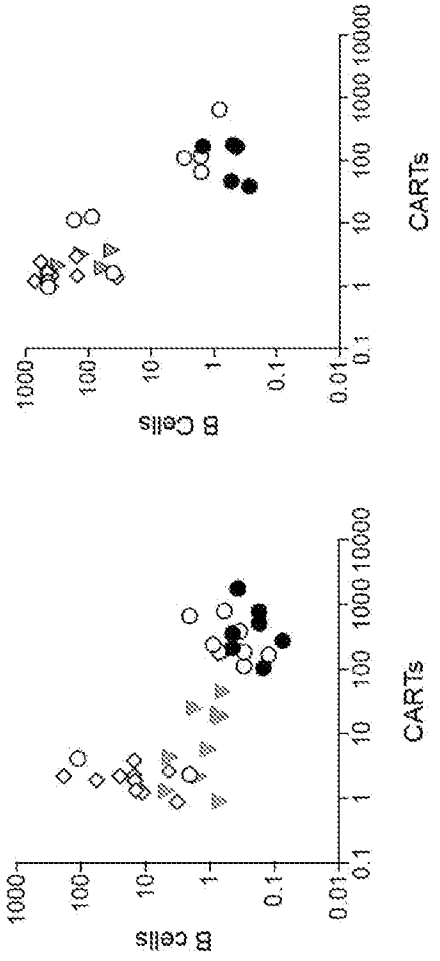


FIG. 45A

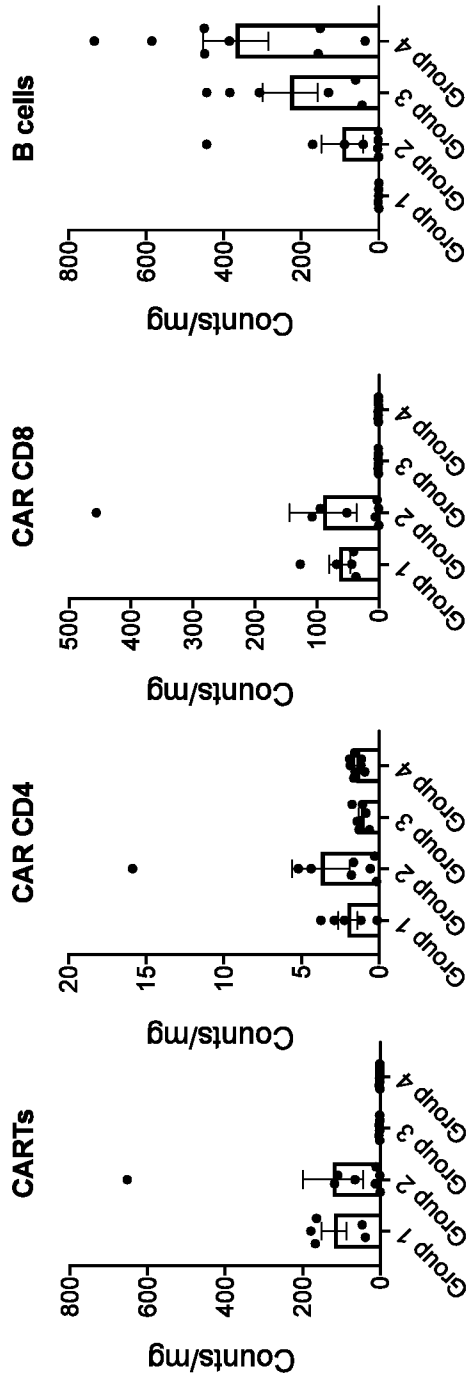
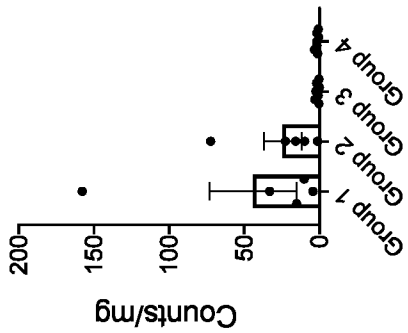
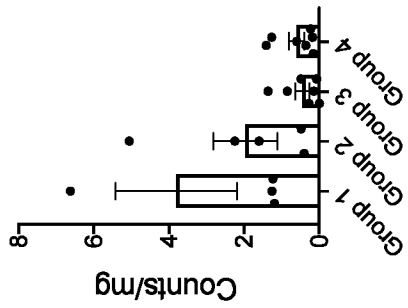


FIG. 45B

Group 1: Free virus + MSP-STARTERS + VEGF-C
Group 2: MSP-virus + MSP-STARTERS + VEGF-C
Group 3: Free virus control
Group 4: PBS

FIG. 46A





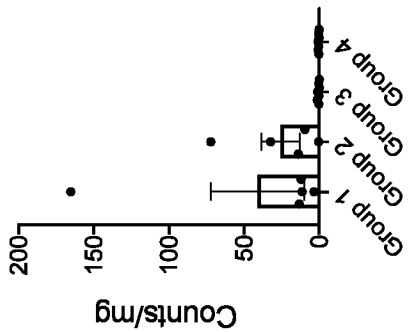
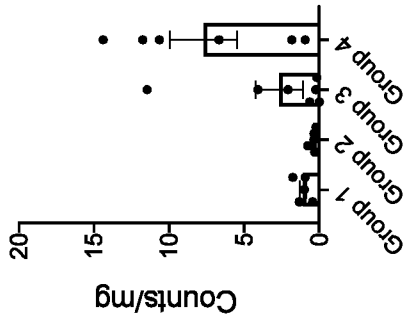
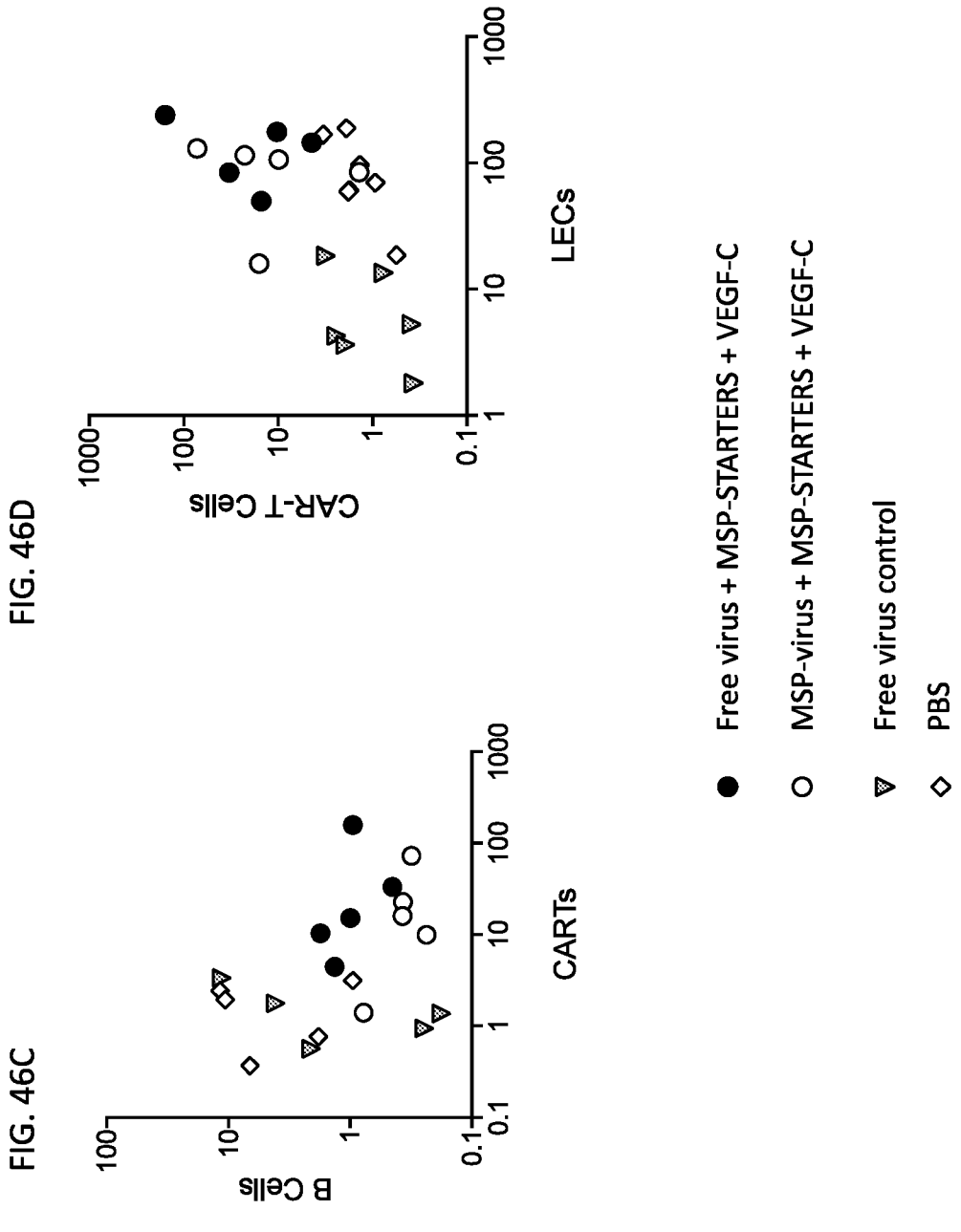


FIG. 46B



Group 1: Free virus + MSP-STARTERS + VEGF-C
Group 2: MSP-virus + MSP-STARTERS + VEGF-C
Group 3: Free virus control
Group 4: PBS


FIG. 46C
B Cells
100
10
1
0.1
0.1
1
10
100
1000
CARTs
FIG. 46D
CAR-T Cells
1000
100
10
1
0.1
1
10
100
1000
LECs
Free virus + MSP-STARTERS + VEGF-C
MSP-virus + MSP-STARTERS + VEGF-C
Free virus control
PBS

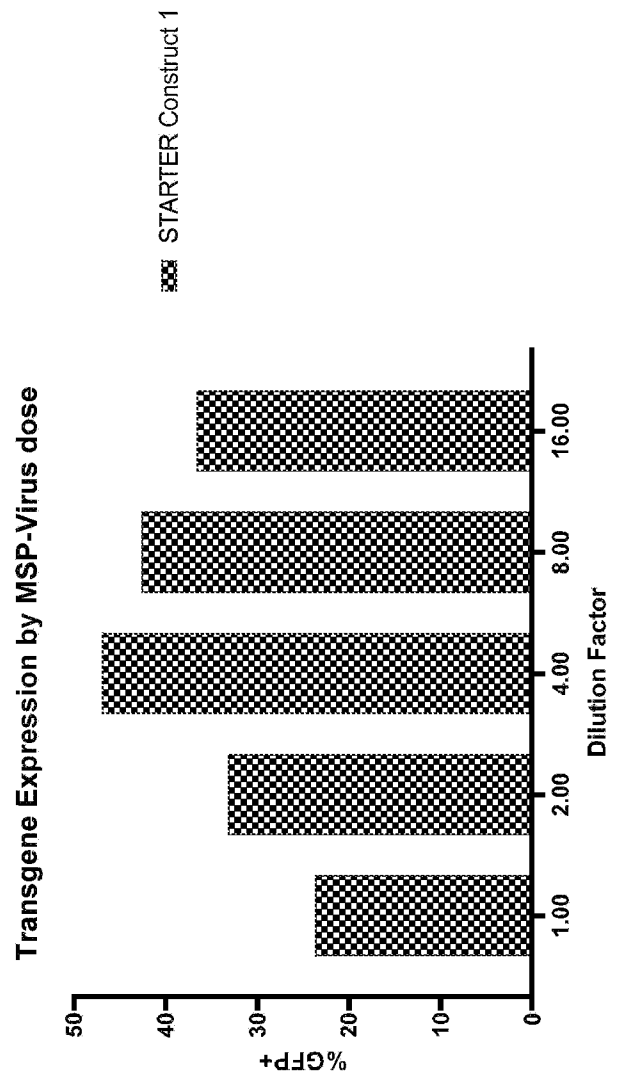

Transgene Expression by MSP-Virus dose
STARTER Construct 1
%GFP+
0
10
20
30
40
50
1.00
2.00
4.00
8.00
16.00
Dilution Factor

FIG. 47

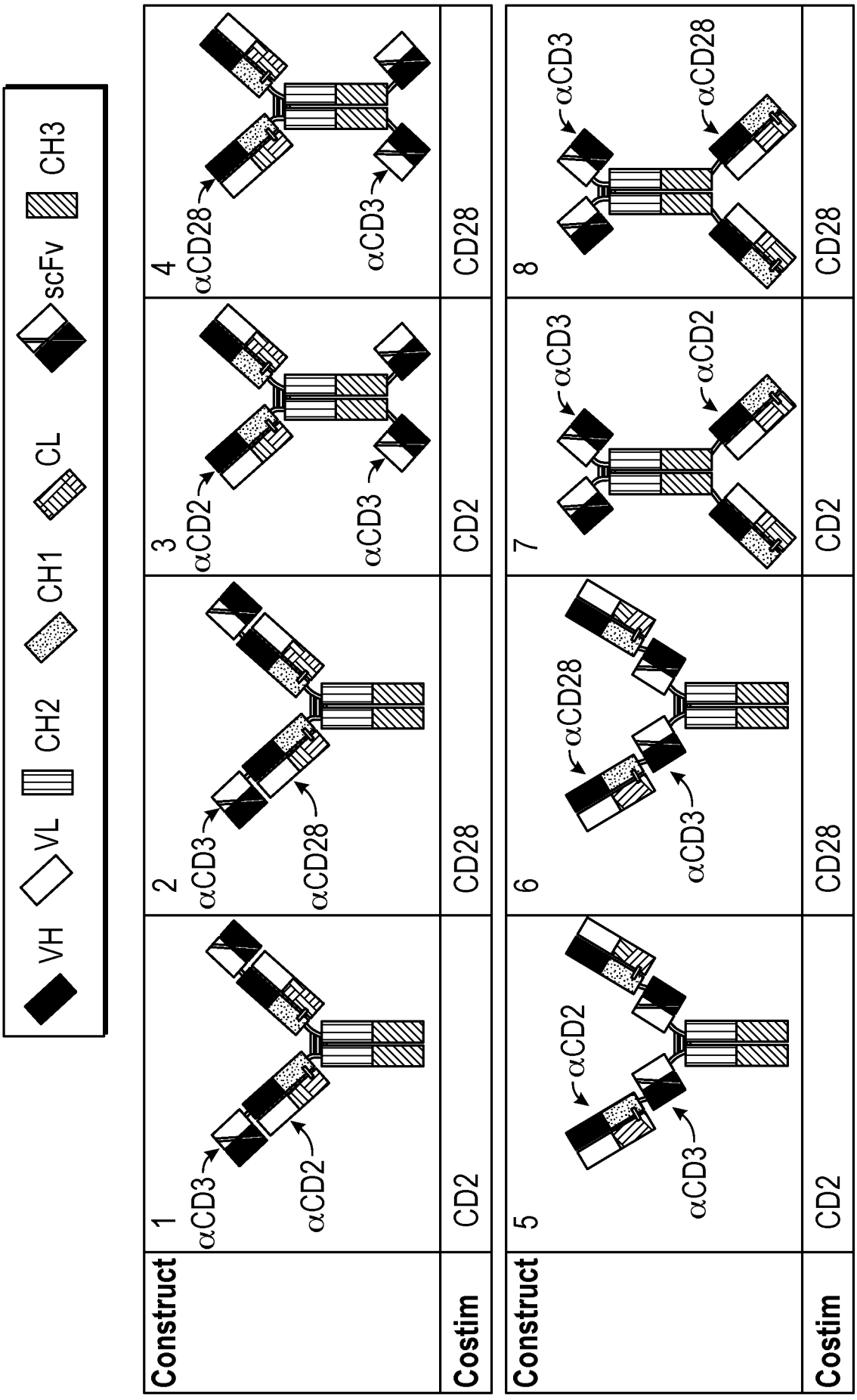

VH
VL
CH2
CH1
CL
scFv
CH3
Construct
1
αCD3
αCD2
2
αCD3
αCD28
3
αCD2
αCD3
4
αCD28
αCD3
Costim
CD2
CD28
CD2
CD28
Construct
5
αCD2
αCD3
6
αCD28
αCD3
7
αCD3
αCD2
8
αCD3
αCD28
Costim
CD2
CD28
CD2
CD28

FIG. 48A

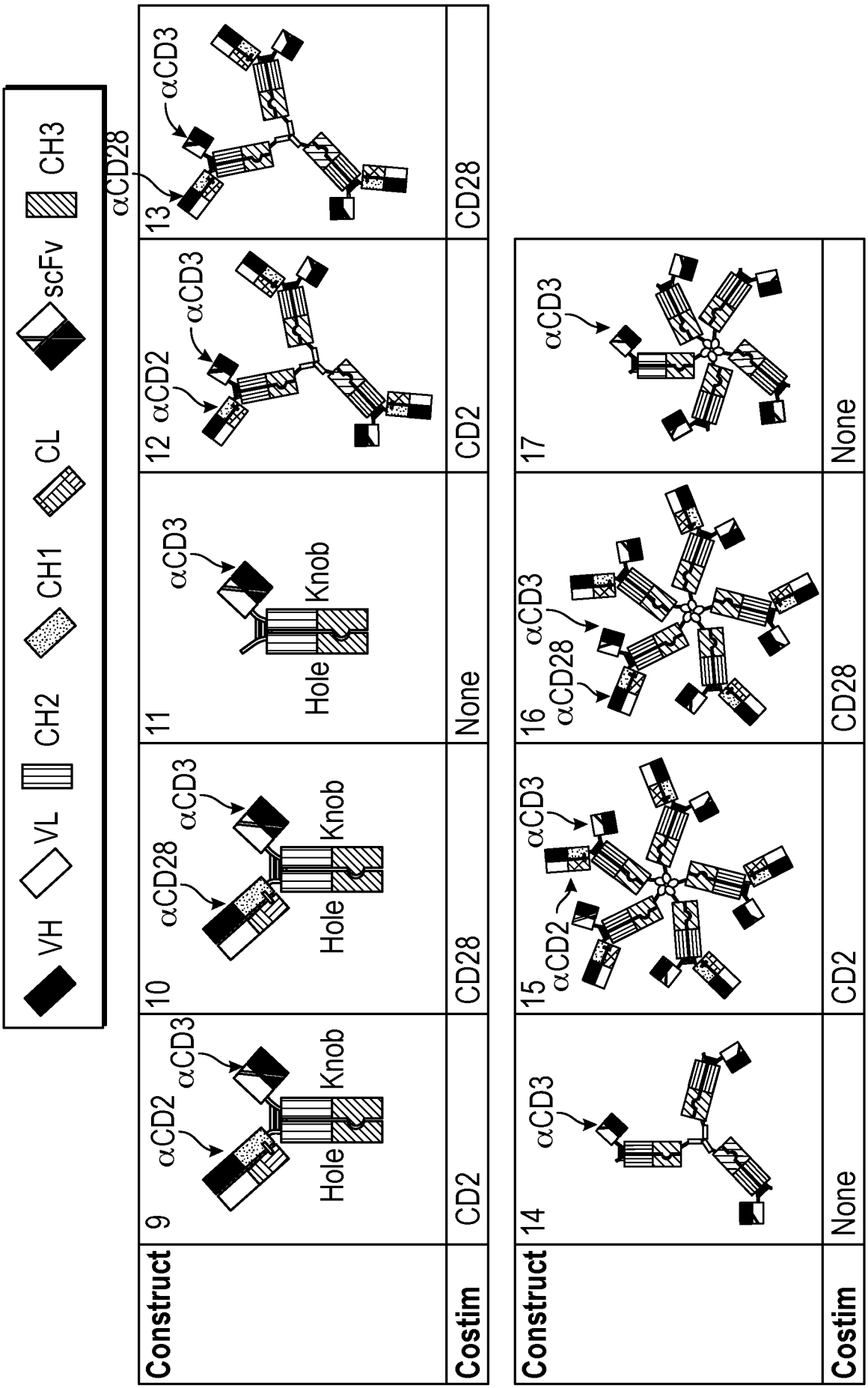

VH
VL
CH2
CH1
CL
scFv
CH3
αCD28
Construct
Costim
9
αCD2
αCD3
Hole
Knob
CD2
10
αCD28
αCD3
Hole
Knob
CD28
11
αCD3
Hole
Knob
None
12
αCD2
αCD3
CD2
13
αCD3
CD28
14
αCD3
None
15
αCD2
αCD3
CD2
16
αCD28
αCD3
CD28
17
αCD3
None

FIG. 48B

Co-Stimulatory Binders	CD3 Binder	Name	
CD25	ANTI-CD3 (1)	F5 CD25	Alternative Costim
IL6Rb	ANTI-CD3 (1)	F5 IL6Rb	
CD27	ANTI-CD3 (1)	F5 CD27	
41BB	ANTI-CD3 (1)	F5 41BB	
ICOS	ANTI-CD3 (1)	F5 ICOS	
CD2	ANTI-CD3 (2)	F5 ANTI-CD3 (2)	Alternative CD3 Binder

FIG. 49A

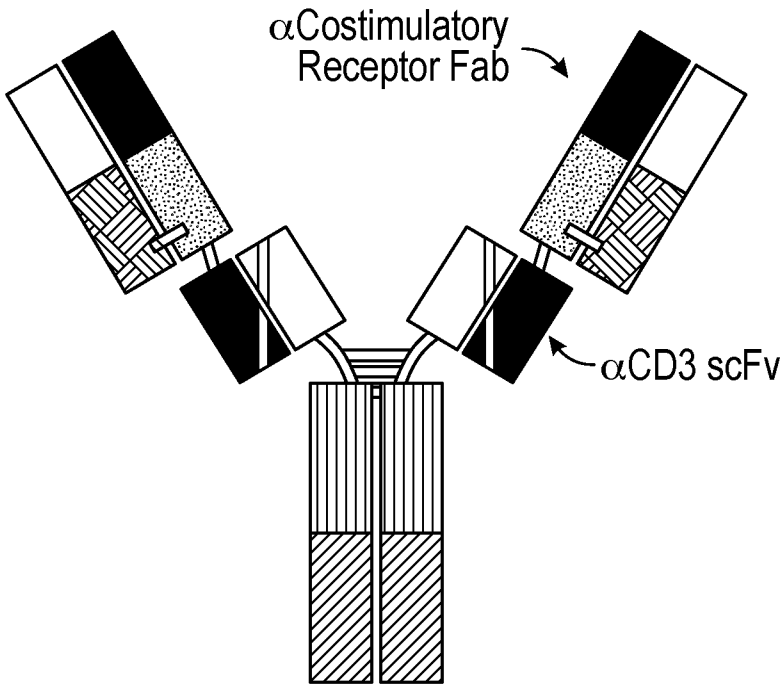


FIG. 49B

Variants	ANTI-CD3 Arm	ANTI-Costim Arm	
NEG2042	ANTI-CD3 (1)	CD2	
NEG2043	ANTI-CD3 (1)	ANTI-CD28 (1)	
NEG2044	ANTI-CD3 (1)	ANTI-CD28 (2)	
NEG2050	ANTI-CD3 (2)	CD2	Alternative CD3 Binders
NEG2051	ANTI-CD3 (3)	CD2	
NEG2052	ANTI-CD3 (2)	ANTI-CD28 (1)	
NEG2053	ANTI-CD3 (3)	ANTI-CD28 (1)	
F5-Not Fc Silenced	ANTI-CD3 (1)	CD2	
Transact		CD28	

FIG. 50A

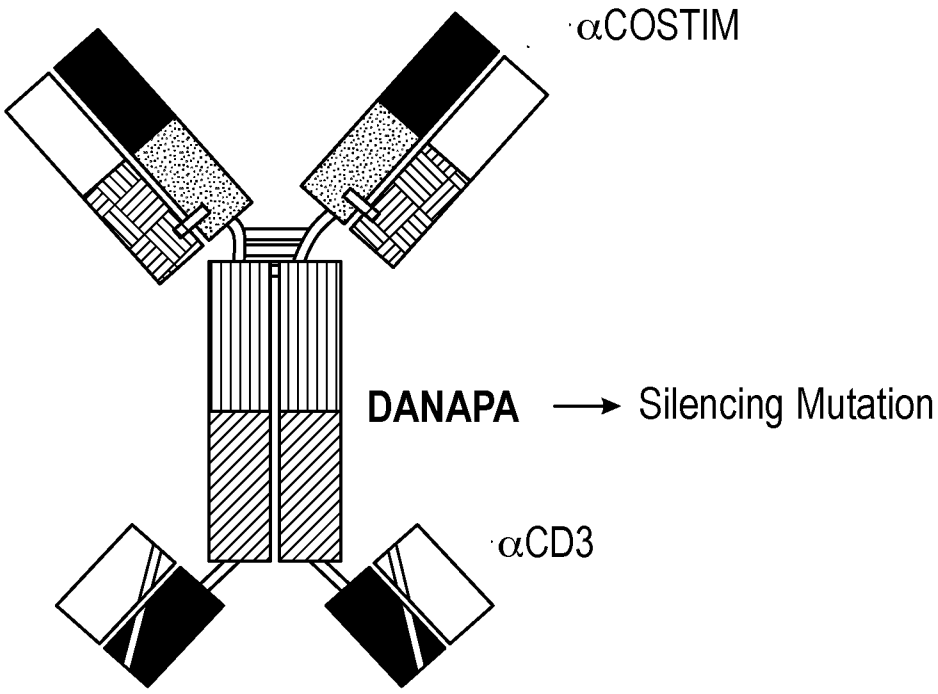


FIG. 50B

FIG. 51A

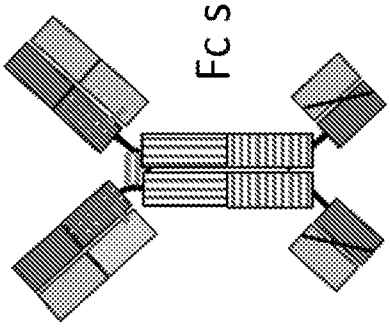


FIG. 51B

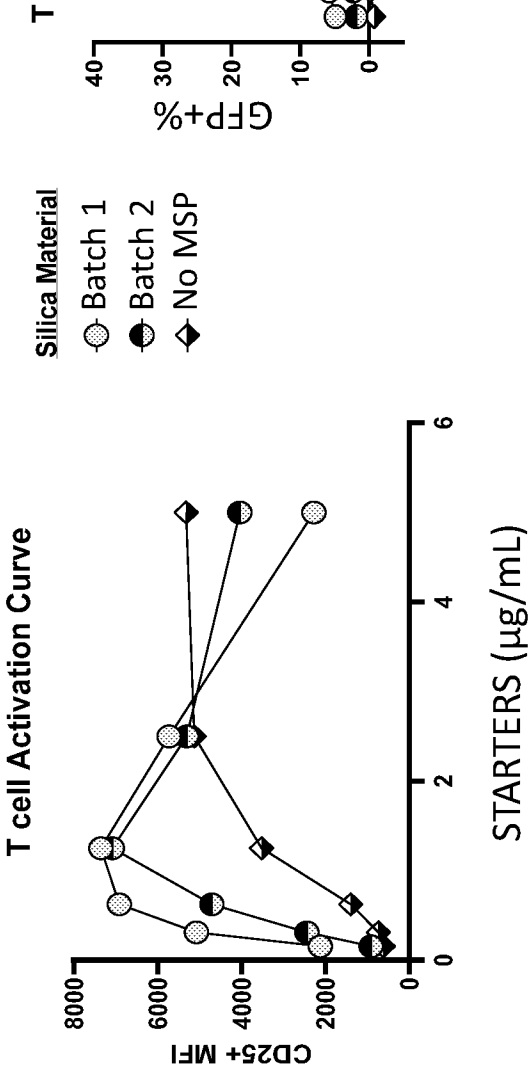
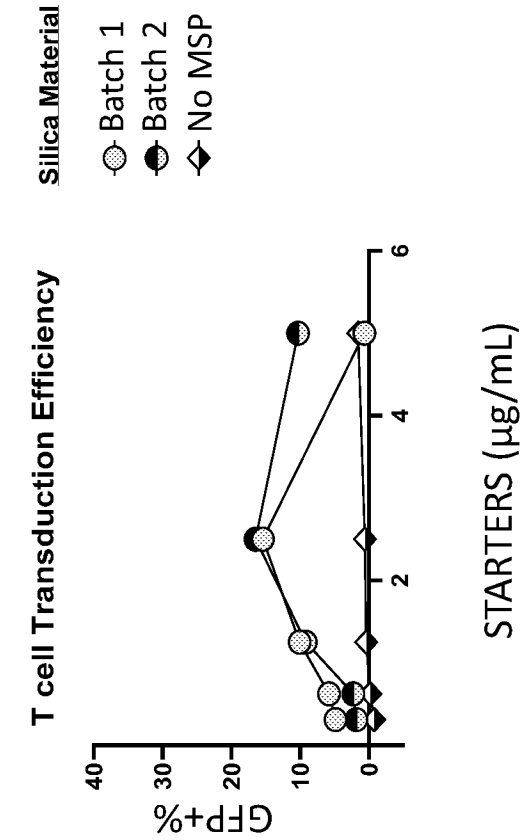


FIG. 51C



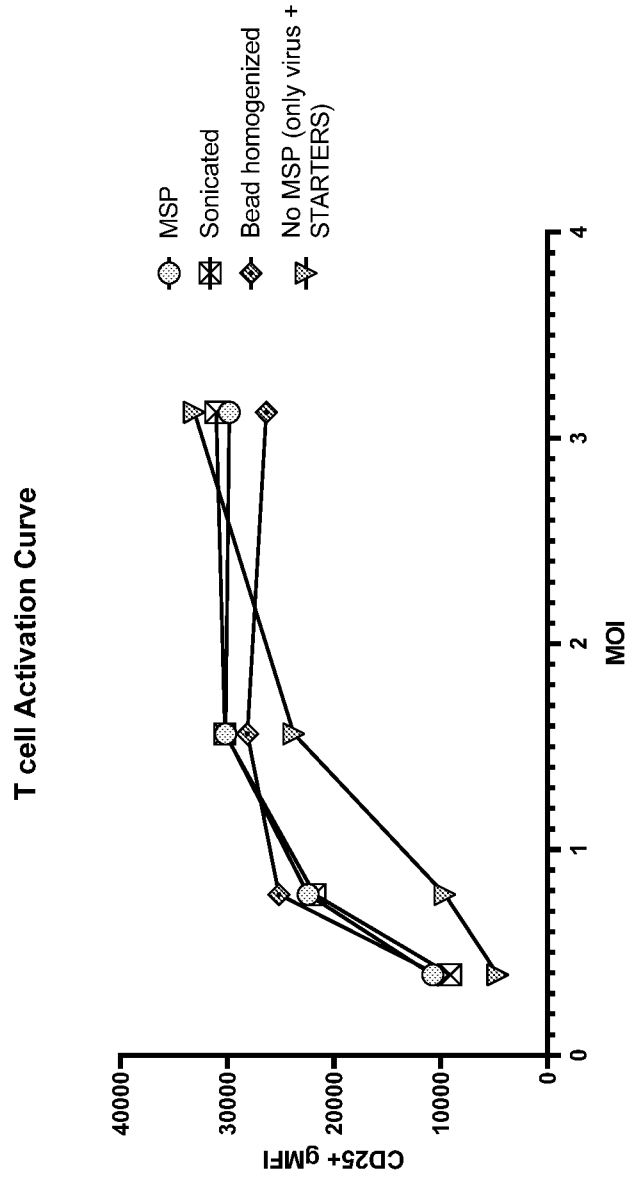


FIG. 52A

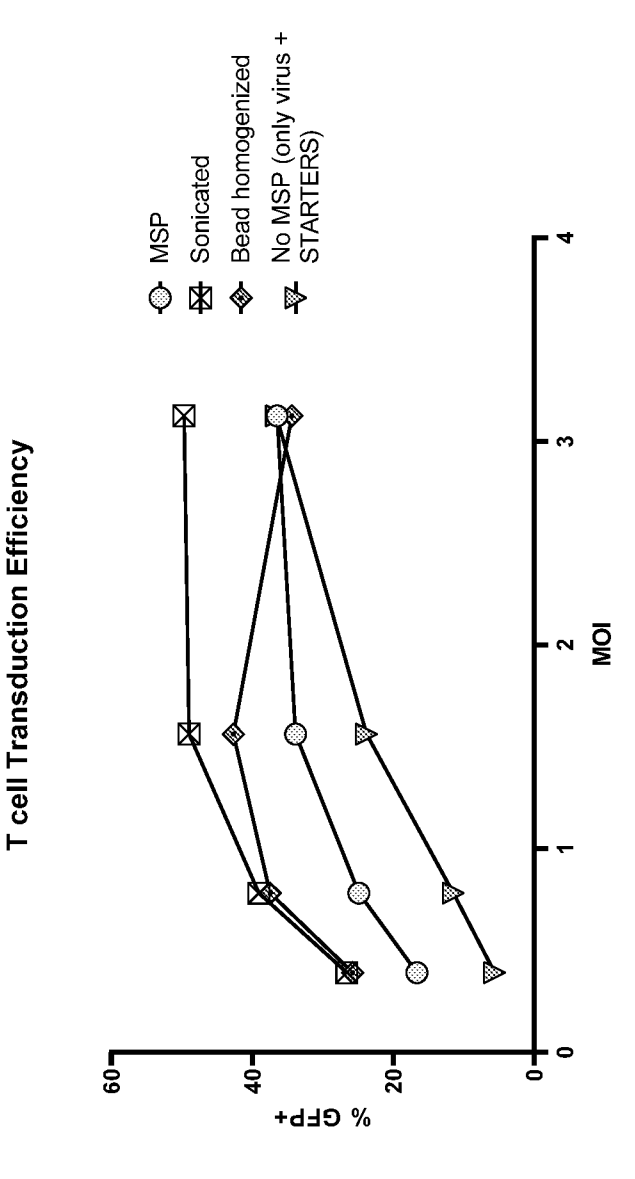
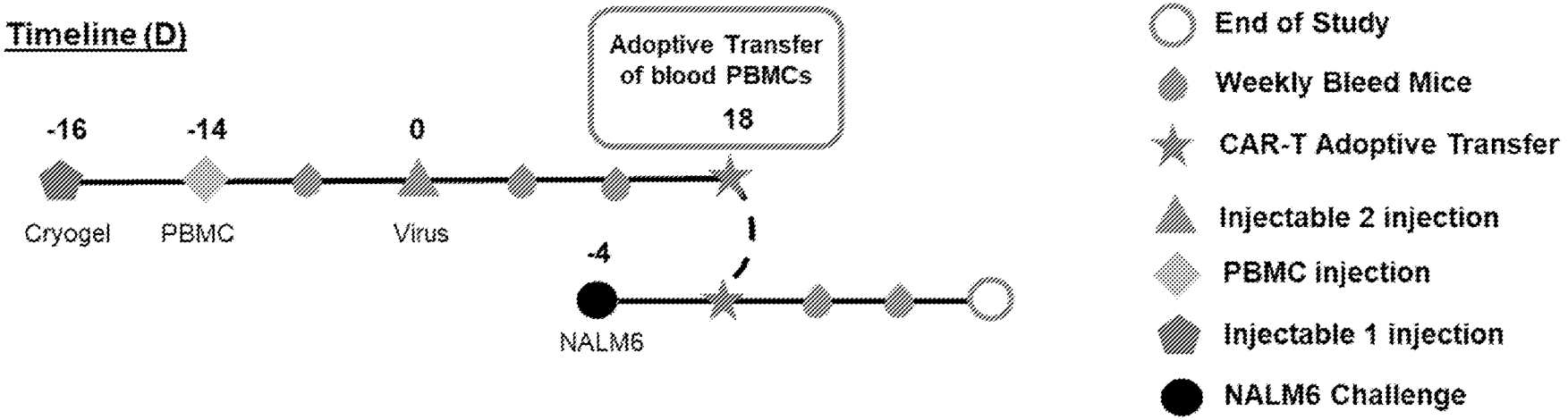


FIG. 52B

FIG. 53A



Groups

1) MSPs with virus and STARTERS
2) Free virus + MSPs with STARTERS
3) PBS + MSPs with STARTERS
4) MSPs with virus (No STARTERS)

VEGF-C Gels

5) MSPs with virus and STARTERS

Blank Gels

FIG. 53B

	Alginate Cryogel	Laponite	VEGF-C Protein	TMA MSPs	STARTERS	CD19 CAR Virus
Injectable 1	+	+	+	-	-	-
Injectable 2	-	-	-	+	+	+

FIG. 53C

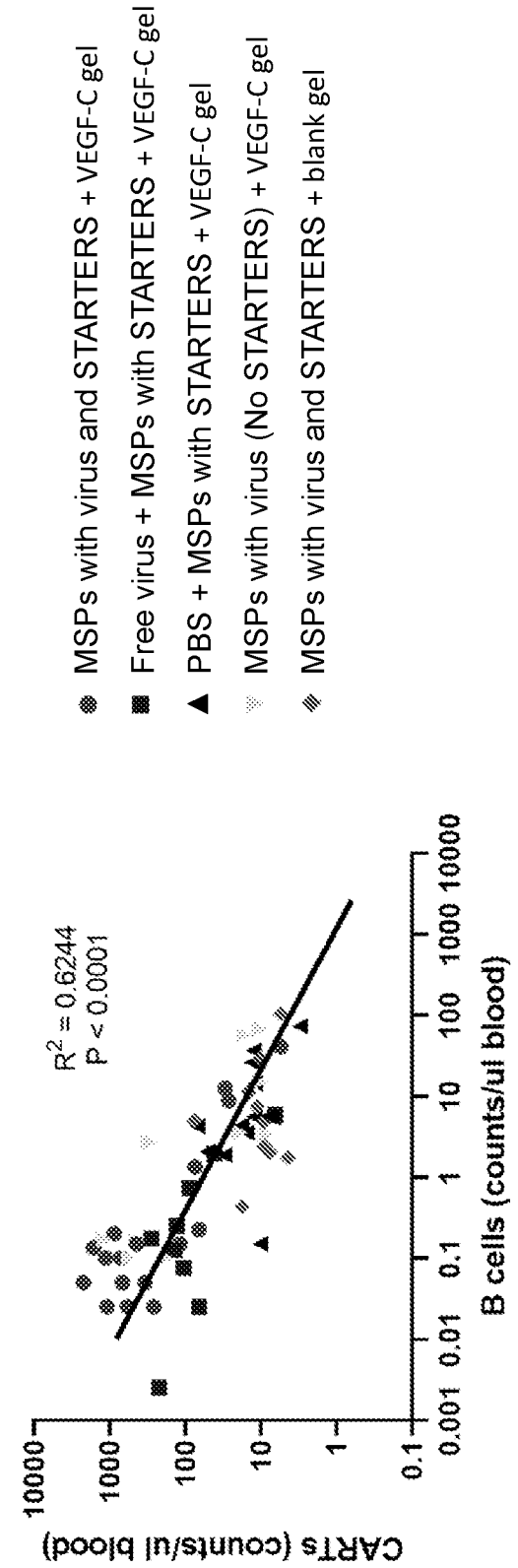


FIG. 53D

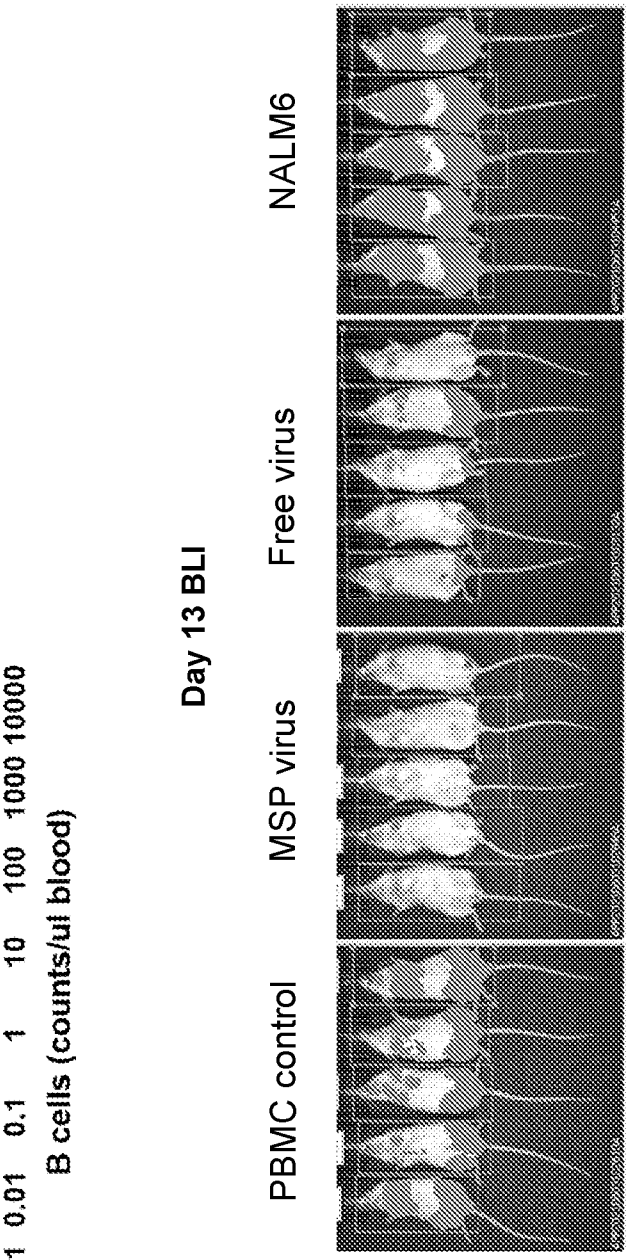


FIG. 53E

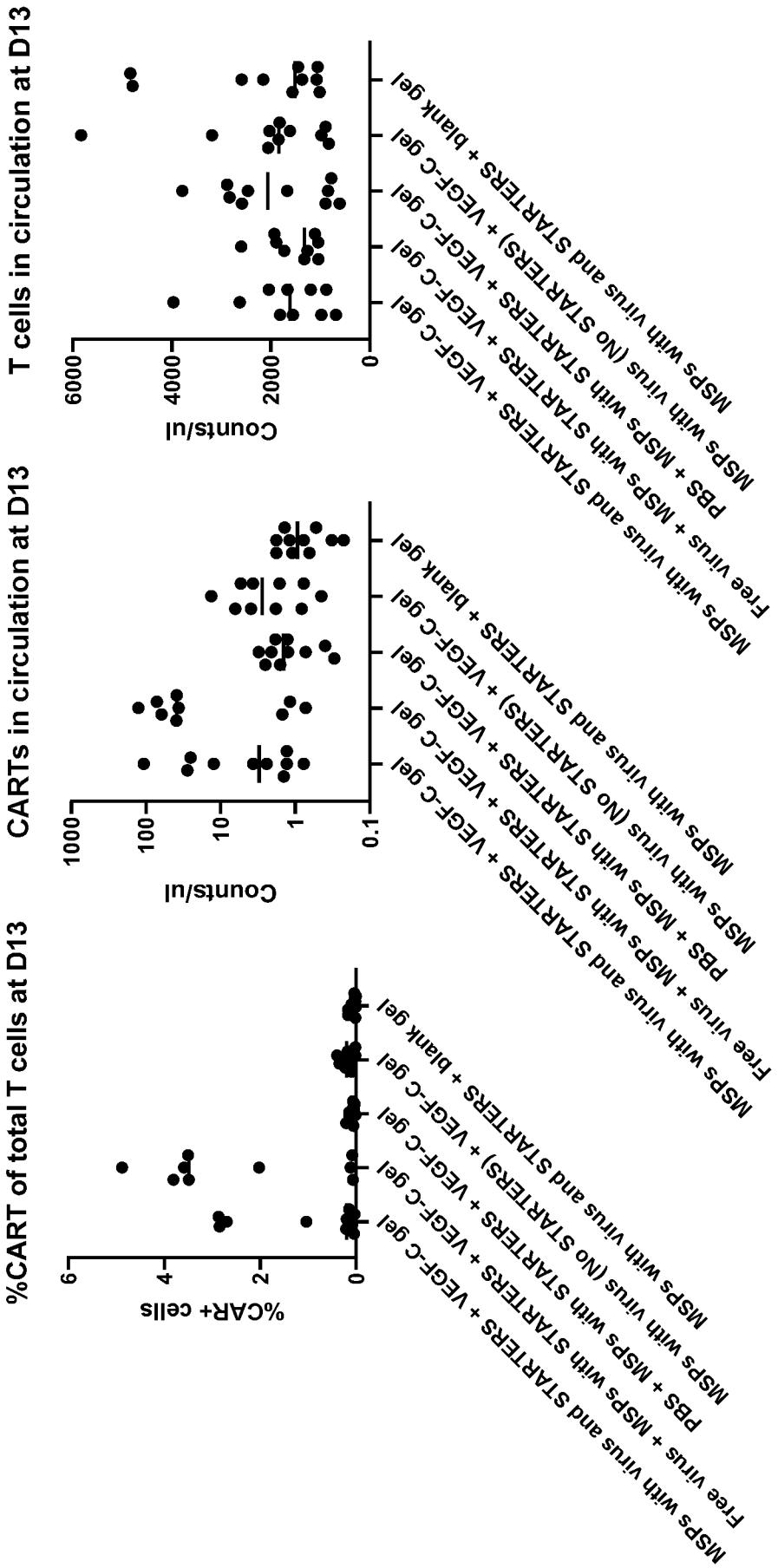


FIG. 53F

FIG. 53G

FIG. 53H

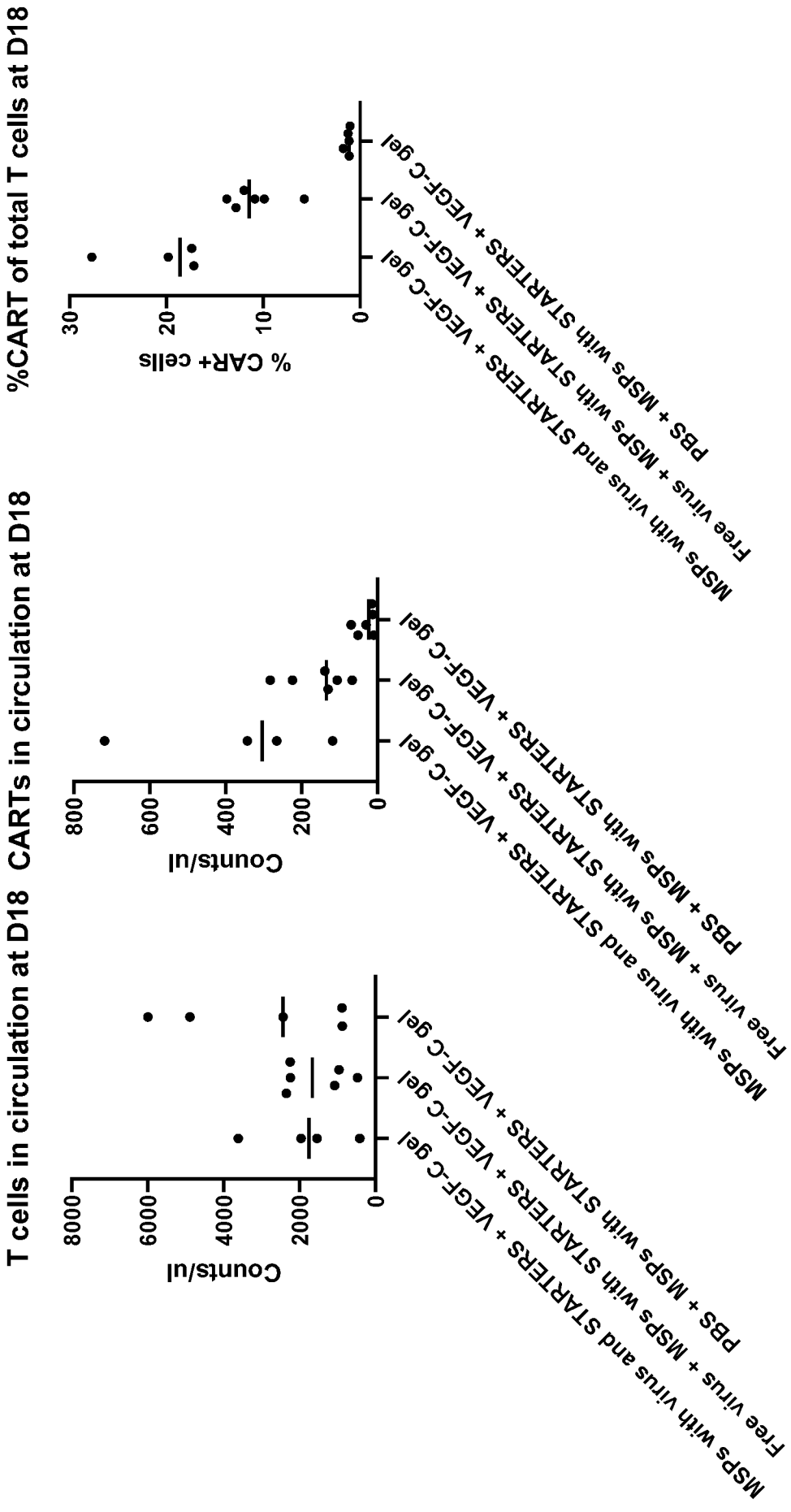


FIG. 53I

FIG. 53J

FIG. 53K

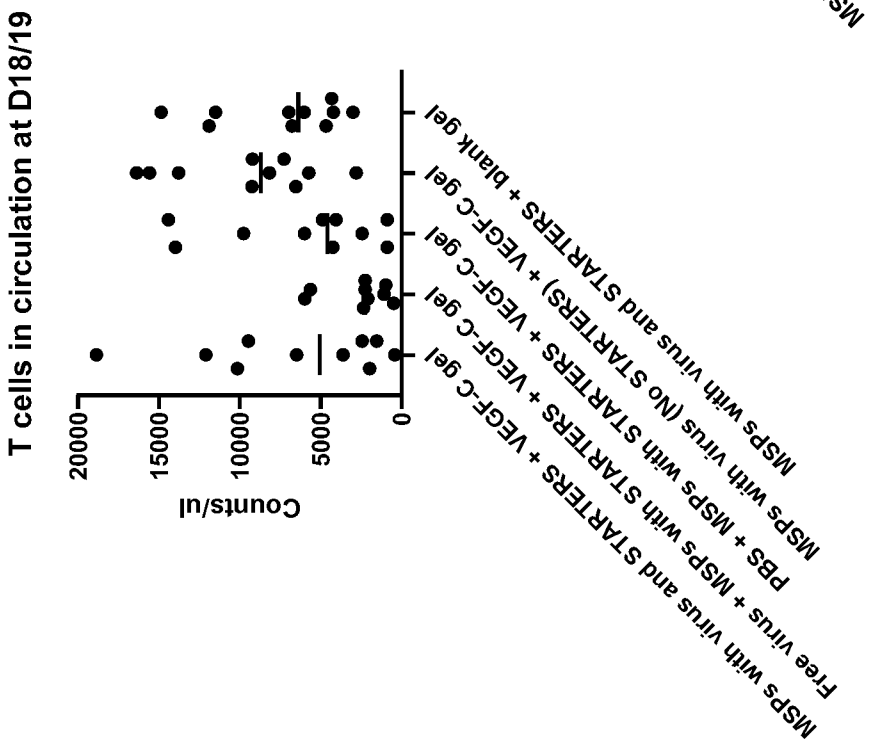


FIG. 53L

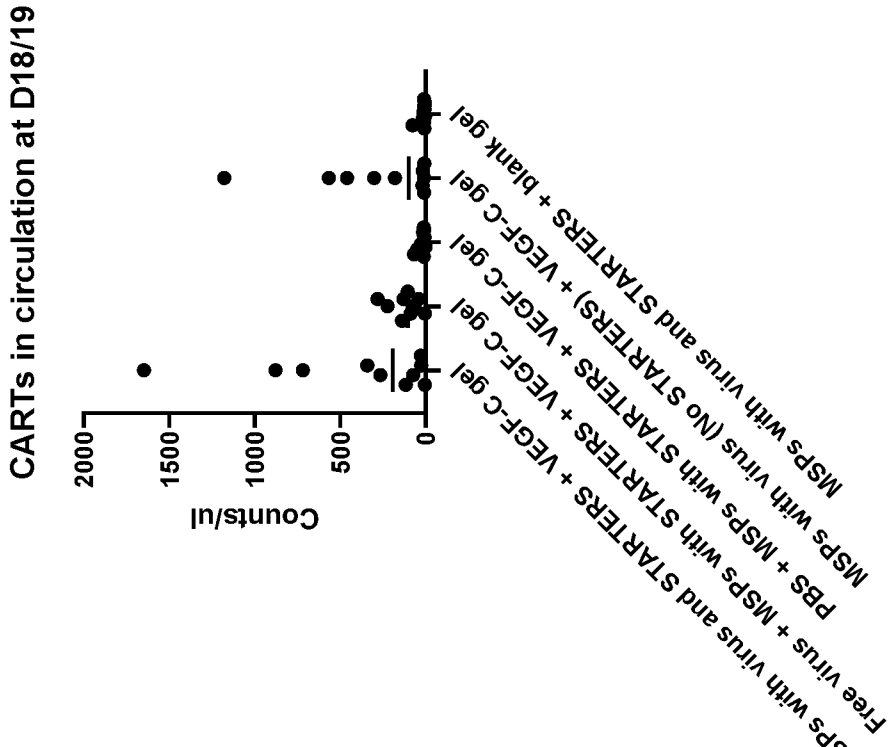


FIG. 54A

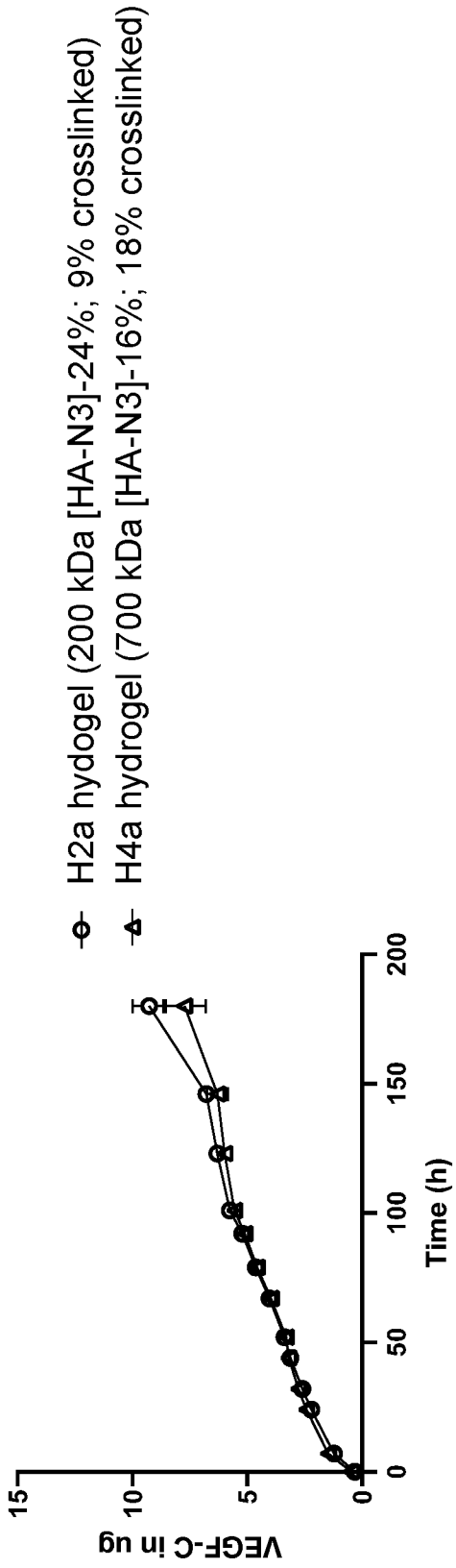


FIG. 54B

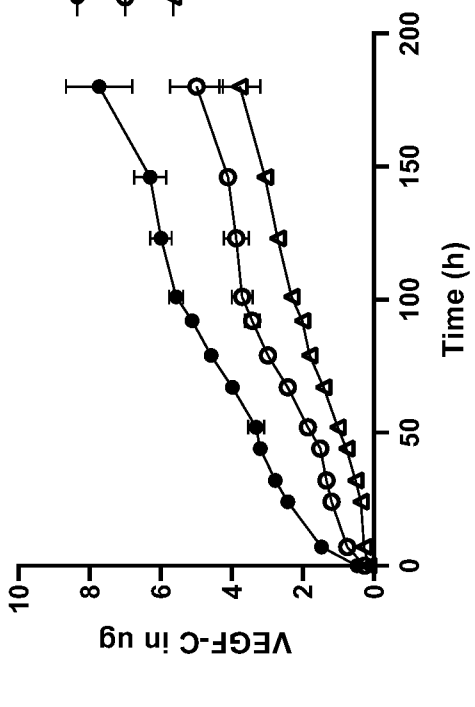


FIG. 54C

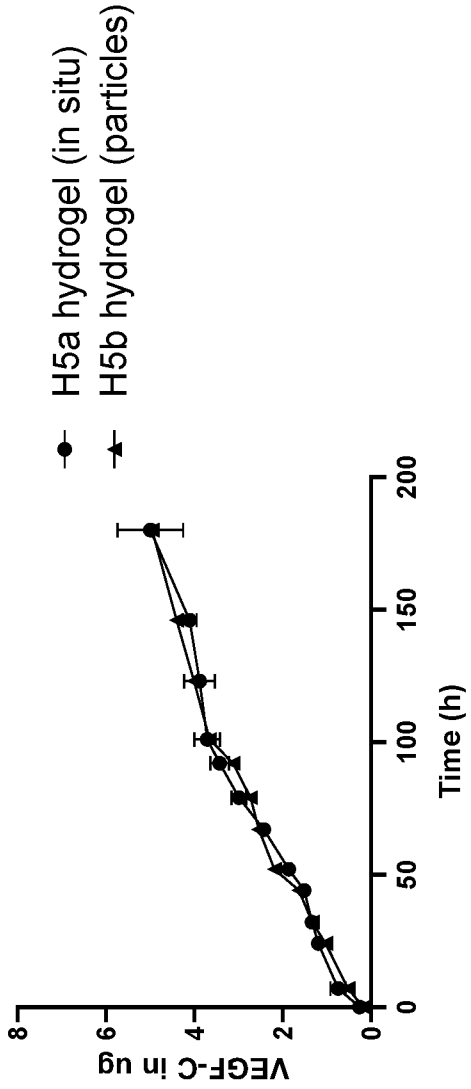


FIG. 54D

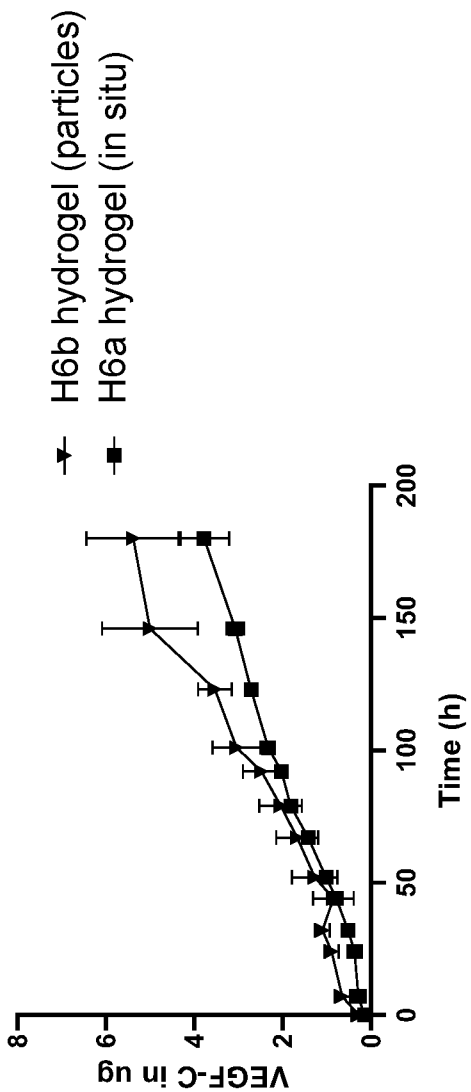


FIG. 55A

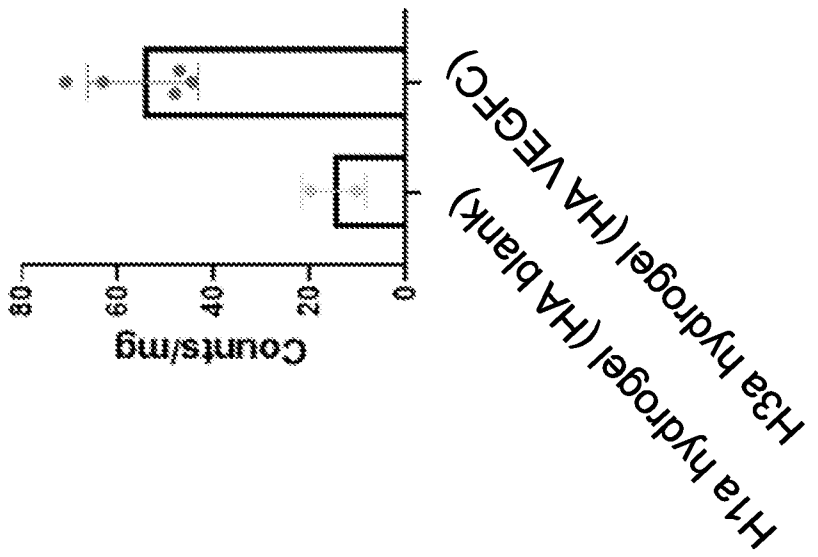
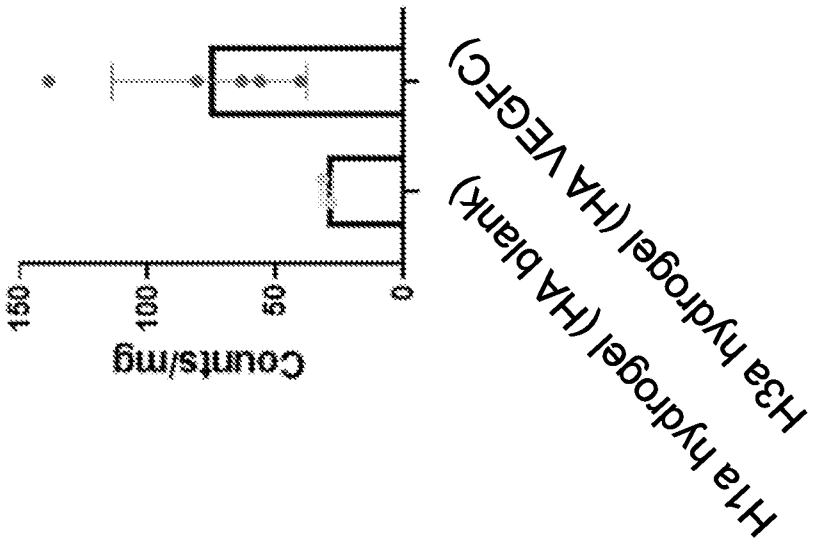


FIG. 55B



SEQUENCE LISTING

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<120> COMPOSITIONS AND METHODS FOR IN VIVO GENERATION OF CAR EXPRESSING CELLS

<130> N2067-7176WO

<140>
<141>

<150> 63/154,609
<151> 2021-02-26

<150> 63/068,876
<151> 2020-08-21

<160> 1417

<170> PatentIn version 3.5

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aaagtgatgt cgtgtactgg ctccgccttt ttcccgaggg tgggggagaa ccgtatataa 180

gtgcagtagt cgccgtgaac gttcttttttc gcaacgggtt tgccgccaga acacaggtaa 240

gtgccgtgtg tggttcccgc gggcctggcc tctttacggg ttatggccct tgcgtgcctt 300

gaattacttc cacctggctg cagtacgtga ttcttgatcc cgagcttcgg gttggaagtg 360

ggtgggagag ttcgaggcct tgcgcttaag gagcccttc gcctcgtgct tgagttgagg 420

cctggcctgg gcgctggggc cgccgcgtgc gaatctggtg gcaccttcgc gcctgtctcg 480

ctgctttcga taagtctcta gccatttaaa atttttgatg acctgctgcg acgcttttt 540

tctggcaaga tagtcttgta aatgcgggcc aagatctgca cactggtatt tcggtttttg 600

gggccgcggg cggcgacggg gcccgtgcgt cccagcgcac atgttcggcg aggcggggcc 660

tgcgagcgcg gccaccgaga atcggacggg ggtagtctca agctggccgg cctgctctgg 720

tgcctggcct cgcgccgccg tgtatcgccc cgccctgggc ggcaaggctg gcccggtcgg 780

caccagttgc gtgagcggaa agatggccgc ttcccggccc tgctgcaggg agctcaaaat 840

ggaggacgcg gcgctcggga gagcgggcgg gtgagtcacc cacacaaagg aaaagggcct 900

ttccgtcctc agccgtcgct tcatgtgact ccacggagta ccgggcgccg tccaggcacc 960

tcgattagtt ctcgagcttt tggagtacgt cgtctttagg ttgggggggag gggttttatg 1020

cgatggagtt tccccacact gagtgggtgg agactgaagt taggccagct tggcacttga 1080

tgtaattctc cttggaattt gccctttttg agtttggatc ttggttcatt ctcaagcctc 1140

agacagtggt tcaaagtttt tttcttccat ttcaggtgtc gtga 1184

<210> 2
<211> 21
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 2
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro
20

<210> 3
<211> 63
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 3
atggccctgc ctgtgacagc cctgctgctg cctctggctc tgctgctgca tgccgctaga 60

ccc 63

<210> 4
<211> 45
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 4
Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala
1 5 10 15

Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly
20 25 30

Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp
35 40 45

<210> 5
<211> 135
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 5
accacgacgc cagcgccgcg accaccaaca ccggcgccca ccatcgcgtc gcagcccctg 60

tccctgcgcc cagaggcgtg ccggccagcg gcgggggcg cagtgcacac gagggggctg 120

gacttcgcct gtgat 135

<210> 6
<211> 230
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 6
Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe

```
1               5                   10                  15

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
            20                  25                  30

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
        35                  40                  45

Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val
    50                  55                  60

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser
65                  70                  75                  80

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
                85                  90                  95

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser
            100                 105                 110

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
        115                 120                 125

Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln
    130                 135                 140

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
145                 150                 155                 160

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
                165                 170                 175

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu
            180                 185                 190

Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser
        195                 200                 205

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
    210                 215                 220
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Leu Ser Leu Gly Lys Met
225 230

<210> 7
<211> 690
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 7
gagagcaagt acggccctcc ctgcccccct tgccctgccc ccgagttcct gggcggaccc 60

agcgtgttcc tgttcccccc caagcccaag gacaccctga tgatcagccg gacccccgag 120

gtgacctgtg tggtggtgga cgtgtcccag gaggaccccg aggtccagtt caactggtac 180

gtggacggcg tggaggtgca caacgccaag accaagcccc gggaggagca gttcaatagc 240

acctaccggg tggtgtccgt gctgaccgtg ctgcaccagg actggctgaa cggcaaggaa 300

tacaagtgta aggtgtccaa caagggcctg cccagcagca tcgagaaaac catcagcaag 360

gccaagggcc agcctcggga gccccaggtg tacaccctgc cccctagcca agaggagatg 420

accaagaacc aggtgtccct gacctgcctg gtgaagggct tctaccccag cgacatcgcc 480

gtggagtggg agagcaacgg ccagcccgag aacaactaca agaccacccc ccctgtgctg 540

gacagcgacg gcagcttctt cctgtacagc cggctgaccg tggacaagag ccggtggcag 600

gagggcaacg tctttagctg ctccgtgatg cacgaggccc tgcacaacca ctacacccag 660

aagagcctga gcctgtccct gggcaagatg 690

<210> 8
<211> 282
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 8
Arg Trp Pro Glu Ser Pro Lys Ala Gln Ala Ser Ser Val Pro Thr Ala
1 5 10 15

```
Gln Pro Gln Ala Glu Gly Ser Leu Ala Lys Ala Thr Thr Ala Pro Ala
            20                  25                  30

Thr Thr Arg Asn Thr Gly Arg Gly Gly Glu Glu Lys Lys Lys Glu Lys
        35                  40                  45

Glu Lys Glu Glu Gln Glu Glu Arg Glu Thr Lys Thr Pro Glu Cys Pro
    50                  55                  60

Ser His Thr Gln Pro Leu Gly Val Tyr Leu Leu Thr Pro Ala Val Gln
65                  70                  75                  80

Asp Leu Trp Leu Arg Asp Lys Ala Thr Phe Thr Cys Phe Val Val Gly
                85                  90                  95

Ser Asp Leu Lys Asp Ala His Leu Thr Trp Glu Val Ala Gly Lys Val
            100                 105                 110

Pro Thr Gly Gly Val Glu Glu Gly Leu Leu Glu Arg His Ser Asn Gly
        115                 120                 125

Ser Gln Ser Gln His Ser Arg Leu Thr Leu Pro Arg Ser Leu Trp Asn
    130                 135                 140

Ala Gly Thr Ser Val Thr Cys Thr Leu Asn His Pro Ser Leu Pro Pro
145                 150                 155                 160

Gln Arg Leu Met Ala Leu Arg Glu Pro Ala Ala Gln Ala Pro Val Lys
                165                 170                 175

Leu Ser Leu Asn Leu Leu Ala Ser Ser Asp Pro Pro Glu Ala Ala Ser
            180                 185                 190

Trp Leu Leu Cys Glu Val Ser Gly Phe Ser Pro Pro Asn Ile Leu Leu
        195                 200                 205

Met Trp Leu Glu Asp Gln Arg Glu Val Asn Thr Ser Gly Phe Ala Pro
    210                 215                 220
```

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Ala Arg Pro Pro Pro Gln Pro Gly Ser Thr Thr Phe Trp Ala Trp Ser
225                 230                 235                 240


Val Leu Arg Val Pro Ala Pro Pro Ser Pro Gln Pro Ala Thr Tyr Thr
                245                 250                 255


Cys Val Val Ser His Glu Asp Ser Arg Thr Leu Leu Asn Ala Ser Arg
            260                 265                 270


Ser Leu Glu Val Ser Tyr Val Thr Asp His
        275                 280


<210> 9
<211> 847
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 9
aggtggcccg aaagtcccaa ggcccaggca tctagtgttc ctactgcaca gccccaggca       60

gaaggcagcc tagccaaagc tactactgca cctgccacta cgcgcaatac tggccgtggc      120

ggggaggaga agaaaaagga gaaagagaaa gaagaacagg aagagaggga gaccaagacc      180

cctgaatgtc catcccatac ccagccgctg ggcgtctatc tcttgactcc cgcagtacag      240

gacttgtggc ttagagataa ggccaccttt acatgtttcg tcgtgggctc tgacctgaag      300

gatgcccatt tgacttggga ggttgccgga aaggtaccca cagggggggt tgaggaaggg      360

ttgctggagc gccattccaa tggctctcag agccagcact caagactcac ccttccgaga      420

tccctgtgga acgccgggac ctctgtcaca tgtactctaa atcatcctag cctgccccca      480

cagcgtctga tggcccttag agagccagcc gcccaggcac cagttaagct tagcctgaat      540

ctgctcgcca gtagtgatcc cccagaggcc gccagctggc tcttatgcga agtgtccggc      600

tttagcccgc ccaacatctt gctcatgtgg ctggaggacc agcgagaagt gaacaccagc      660

ggcttcgctc cagcccggcc cccaccccag ccgggttcta ccacattctg ggcctggagt      720

gtcttaaggg tcccagcacc acctagcccc cagccagcca catacacctg tgttgtgtcc      780

catgaagata gcaggaccct gctaaatgct tctaggagtc tggaggtttc ctacgtgact      840
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gaccatt 847

<210> 10
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 10
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10

<210> 11
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 11
ggtggcggag gttctggagg tggaggttcc 30

<210> 12
<211> 24
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 12
Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu
1 5 10 15

Ser Leu Val Ile Thr Leu Tyr Cys
20

<210> 13
<211> 72

<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 13
atctacatct gggcgccctt ggccgggact tgtggggtcc ttctcctgtc actggttatc 60

acccttttact gc 72

<210> 14
<211> 42
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 14
Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
1 5 10 15

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
20 25 30

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu
35 40

<210> 15
<211> 126
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 15
aaacggggca gaaagaaact cctgtatata ttcaaacaac catttatgag accagtacaa 60

actactcaag aggaagatgg ctgtagctgc cgatttccag aagaagaaga aggaggatgt 120

gaactg 126

<210> 16
<211> 48
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 16
Gln Arg Arg Lys Tyr Arg Ser Asn Lys Gly Glu Ser Pro Val Glu Pro
1 5 10 15

Ala Glu Pro Cys Arg Tyr Ser Cys Pro Arg Glu Glu Glu Gly Ser Thr
20 25 30

Ile Pro Ile Gln Glu Asp Tyr Arg Lys Pro Glu Pro Ala Cys Ser Pro
35 40 45

<210> 17
<211> 123
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 17
aggagtaaga ggagcaggct cctgcacagt gactacatga acatgactcc ccgccgcccc 60

gggcccaccc gcaagcatta ccagccctat gccccaccac gcgacttcgc agcctatcgc 120

tcc 123

<210> 18
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 18
Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly

1 5 10 15

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
20 25 30

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
35 40 45

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
50 55 60

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
65 70 75 80

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
85 90 95

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
100 105 110

<210> 19
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 19
agagtgaagt tcagcaggag cgcagacgcc cccgcgtaca agcagggcca gaaccagctc 60

tataacgagc tcaatctagg acgaagagag gagtacgatg ttttggacaa gagacgtggc 120

cgggaccctg agatgggggg aaagccgaga aggaagaacc ctcaggaagg cctgtacaat 180

gaactgcaga aagataagat ggcggaggcc tacagtgaga ttgggatgaa aggcgagcgc 240

cggaggggca aggggcacga tggcctttac cagggtctca gtacagccac caaggacacc 300

tacgacgccc ttcacatgca ggccctgccc cctcgc 336

<210> 20
<211> 112
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 20
Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly
1 5 10 15

Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr
20 25 30

Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
35 40 45

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
50 55 60

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
65 70 75 80

Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala
85 90 95

Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
100 105 110

<210> 21
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 21
agagtgaagt tcagcaggag cgcagacgcc cccgcgtacc agcagggcca gaaccagctc 60

tataacgagc tcaatctagg acgaagagag gagtacgatg ttttggacaa gagacgtggc 120

cgggaccctg agatgggggg aaagccgaga aggaagaacc ctcaggaagg cctgtacaat 180

gaactgcaga aagataagat ggcggaggcc tacagtgaga ttgggatgaa aggcgagcgc 240

cggaggggca aggggcacga tggcctttac cagggtctca gtacagccac caaggacacc 300

tacgacgccc ttcacatgca ggccctgccc cctcgc 336

<210> 22
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<220>
<221> source
<223> /note="See specification as filed for detailed description of substitutions and preferred embodiments"

<400> 22
Gly Gly Gly Gly Ser
1 5

<210> 23
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic oligonucleotide"

<400> 23
ggtggcggag gttctggagg tggaggttcc 30

<210> 24
<211> 150
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 24
Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr
1 5 10 15

Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
            20   25   30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
        35   40   45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
    50   55   60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65   70   75   80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
                85   90   95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
            100   105   110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
        115   120   125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
    130   135   140

Gln Phe Gln Thr Leu Val
145   150

<210> 25
<211> 450
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 25
cccggatggt ttctggactc tccggatcgc ccgtggaatc ccccaacctt ctcaccggca 60

ctcttggttg tgactgaggg cgataatgcg accttcacgt gctcgttctc caacacctcc 120

gaatcattcg tgctgaactg gtaccgcatg agcccgtcaa accagaccga caagctcgcc 180

gcgtttccgg aagatcggtc gcaaccggga caggattgtc ggttccgcgt gactcaactg 240

ccgaatggca gagacttcca catgagcgtg gtccgcgcta ggcgaaacga ctccgggacc 300

tacctgtgcg gagccatctc gctggcgcct aaggcccaaa tcaaagagag cttgagggcc 360

gaactgagag tgaccgagcg cagagctgag gtgccaactg cacatccatc cccatcgcct 420

cggcctgcgg ggcagtttca gaccctggtc 450

<210> 26
<211> 394
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 26
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro
20 25 30

Trp Asn Pro Pro Thr Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly
35 40 45

Asp Asn Ala Thr Phe Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe
50 55 60

Val Leu Asn Trp Tyr Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu
65 70 75 80

Ala Ala Phe Pro Glu Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe
85 90 95

Arg Val Thr Gln Leu Pro Asn Gly Arg Asp Phe His Met Ser Val Val
100 105 110

Arg Ala Arg Arg Asn Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser
115 120 125

```
Leu Ala Pro Lys Ala Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg
    130                 135                 140

Val Thr Glu Arg Arg Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser
145                 150                 155                 160

Pro Arg Pro Ala Gly Gln Phe Gln Thr Leu Val Thr Thr Thr Pro Ala
                165                 170                 175

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
            180                 185                 190

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
        195                 200                 205

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
    210                 215                 220

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
225                 230                 235                 240

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
                245                 250                 255

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
            260                 265                 270

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
        275                 280                 285

Ser Ala Asp Ala Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn
    290                 295                 300

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
305                 310                 315                 320

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
                325                 330                 335

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
            340                 345                 350
```

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
355 360 365

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
370 375 380

Ala Leu His Met Gln Ala Leu Pro Pro Arg
385 390

<210> 27
<211> 1182
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 27
atggccctcc ctgtcactgc cctgcttctc cccctcgcac tcctgctcca cgccgctaga 60

ccacccggat ggtttctgga ctctccggat cgcccgtgga atcccccaac cttctcaccg 120

gcactcttgg ttgtgactga gggcgataat gcgaccttca cgtgctcgtt ctccaacacc 180

tccgaatcat tcgtgctgaa ctggtaccgc atgagcccgt caaaccagac cgacaagctc 240

gccgcgtttc cggaagatcg gtcgcaaccg ggacaggatt gtcggttccg cgtgactcaa 300

ctgccgaatg gcagagactt ccacatgagc gtggtccgcg ctaggcgaaa cgactccggg 360

acctacctgt gcggagccat ctcgctggcg cctaaggccc aaatcaaaga gagcttgagg 420

gccgaactga gagtgaccga gcgcagagct gaggtgccaa ctgcacatcc atccccatcg 480

cctcggcctg cggggcagtt tcagaccctg gtcacgacca ctccggcgcc gcgcccaccg 540

actccggccc caactatcgc gagccagccc ctgtcgctga ggccggaagc atgccgccct 600

gccgccggag gtgctgtgca tacccgggga ttggacttcg catgcgacat ctacatttgg 660

gctcctctcg ccggaacttg tggcgtgctc cttctgtccc tggtcatcac cctgtactgc 720

aagcggggtc ggaaaaagct tctgtacatt ttcaagcagc ccttcatgag gcccgtgcaa 780

accacccagg aggaggacgg ttgctcctgc cggttccccg aagaggaaga aggaggttgc 840

gagctgcgcg tgaagttctc ccggagcgcc gacgcccccg cctataagca gggccagaac 900

cagctgtaca acgaactgaa cctgggacgg cgggaagagt acgatgtgct ggacaagcgg 960

cgcggccggg accccgaaat gggcgggaag cctagaagaa agaaccctca ggaaggcctg 1020

tataacgagc tgcagaagga caagatggcc gaggcctact ccgaaattgg gatgaaggga 1080

gagcggcgga ggggaaaggg gcacgacggc ctgtaccaag gactgtccac cgccaccaag 1140

gacacatacg atgccctgca catgcaggcc cttccccctc gc 1182

<210> 28
<211> 40
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<220>
<221> SITE
<222> (1)..(40)
<223> /note="This sequence may encompass 1-10 'Gly Gly Gly Ser'
repeating units"

<400> 28
Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
20 25 30

Gly Gly Gly Ser Gly Gly Gly Ser
35 40

<210> 29
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 29
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly

1 5 10 15

Gly Gly Gly Ser
20

<210> 30
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 30
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 31
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 31
Gly Gly Gly Ser
1

<210> 32

<400> 32
000

<210> 33

<400> 33
000

<210> 34
<211> 5000
<212> RNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<220>
<221> SITE
<222> (1)..(5000)
<223> /note="This sequence may encompass 50-5000
nucleotides"

<220>
<221> source
<223> /note="See specification as filed for detailed description of
substitutions and preferred embodiments"

<400> 34
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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 300

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 360

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aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 480

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 540

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 600

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 660

aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa 720

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<210> 36

<400> 36
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<210> 37

<400> 37
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<210> 38

<400> 38
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<210> 39
<211> 373
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 39
Pro Gly Trp Phe Leu Asp Ser Pro Asp Arg Pro Trp Asn Pro Pro Thr
1 5 10 15

Phe Ser Pro Ala Leu Leu Val Val Thr Glu Gly Asp Asn Ala Thr Phe
20 25 30

Thr Cys Ser Phe Ser Asn Thr Ser Glu Ser Phe Val Leu Asn Trp Tyr
35 40 45

Arg Met Ser Pro Ser Asn Gln Thr Asp Lys Leu Ala Ala Phe Pro Glu
50 55 60

Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg Phe Arg Val Thr Gln Leu
65 70 75 80

Pro Asn Gly Arg Asp Phe His Met Ser Val Val Arg Ala Arg Arg Asn
85 90 95

Asp Ser Gly Thr Tyr Leu Cys Gly Ala Ile Ser Leu Ala Pro Lys Ala
100 105 110

Gln Ile Lys Glu Ser Leu Arg Ala Glu Leu Arg Val Thr Glu Arg Arg
115 120 125

Ala Glu Val Pro Thr Ala His Pro Ser Pro Ser Pro Arg Pro Ala Gly
130 135 140

Gln Phe Gln Thr Leu Val Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr
145 150 155 160

Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala
165 170 175

Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe
180 185 190

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Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val
        195                 200                 205

Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys
    210                 215                 220

Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr
225                 230                 235                 240

Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu
                245                 250                 255

Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro
            260                 265                 270

Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly
        275                 280                 285

Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro
    290                 295                 300

Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr
305                 310                 315                 320

Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly
                325                 330                 335

Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln
            340                 345                 350

Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln
        355                 360                 365

Ala Leu Pro Pro Arg
    370
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<210> 40

<400> 40
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<210> 41

<400> 41
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<210> 42

<400> 42
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<210> 43

<400> 43
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<210> 44
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 44
Ser Tyr Ala Met Ser
1 5

<210> 45
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 45
Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 46
<211> 14

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 46
Arg Glu Trp Val Pro Tyr Asp Val Ser Trp Tyr Phe Asp Tyr
1 5 10

<210> 47
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 47
Gly Phe Thr Phe Ser Ser Tyr
1 5

<210> 48
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 48
Ser Gly Ser Gly Gly Ser
1 5

<210> 49
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 49

Gly Phe Thr Phe Ser Ser Tyr Ala
1 5

<210> 50
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 50
Ile Ser Gly Ser Gly Gly Ser Thr
1 5

<210> 51
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 51
Ala Arg Arg Glu Trp Val Pro Tyr Asp Val Ser Trp Tyr Phe Asp Tyr
1 5 10 15

<210> 52
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 52
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val

35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Glu Trp Val Pro Tyr Asp Val Ser Trp Tyr Phe Asp Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 53
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 53
gaagtgcagt tgctggagtc aggcggagga ctggtgcagc ccggaggatc gcttcgcttg 60

agctgcgcag cctcaggctt taccttctcc tcctacgcca tgtcctgggt cagacaggct 120

cccgggaagg gactggaatg ggtgtccgcc attagcggtt ccggcggaag cacttactat 180

gccgactctg tgaagggccg cttcactatc tcccgggaca actccaagaa caccctgtat 240

ctccaaatga attccctgag ggccgaagat accgcggtgt actactgcgc tagacgggag 300

tgggtgccct acgatgtcag ctggtacttc gactactggg gacagggcac tctcgtgact 360

gtgtcctcc 369

<210> 54
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 54
Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
1 5 10

<210> 55
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 55
Ala Ala Ser Ser Leu Gln Ser
1 5

<210> 56
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 56
Gln Gln Ser Tyr Ser Thr Pro Leu Thr
1 5

<210> 57
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 57
Ser Gln Ser Ile Ser Ser Tyr
1 5

<210> 58
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 58
Ala Ala Ser
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<210> 59
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 59
Ser Tyr Ser Thr Pro Leu
1 5

<210> 60
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 60
Gln Ser Ile Ser Ser Tyr
1 5

<210> 61
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 61
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 62
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 62
gacattcaaa tgactcagtc cccgtcctcc ctctccgcct ccgtgggaga tcgcgtcacg 60

atcacgtgca gggccagcca gagcatctcc agctacctga actggtacca gcagaagcca 120

gggaaggcac cgaagctcct gatctacgcc gctagctcgc tgcagtccgg cgtcccttca 180

cggttctcgg gatcgggctc aggcaccgac ttcaccctga ccattagcag cctgcagccg 240

gaggacttcg cgacatacta ctgtcagcag tcatactcca cccctctgac cttcggccaa 300

gggaccaaag tggagatcaa g 321

<210> 63
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 63
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> 64
<211> 250
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 64
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

```
Ala Arg Arg Glu Trp Val Pro Tyr Asp Val Ser Trp Tyr Phe Asp Tyr
            100                 105                 110


Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125


Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
    130                 135                 140


Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
145                 150                 155                 160


Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu
                165                 170                 175


Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
            180                 185                 190


Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
        195                 200                 205


Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
    210                 215                 220


Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr
225                 230                 235                 240


Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
                245                 250


<210> 65
<211> 750
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 65
gaagtgcagt tgctggagtc aggcggagga ctggtgcagc ccggaggatc gcttcgcttg       60
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agctgcgcag cctcaggctt taccttctcc tcctacgcca tgtcctgggt cagacaggct 120

cccgggaagg gactggaatg ggtgtccgcc attagcggtt ccggcggaag cacttactat 180

gccgactctg tgaagggccg cttcactatc tcccgggaca actccaagaa caccctgtat 240

ctccaaatga attccctgag ggccgaagat accgcggtgt actactgcgc tagacgggag 300

tgggtgccct acgatgtcag ctggtacttc gactactggg gacagggcac tctcgtgact 360

gtgtcctccg gtggtggtgg atcgggggt ggtggttcgg gcggaggagg atctggagga 420

ggagggtcgg acattcaaat gactcagtcc ccgtcctccc tctccgcctc cgtgggagat 480

cgcgtcacga tcacgtgcag ggccagccag agcatctcca gctacctgaa ctggtaccag 540

cagaagccag ggaaggcacc gaagctcctg atctacgccg ctagctcgct gcagtccggc 600

gtcccttcac ggttctcggg atcgggctca ggcaccgact tcaccctgac cattagcagc 660

ctgcagccgg aggacttcgc gacatactac tgtcagcagt catactccac ccctctgacc 720

ttcggccaag ggaccaaagt ggagatcaag 750

<210> 66
<211> 473
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 66
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

```
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Arg Glu Trp Val Pro Tyr Asp Val Ser Trp Tyr Phe Asp Tyr
            100                 105                 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
    130                 135                 140

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
145                 150                 155                 160

Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu
                165                 170                 175

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
            180                 185                 190

Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
        195                 200                 205

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
    210                 215                 220

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr
225                 230                 235                 240

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro
                245                 250                 255

Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu
            260                 265                 270

Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg
        275                 280                 285
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Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly
    290                 295                 300

Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys
305                 310                 315                 320

Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg
                325                 330                 335

Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro
            340                 345                 350

Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser
        355                 360                 365

Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu
    370                 375                 380

Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg
385                 390                 395                 400

Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln
                405                 410                 415

Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr
            420                 425                 430

Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp
        435                 440                 445

Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala
    450                 455                 460

Leu His Met Gln Ala Leu Pro Pro Arg
465                 470
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<210> 67
<211> 1419
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 67
gaagtgcagt tgctggagtc aggcggagga ctggtgcagc ccggaggatc gcttcgcttg 60

agctgcgcag cctcaggctt taccttctcc tcctacgcca tgtcctgggt cagacaggct 120

cccgggaagg gactggaatg ggtgtccgcc attagcggtt ccggcggaag cacttactat 180

gccgactctg tgaagggccg cttcactatc tcccgggaca actccaagaa caccctgtat 240

ctccaaatga attccctgag ggccgaagat accgcggtgt actactgcgc tagacgggag 300

tgggtgccct acgatgtcag ctggtacttc gactactggg gacagggcac tctcgtgact 360

gtgtcctccg gtggtggtgg atcgggggt ggtggttcgg gcggaggagg atctggagga 420

ggagggtcgg acattcaaat gactcagtcc ccgtcctccc tctccgcctc cgtgggagat 480

cgcgtcacga tcacgtgcag ggccagccag agcatctcca gctacctgaa ctggtaccag 540

cagaagccag ggaaggcacc gaagctcctg atctacgccg ctagctcgct gcagtccggc 600

gtcccttcac ggttctcggg atcgggctca ggcaccgact tcaccctgac cattagcagc 660

ctgcagccgg aggacttcgc gacatactac tgtcagcagt catactccac ccctctgacc 720

ttcggccaag ggaccaaagt ggagatcaag accactaccc cagcaccgag gccacccacc 780

ccggctccta ccatcgcctc ccagcctctg tccctgcgtc cggaggcatg tagacccgca 840

gctggtgggg ccgtgcatac ccggggtctt gacttcgcct gcgatatcta catttgggcc 900

cctctggctg gtacttgcgg ggtcctgctg ctttcactcg tgatcactct ttactgtaag 960

cgcggtcgga agaagctgct gtacatcttt aagcaaccct tcatgaggcc tgtgcagact 1020

actcaagagg aggacggctg ttcatgccgg ttcccagagg aggaggaagg cggctgcgaa 1080

ctgcgcgtga aattcagccg cagcgcagat gctccagcct accagcaggg gcagaaccag 1140

ctctacaacg aactcaatct tggtcggaga gaggagtacg acgtgctgga caagcggaga 1200

ggacgggacc cagaaatggg cgggaagccg cgcagaaaga atccccaaga gggcctgtac 1260

aacgagctcc aaaaggataa gatggcagaa gcctatagcg agattggtat gaaaggggaa 1320

cgcagaagag gcaaaggcca cgacggactg taccagggac tcagcaccgc caccaaggac 1380

acctatgacg ctcttcacat gcaggccctg ccgcctcgg 1419

<210> 68
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 68
Arg Glu Trp Trp Tyr Asp Asp Trp Tyr Leu Asp Tyr
1 5 10

<210> 69
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 69
Ala Arg Arg Glu Trp Trp Tyr Asp Asp Trp Tyr Leu Asp Tyr
1 5 10

<210> 70
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 70
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val

50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Glu Trp Trp Tyr Asp Asp Trp Tyr Leu Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 71
<211> 363
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 71
gaagtgcagt tgctggagtc aggcggagga ctggtgcagc ccggaggatc gcttcgcttg 60

agctgcgcag cctcaggctt taccttctcc tcctacgcca tgtcctgggt cagacaggct 120

cccgggaagg gactggaatg ggtgtccgcc attagcggtt ccggcggaag cacttactat 180

gccgactctg tgaagggccg cttcactatc tcccgggaca actccaagaa caccctgtat 240

ctccaaatga attccctgag ggccgaagat accgcggtgt actactgcgc tagacgggag 300

tggtggtacg acgattggta cctggactac tggggacagg gcactctcgt gactgtgtcc 360

tcc 363

<210> 72
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 72
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20   25   30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Arg Glu Trp Trp Tyr Asp Asp Trp Tyr Leu Asp Tyr Trp Gly
            100   105   110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115   120   125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
    130   135   140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145   150   155   160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165   170   175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180   185   190

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195   200   205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
210 215 220

Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225 230 235 240

Gln Gly Thr Lys Val Glu Ile Lys
245

<210> 73
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 73
gaagtgcagt tgctggagtc aggcggagga ctggtgcagc ccggaggatc gcttcgcttg 60

agctgcgcag cctcaggctt taccttctcc tcctacgcca tgtcctgggt cagacaggct 120

cccgggaagg gactggaatg ggtgtccgcc attagcggtt ccggcggaag cacttactat 180

gccgactctg tgaagggccg cttcactatc tcccgggaca actccaagaa caccctgtat 240

ctccaaatga attccctgag ggccgaagat accgcggtgt actactgcgc tagacgggag 300

tggtggtacg acgattggta cctggactac tggggacagg gcactctcgt gactgtgtcc 360

tccggtggtg gtggatcggg gggtggtggt tcgggcggag gaggatctgg aggaggaggg 420

tcggacattc aaatgactca gtccccgtcc tccctctccg cctccgtggg agatcgcgtc 480

acgatcacgt gcagggccag ccagagcatc tccagctacc tgaactggta ccagcagaag 540

ccagggaagg caccgaagct cctgatctac gccgctagct cgctgcagtc cggcgtccct 600

tcacggttct cgggatcggg ctcaggcacc gacttcaccc tgaccattag cagcctgcag 660

ccggaggact tcgcgacata ctactgtcag cagtcatact ccacccctct gaccttcggc 720

caagggacca aagtggagat caag 744

<210> 74
<211> 471
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 74
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Glu Trp Trp Tyr Asp Asp Trp Tyr Leu Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
130 135 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145 150 155 160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
165 170 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
180 185 190

```
Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro
                245                 250                 255

Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
            260                 265                 270

Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
        275                 280                 285

Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
    290                 295                 300

Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly
305                 310                 315                 320

Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val
                325                 330                 335

Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu
            340                 345                 350

Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp
        355                 360                 365

Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
    370                 375                 380

Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
385                 390                 395                 400

Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
```

405 410 415

Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
420 425 430

Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
435 440 445

Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
450 455 460

Met Gln Ala Leu Pro Pro Arg
465 470

<210> 75
<211> 1413
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 75
gaagtgcagt tgctggagtc aggcggagga ctggtgcagc ccggaggatc gcttcgcttg 60

agctgcgcag cctcaggctt taccttctcc tcctacgcca tgtcctgggt cagacaggct 120

cccgggaagg gactggaatg ggtgtccgcc attagcggtt ccggcggaag cacttactat 180

gccgactctg tgaagggccg cttcactatc tcccgggaca actccaagaa caccctgtat 240

ctccaaatga attccctgag ggccgaagat accgcggtgt actactgcgc tagacgggag 300

tggtggtacg acgattggta cctggactac tggggacagg gcactctcgt gactgtgtcc 360

tccggtggtg gtggatcggg gggtggtggt tcgggcggag gaggatctgg aggaggaggg 420

tcggacattc aaatgactca gtccccgtcc tccctctccg cctccgtggg agatcgcgtc 480

acgatcacgt gcagggccag ccagagcatc tccagctacc tgaactggta ccagcagaag 540

ccagggaagg caccgaagct cctgatctac gccgctagct cgctgcagtc cggcgtccct 600

tcacggttct cgggatcggg ctcaggcacc gacttcaccc tgaccattag cagcctgcag 660

ccggaggact tcgcgacata ctactgtcag cagtcatact ccacccctct gaccttcggc 720

caagggacca aagtggagat caagaccact accccagcac cgaggccacc caccccggct 780

cctaccatcg cctcccagcc tctgtccctg cgtccggagg catgtagacc cgcagctggt 840

ggggccgtgc atacccgggg tcttgacttc gcctgcgata tctacatttg ggcccctctg 900

gctggtactt gcggggtcct gctgctttca ctcgtgatca ctctttactg taagcgcggt 960

cggaagaagc tgctgtacat ctttaagcaa cccttcatga ggcctgtgca gactactcaa 1020

gaggaggacg gctgttcatg ccggttccca gaggaggagg aaggcggctg cgaactgcgc 1080

gtgaaattca gccgcagcgc agatgctcca gcctaccagc aggggcagaa ccagctctac 1140

aacgaactca atcttggtcg gagagaggag tacgacgtgc tggacaagcg gagaggacgg 1200

gacccagaaa tgggcgggaa gccgcgcaga aagaatcccc aagagggcct gtacaacgag 1260

ctccaaaagg ataagatggc agaagcctat agcgagattg gtatgaaagg ggaacgcaga 1320

agaggcaaag gccacgacgg actgtaccag ggactcagca ccgccaccaa ggacacctat 1380

gacgctcttc acatgcaggc cctgccgcct cgg 1413

<210> 76
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 76
Arg Glu Trp Trp Gly Glu Ser Trp Leu Phe Asp Tyr
1 5 10

<210> 77
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 77
Ala Arg Arg Glu Trp Trp Gly Glu Ser Trp Leu Phe Asp Tyr
1 5 10

<210> 78
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 78
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Glu Trp Trp Gly Glu Ser Trp Leu Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 79
<211> 363
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 79
gaagtgcagt tgctggagtc aggcggagga ctggtgcagc ccggaggatc gcttcgcttg 60

agctgcgcag cctcaggctt taccttctcc tcctacgcca tgtcctgggt cagacaggct 120

cccgggaagg gactggaatg ggtgtccgcc attagcggtt ccggcggaag cacttactat 180

gccgactctg tgaagggccg cttcactatc tcccgggaca actccaagaa caccctgtat 240

ctccaaatga attccctgag ggccgaagat accgcggtgt actactgcgc tagacgggag 300

tggtggggag aaagctggct gttcgactac tggggacagg gcactctcgt gactgtgtcc 360

tcc 363

<210> 80
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 80
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Glu Trp Trp Gly Glu Ser Trp Leu Phe Asp Tyr Trp Gly
100 105 110

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Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125


Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
    130                 135                 140


Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160


Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175


Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190


Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205


Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220


Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240


Gln Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 81
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 81
gaagtgcagt tgctggagtc aggcggagga ctggtgcagc ccggaggatc gcttcgcttg 60

agctgcgcag cctcaggctt taccttctcc tcctacgcca tgtcctgggt cagacaggct 120

cccgggaagg gactggaatg ggtgtccgcc attagcggtt ccggcggaag cacttactat 180

gccgactctg tgaagggccg cttcactatc tcccgggaca actccaagaa caccctgtat 240

ctccaaatga attccctgag ggccgaagat accgcggtgt actactgcgc tagacgggag 300

tggtggggag aaagctggct gttcgactac tggggacagg gcactctcgt gactgtgtcc 360

tccggtggtg gtggatcggg gggtggtggt tcgggcggag gaggatctgg aggaggaggg 420

tcggacattc aaatgactca gtccccgtcc tccctctccg cctccgtggg agatcgcgtc 480

acgatcacgt gcagggccag ccagagcatc tccagctacc tgaactggta ccagcagaag 540

ccagggaagg caccgaagct cctgatctac gccgctagct cgctgcagtc cggcgtccct 600

tcacggttct cgggatcggg ctcaggcacc gacttcaccc tgaccattag cagcctgcag 660

ccggaggact tcgcgacata ctactgtcag cagtcatact ccacccctct gaccttcggc 720

caagggacca aagtggagat caag 744

<210> 82
<211> 471
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 82
Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

```
Ala Arg Arg Glu Trp Trp Gly Glu Ser Trp Leu Phe Asp Tyr Trp Gly
            100                 105                 110

Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
        115                 120                 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
    130                 135                 140

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
145                 150                 155                 160

Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Ala Ala
            180                 185                 190

Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Leu Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Val Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg Pro
                245                 250                 255

Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
            260                 265                 270

Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
        275                 280                 285

Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
    290                 295                 300
```

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Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly
305                 310                 315                 320


Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val
                325                 330                 335


Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu
            340                 345                 350


Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp
        355                 360                 365


Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
    370                 375                 380


Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
385                 390                 395                 400


Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
                405                 410                 415


Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
            420                 425                 430


Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
        435                 440                 445


Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
    450                 455                 460


Met Gln Ala Leu Pro Pro Arg
465                 470


<210> 83
<211> 1413
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"
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<400> 83
gaagtgcagt tgctggagtc aggcggagga ctggtgcagc ccggaggatc gcttcgcttg 60

agctgcgcag cctcaggctt taccttctcc tcctacgcca tgtcctgggt cagacaggct 120

cccgggaagg gactggaatg ggtgtccgcc attagcggtt ccggcggaag cacttactat 180

gccgactctg tgaagggccg cttcactatc tcccgggaca actccaagaa caccctgtat 240

ctccaaatga attccctgag ggccgaagat accgcggtgt actactgcgc tagacgggag 300

tggtggggag aaagctggct gttcgactac tggggacagg gcactctcgt gactgtgtcc 360

tccggtggtg gtggatcggg gggtggtggt tcgggcggag gaggatctgg aggaggaggg 420

tcggacattc aaatgactca gtccccgtcc tccctctccg cctccgtggg agatcgcgtc 480

acgatcacgt gcagggccag ccagagcatc tccagctacc tgaactggta ccagcagaag 540

ccagggaagg caccgaagct cctgatctac gccgctagct cgctgcagtc cggcgtccct 600

tcacggttct cgggatcggg ctcaggcacc gacttcaccc tgaccattag cagcctgcag 660

ccggaggact tcgcgacata ctactgtcag cagtcatact ccacccctct gaccttcggc 720

caagggacca aagtggagat caagaccact accccagcac cgaggccacc caccccggct 780

cctaccatcg cctcccagcc tctgtccctg cgtccggagg catgtagacc cgcagctggt 840

ggggccgtgc atacccgggg tcttgacttc gcctgcgata tctacatttg ggcccctctg 900

gctggtactt gcggggtcct gctgctttca ctcgtgatca ctctttactg taagcgcggt 960

cggaagaagc tgctgtacat ctttaagcaa cccttcatga ggcctgtgca gactactcaa 1020

gaggaggacg gctgttcatg ccggttccca gaggaggagg aaggcggctg cgaactgcgc 1080

gtgaaattca gccgcagcgc agatgctcca gcctaccagc aggggcagaa ccagctctac 1140

aacgaactca atcttggtcg gagagaggag tacgacgtgc tggacaagcg gagaggacgg 1200

gacccagaaa tgggcgggaa gccgcgcaga aagaatcccc aagagggcct gtacaacgag 1260

ctccaaaagg ataagatggc agaagcctat agcgagattg gtatgaaagg ggaacgcaga 1320

agaggcaaag gccacgacgg actgtaccag ggactcagca ccgccaccaa ggacacctat 1380

gacgctcttc acatgcaggc cctgccgcct cgg 1413

<210> 84
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
<221> VARIANT
<222> (4)..(4)
<223> /replace=" "

<220>
<221> VARIANT
<222> (5)..(5)
<223> /replace=" "

<220>
<221> VARIANT
<222> (6)..(6)
<223> /replace="Tyr"

<220>
<221> VARIANT
<222> (7)..(7)
<223> /replace="Tyr" or "Asp"

<220>
<221> VARIANT
<222> (8)..(8)
<223> /replace="Asp" or "Val"

<220>
<221> VARIANT
<222> (9)..(9)
<223> /replace="Asp"

<220>
<221> VARIANT
<222> (11)..(11)
<223> /replace="Tyr"

<220>
<221> VARIANT
<222> (12)..(12)
<223> /replace="Leu"

<220>
<221> SITE
<222> (1)..(14)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 84
Arg Glu Trp Val Pro Trp Gly Glu Ser Trp Leu Phe Asp Tyr
1   5   10

<210> 85
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<220>
<221> VARIANT
<222> (6)..(6)
<223> /replace=" "

<220>
<221> VARIANT
<222> (7)..(7)
<223> /replace=" "

<220>
<221> VARIANT
<222> (8)..(8)
<223> /replace="Tyr"

<220>
<221> VARIANT
<222> (9)..(9)
<223> /replace="Tyr" or "Asp"

<220>
<221> VARIANT
<222> (10)..(10)
<223> /replace="Asp" or "Val"

<220>
<221> VARIANT
<222> (11)..(11)
<223> /replace="Asp"

<220>
<221> VARIANT
<222> (13)..(13)
<223> /replace="Tyr"

<220>
<221> VARIANT
<222> (14)..(14)

<223> /replace="Leu"

<220>
<221> SITE
<222> (1)..(16)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 85
Ala Arg Arg Glu Trp Val Pro Trp Gly Glu Ser Trp Leu Phe Asp Tyr
1 5 10 15

<210> 86
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 86
Ser Tyr Gly Met His
1 5

<210> 87
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 87
Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 88
<211> 14
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 88
Ser Gly Tyr Ala Leu His Asp Asp Tyr Tyr Gly Leu Asp Val
1 5 10

<210> 89
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 89
Ser Tyr Asp Gly Ser Asn
1 5

<210> 90
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 90
Gly Phe Thr Phe Ser Ser Tyr Gly
1 5

<210> 91
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 91
Ile Ser Tyr Asp Gly Ser Asn Lys
1 5

<210> 92
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 92
Gly Gly Ser Gly Tyr Ala Leu His Asp Asp Tyr Tyr Gly Leu Asp Val
1   5   10   15

<210> 93
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 93
Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20   25   30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Gly Gly Ser Gly Tyr Ala Leu His Asp Asp Tyr Tyr Gly Leu Asp Val
            100   105   110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 94
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 94
caagtgcagc tgcaggaatc cggtggcgga gtcgtgcagc ctggaaggag cctgagactc 60

tcatgcgccg cgtcagggtt caccttttcc tcctacggga tgcattgggt cagacaggcc 120

cccggaaagg gactcgaatg ggtggctgtg atcagctacg acggctccaa caagtactac 180

gccgactccg tgaaaggccg gttcactatc tcccgggaca actccaagaa cacgctgtat 240

ctgcaaatga attcactgcg cgcggaggat accgctgtgt actactgcgg tggctccggt 300

tacgccctgc acgatgacta ttacggcctt gacgtctggg gccagggaac cctcgtgact 360

gtgtccagc 369

<210> 95
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 95
Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
1 5 10

<210> 96
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 96
Asp Val Ser Asn Arg Pro Ser
1   5

<210> 97
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 97
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1   5   10

<210> 98
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 98
Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr
1   5   10

<210> 99
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 99
Asp Val Ser
1

<210> 100
<211> 8
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 100
Tyr Thr Ser Ser Ser Thr Leu Tyr
1 5

<210> 101
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 101
Ser Ser Asp Val Gly Gly Tyr Asn Tyr
1 5

<210> 102
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 102
Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Leu Tyr Val Phe Gly Ser Gly Thr Lys Val Thr Val Leu
100 105 110

<210> 103
<211> 333
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 103
cagagcgcac tgactcagcc ggcatccgtg tccggtagcc ccggacagtc gattaccatc 60

tcctgtaccg gcacctcctc cgacgtggga gggtacaact acgtgtcgtg gtaccagcag 120

cacccaggaa aggcccctaa gttgatgatc tacgatgtgt caaaccgccc gtctggagtc 180

tccaaccggt tctccggctc caagtccggc aacaccgcca gcctgaccat tagcgggctg 240

caagccgagg atgaggccga ctactactgc tcgagctaca catcctcgag caccctctac 300

gtgttcggct cggggactaa ggtcaccgtg ctg 333

<210> 104
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 104
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> 105
<211> 249
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 105
Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Gly Gly Ser Gly Tyr Ala Leu His Asp Asp Tyr Tyr Gly Leu Asp Val
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ser Ala Leu Thr Gln
130 135 140

Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser Ile Thr Ile Ser Cys
145 150 155 160

Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr
165 170 175

Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Asp Val Ser
180 185 190

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Asn Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly
        195                 200                 205


Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala
    210                 215                 220


Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val Phe
225                 230                 235                 240


Gly Ser Gly Thr Lys Val Thr Val Leu
                245


<210> 106
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 106
caagtgcagc tgcaggaatc cggtggcgga gtcgtgcagc ctggaaggag cctgagactc       60

tcatgcgccg cgtcagggtt caccttttcc tcctacggga tgcattgggt cagacaggcc      120

cccggaaagg gactcgaatg ggtggctgtg atcagctacg acggctccaa caagtactac      180

gccgactccg tgaaaggccg gttcactatc tcccgggaca actccaagaa cacgctgtat      240

ctgcaaatga attcactgcg cgcggaggat accgctgtgt actactgcgg tggctccggt      300

tacgccctgc acgatgacta ttacggcctt gacgtctggg gccagggaac cctcgtgact      360

gtgtccagcg gtggaggagg ttcgggcgga ggaggatcag gaggggtgg atcgcagagc       420

gcactgactc agccggcatc cgtgtccggt agccccggac agtcgattac catctcctgt      480

accggcacct cctccgacgt gggagggtac aactacgtgt cgtggtacca gcagcaccca      540

ggaaaggccc ctaagttgat gatctacgat gtgtcaaacc gcccgtctgg agtctccaac      600

cggttctccg gctccaagtc cggcaacacc gccagcctga ccattagcgg gctgcaagcc      660

gaggatgagg ccgactacta ctgctcgagc tacacatcct cgagcaccct ctacgtgttc      720

ggctcgggga ctaaggtcac cgtgctg                                          747
```

<210> 107
<211> 472
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 107
Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Gly Gly Ser Gly Tyr Ala Leu His Asp Asp Tyr Tyr Gly Leu Asp Val
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ser Ala Leu Thr Gln
130 135 140

Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser Ile Thr Ile Ser Cys
145 150 155 160

Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr

```
                165                 170                 175

Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Asp Val Ser
            180                 185                 190

Asn Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly
        195                 200                 205

Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala
    210                 215                 220

Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val Phe
225                 230                 235                 240

Gly Ser Gly Thr Lys Val Thr Val Leu Thr Thr Thr Pro Ala Pro Arg
                245                 250                 255

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
            260                 265                 270

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
        275                 280                 285

Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
    290                 295                 300

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg
305                 310                 315                 320

Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro
                325                 330                 335

Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu
            340                 345                 350

Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala
        355                 360                 365

Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
    370                 375                 380
```

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
385 390 395 400

Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
405 410 415

Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
420 425 430

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
435 440 445

Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
450 455 460

His Met Gln Ala Leu Pro Pro Arg
465 470

<210> 108
<211> 1416
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 108
caagtgcagc tgcaggaatc cggtggcgga gtcgtgcagc ctggaaggag cctgagactc 60

tcatgcgccg cgtcagggtt caccttttcc tcctacggga tgcattgggt cagacaggcc 120

cccggaaagg gactcgaatg ggtggctgtg atcagctacg acggctccaa caagtactac 180

gccgactccg tgaaaggccg gttcactatc tcccgggaca actccaagaa cacgctgtat 240

ctgcaaatga attcactgcg cgcggaggat accgctgtgt actactgcgg tggctccggt 300

tacgccctgc acgatgacta ttacggcctt gacgtctggg gccagggaac cctcgtgact 360

gtgtccagcg gtggaggagg ttcgggcgga ggaggatcag gaggggtgg atcgcagagc 420

gcactgactc agccggcatc cgtgtccggt agccccggac agtcgattac catctcctgt 480

accggcacct cctccgacgt gggagggtac aactacgtgt cgtggtacca gcagcaccca 540

ggaaaggccc ctaagttgat gatctacgat gtgtcaaacc gcccgtctgg agtctccaac 600

cggttctccg gctccaagtc cggcaacacc gccagcctga ccattagcgg gctgcaagcc 660

gaggatgagg ccgactacta ctgctcgagc tacacatcct cgagcaccct ctacgtgttc 720

ggctcgggga ctaaggtcac cgtgctgacc actaccccag caccgaggcc acccaccccg 780

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 840

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccccc 900

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 960

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1020

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1080

cgcgtgaaat tcagccgcag cgcagatgct ccagcctacc agcaggggca gaaccagctc 1140

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1200

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1260

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1320

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1380

tatgacgctc ttcacatgca ggccctgccg cctcgg 1416

<210> 109
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 109
Val Ile Ser Tyr Lys Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 110
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 110
Ser Tyr Lys Gly Ser Asn
1 5

<210> 111
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 111
Ile Ser Tyr Lys Gly Ser Asn Lys
1 5

<210> 112
<211> 123
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 112
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Ser Tyr Lys Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr

65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Gly Gly Ser Gly Tyr Ala Leu His Asp Asp Tyr Tyr Gly Leu Asp Val
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 113
<211> 369
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 113
caagtgcagc ttgtcgaatc gggaggcgga gtggtgcagc ctggacgatc gctccggctc 60

tcatgtgccg cgagcggatt caccttctcg agctacggca tgcactgggt cagacaagcc 120

ccaggaaagg gcctggaatg ggtggctgtc atctcgtaca agggctcaaa caagtactac 180

gccgactccg tgaagggccg gttcaccatc tcccgcgata actccaagaa taccctctat 240

ctgcaaatga acagcctgag ggccgaggat actgcagtgt actactgcgg gggttcaggc 300

tacgcgctgc acgacgacta ctacggattg gacgtctggg gccaaggaac tcttgtgacc 360

gtgtcctct 369

<210> 114
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 114
Glu Val Ser Asn Arg Leu Arg
1 5

<210> 115
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 115
Ser Ser Tyr Thr Ser Ser Ser Ala Leu Tyr Val
1 5 10

<210> 116
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 116
Glu Val Ser
1

<210> 117
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 117
Tyr Thr Ser Ser Ser Ala Leu Tyr
1 5

<210> 118
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 118
Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Val Ser Asn Arg Leu Arg Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Ala Leu Tyr Val Phe Gly Ser Gly Thr Lys Val Thr Val Leu
100 105 110

<210> 119
<211> 333
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 119
cagagcgcgc tgactcagcc tgcctccgtg agcggttcgc cgggacagtc cattaccatt 60

tcgtgcaccg ggacctcctc cgacgtggga ggctacaact acgtgtcctg gtaccagcag 120

catcccggaa aggccccgaa gctgatgatc tacgaagtgt cgaacagact gcggggagtc 180

tccaaccgct tttccgggtc caagtccggc aacaccgcca gcctgaccat cagcgggctc 240

caggcagaag atgaggctga ctattactgc tcctcctaca cgtcaagctc cgccctctac 300

gtgttcgggt ccgggaccaa agtcactgtg ctg 333

<210> 120
<211> 254
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 120
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Ser Tyr Lys Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Gly Gly Ser Gly Tyr Ala Leu His Asp Asp Tyr Tyr Gly Leu Asp Val
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
130 135 140

Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser
145 150 155 160

Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn

```
                165                 170                 175

Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met
            180                 185                 190

Ile Tyr Glu Val Ser Asn Arg Leu Arg Gly Val Ser Asn Arg Phe Ser
        195                 200                 205

Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln
    210                 215                 220

Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser
225                 230                 235                 240

Ala Leu Tyr Val Phe Gly Ser Gly Thr Lys Val Thr Val Leu
                245                 250
```

<210> 121
<211> 762
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 121
caagtgcagc ttgtcgaatc gggaggcgga gtggtgcagc ctggacgatc gctccggctc 60

tcatgtgccg cgagcggatt caccttctcg agctacggca tgcactgggt cagacaagcc 120

ccaggaaagg gcctggaatg ggtggctgtc atctcgtaca agggctcaaa caagtactac 180

gccgactccg tgaagggccg gttcaccatc tcccgcgata actccaagaa taccctctat 240

ctgcaaatga acagcctgag ggccgaggat actgcagtgt actactgcgg gggttcaggc 300

tacgcgctgc acgacgacta ctacggattg gacgtctggg gccaaggaac tcttgtgacc 360

gtgtcctctg gtggaggcgg atcaggggt ggcggatctg ggggtggtgg ttccggggga 420

ggaggatcgc agagcgcgct gactcagcct gcctccgtga gcggttcgcc gggacagtcc 480

attaccattt cgtgcaccgg gacctcctcc gacgtgggag gctacaacta cgtgtcctgg 540

taccagcagc atcccggaaa ggccccgaag ctgatgatct acgaagtgtc gaacagactg 600

cggggagtct ccaaccgctt ttccgggtcc aagtccggca acaccgccag cctgaccatc 660

agcgggctcc aggcagaaga tgaggctgac tattactgct cctcctacac gtcaagctcc 720

gccctctacg tgttcgggtc cgggaccaaa gtcactgtgc tg 762

<210> 122
<211> 477
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 122
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Ser Tyr Lys Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Gly Gly Ser Gly Tyr Ala Leu His Asp Asp Tyr Tyr Gly Leu Asp Val
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
130 135 140

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Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser
145                 150                 155                 160

Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn
                165                 170                 175

Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met
            180                 185                 190

Ile Tyr Glu Val Ser Asn Arg Leu Arg Gly Val Ser Asn Arg Phe Ser
        195                 200                 205

Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln
    210                 215                 220

Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser
225                 230                 235                 240

Ala Leu Tyr Val Phe Gly Ser Gly Thr Lys Val Thr Val Leu Thr Thr
                245                 250                 255

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
            260                 265                 270

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
        275                 280                 285

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
    290                 295                 300

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
305                 310                 315                 320

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
                325                 330                 335

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
            340                 345                 350

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
        355                 360                 365
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Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
    370                 375                 380

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
385                 390                 395                 400

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
                405                 410                 415

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
            420                 425                 430

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
        435                 440                 445

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
    450                 455                 460

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
465                 470                 475
```

<210> 123
<211> 1431
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 123
caagtgcagc ttgtcgaatc gggaggcgga gtggtgcagc ctggacgatc gctccggctc 60

tcatgtgccg cgagcggatt caccttctcg agctacggca tgcactgggt cagacaagcc 120

ccaggaaagg gcctggaatg ggtggctgtc atctcgtaca agggctcaaa caagtactac 180

gccgactccg tgaagggccg gttcaccatc tcccgcgata actccaagaa taccctctat 240

ctgcaaatga acagcctgag ggccgaggat actgcagtgt actactgcgg gggttcaggc 300

tacgcgctgc acgacgacta ctacggattg gacgtctggg gccaaggaac tcttgtgacc 360

gtgtcctctg gtggaggcgg atcaggggt ggcggatctg ggggtggtgg ttccggggga 420

ggaggatcgc agagcgcgct gactcagcct gcctccgtga gcggttcgcc gggacagtcc 480

attaccattt cgtgcaccgg gacctcctcc gacgtgggag gctacaacta cgtgtcctgg 540

taccagcagc atcccggaaa ggccccgaag ctgatgatct acgaagtgtc gaacagactg 600

cggggagtct ccaaccgctt ttccgggtcc aagtccggca acaccgccag cctgaccatc 660

agcgggctcc aggcagaaga tgaggctgac tattactgct cctcctacac gtcaagctcc 720

gccctctacg tgttcgggtc cgggaccaaa gtcactgtgc tgaccactac cccagcaccg 780

aggccaccca ccccggctcc taccatcgcc tcccagcctc tgtccctgcg tccggaggca 840

tgtagacccg cagctggtgg ggccgtgcat acccggggtc ttgacttcgc ctgcgatatc 900

tacatttggg cccctctggc tggtacttgc ggggtcctgc tgctttcact cgtgatcact 960

ctttactgta agcgcggtcg gaagaagctg ctgtacatct ttaagcaacc cttcatgagg 1020

cctgtgcaga ctactcaaga ggaggacggc tgttcatgcc ggttcccaga ggaggaggaa 1080

ggcggctgcg aactgcgcgt gaaattcagc cgcagcgcag atgctccagc ctaccagcag 1140

gggcagaacc agctctacaa cgaactcaat cttggtcgga gagaggagta cgacgtgctg 1200

gacaagcgga gaggacggga cccagaaatg ggcgggaagc cgcgcagaaa gaatccccaa 1260

gagggcctgt acaacgagct ccaaaaggat aagatggcag aagcctatag cgagattggt 1320

atgaaagggg aacgcagaag aggcaaaggc cacgacggac tgtaccaggg actcagcacc 1380

gccaccaagg acacctatga cgctcttcac atgcaggccc tgccgcctcg g 1431

<210> 124
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 124
Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Val Ser Asn Arg Leu Arg Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Leu Tyr Val Phe Gly Ser Gly Thr Lys Val Thr Val Leu
100 105 110

<210> 125
<211> 333
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 125
cagagcgcgc tgactcagcc tgcctccgtg agcggttcgc cgggacagtc cattaccatt 60

tcgtgcaccg ggacctcctc cgacgtggga ggctacaact acgtgtcctg gtaccagcag 120

catcccggaa aggccccgaa gctgatgatc tacgaagtgt cgaacagact gcggggagtc 180

tccaaccgct tttccgggtc caagtccggc aacaccgcca gcctgaccat cagcgggctc 240

caggcagaag atgaggctga ctattactgc tcctcctaca cgtcaagctc caccctctac 300

gtgttcgggt ccgggaccaa agtcactgtg ctg 333

<210> 126
<211> 254
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 126
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
            20   25   30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35   40   45

Ala Val Ile Ser Tyr Lys Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Gly Gly Ser Gly Tyr Ala Leu His Asp Asp Tyr Tyr Gly Leu Asp Val
            100   105   110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
        115   120   125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
    130   135   140

Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser
145   150   155   160

Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn
                165   170   175

Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met
            180   185   190

Ile Tyr Glu Val Ser Asn Arg Leu Arg Gly Val Ser Asn Arg Phe Ser
        195   200   205

Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln
210 215 220

Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser
225 230 235 240

Thr Leu Tyr Val Phe Gly Ser Gly Thr Lys Val Thr Val Leu
245 250

<210> 127
<211> 762
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 127
caagtgcagc ttgtcgaatc gggaggcgga gtggtgcagc ctggacgatc gctccggctc 60

tcatgtgccg cgagcggatt caccttctcg agctacggca tgcactgggt cagacaagcc 120

ccaggaaagg gcctggaatg ggtggctgtc atctcgtaca agggctcaaa caagtactac 180

gccgactccg tgaagggccg gttcaccatc tcccgcgata actccaagaa taccctctat 240

ctgcaaatga acagcctgag ggccgaggat actgcagtgt actactgcgg gggttcaggc 300

tacgcgctgc acgacgacta ctacggattg gacgtctggg gccaaggaac tcttgtgacc 360

gtgtcctctg gtggaggcgg atcagggggt ggcggatctg ggggtggtgg ttccgggggа 420

ggaggatcgc agagcgcgct gactcagcct gcctccgtga gcggttcgcc gggacagtcc 480

attaccattt cgtgcaccgg gacctcctcc gacgtgggag gctacaacta cgtgtcctgg 540

taccagcagc atcccggaaa ggccccgaag ctgatgatct acgaagtgtc gaacagactg 600

cggggagtct ccaaccgctt ttccgggtcc aagtccggca acaccgccag cctgaccatc 660

agcgggctcc aggcagaaga tgaggctgac tattactgct cctcctacac gtcaagctcc 720

accctctacg tgttcgggtc cgggaccaaa gtcactgtgc tg 762

<210> 128
<211> 477
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 128
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Ser Tyr Lys Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Gly Gly Ser Gly Tyr Ala Leu His Asp Asp Tyr Tyr Gly Leu Asp Val
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
130 135 140

Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser
145 150 155 160

Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn
165 170 175

Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met
180 185 190

```
Ile Tyr Glu Val Ser Asn Arg Leu Arg Gly Val Ser Asn Arg Phe Ser
        195                 200                 205

Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln
    210                 215                 220

Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser
225                 230                 235                 240

Thr Leu Tyr Val Phe Gly Ser Gly Thr Lys Val Thr Val Leu Thr Thr
                245                 250                 255

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
            260                 265                 270

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
        275                 280                 285

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
    290                 295                 300

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
305                 310                 315                 320

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
                325                 330                 335

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
            340                 345                 350

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
        355                 360                 365

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
    370                 375                 380

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
385                 390                 395                 400

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
```

405 410 415

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
420 425 430

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
435 440 445

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
450 455 460

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
465 470 475

<210> 129
<211> 1431
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 129
caagtgcagc ttgtcgaatc gggaggcgga gtggtgcagc ctggacgatc gctccggctc 60

tcatgtgccg cgagcggatt caccttctcg agctacggca tgcactgggt cagacaagcc 120

ccaggaaagg gcctggaatg ggtggctgtc atctcgtaca agggctcaaa caagtactac 180

gccgactccg tgaagggccg gttcaccatc tcccgcgata actccaagaa taccctctat 240

ctgcaaatga acagcctgag ggccgaggat actgcagtgt actactgcgg gggttcaggc 300

tacgcgctgc acgacgacta ctacggattg gacgtctggg gccaaggaac tcttgtgacc 360

gtgtcctctg gtggaggcgg atcagggggt ggcggatctg ggggtggtgg ttccggggga 420

ggaggatcgc agagcgcgct gactcagcct gcctccgtga gcggttcgcc gggacagtcc 480

attaccattt cgtgcaccgg gacctcctcc gacgtgggag gctacaacta cgtgtcctgg 540

taccagcagc atcccggaaa ggccccgaag ctgatgatct acgaagtgtc gaacagactg 600

cggggagtct ccaaccgctt ttccgggtcc aagtccggca acaccgccag cctgaccatc 660

agcgggctcc aggcagaaga tgaggctgac tattactgct cctcctacac gtcaagctcc 720

accctctacg tgttcgggtc cgggaccaaa gtcactgtgc tgaccactac cccagcaccg 780

aggccaccca ccccggctcc taccatcgcc tcccagcctc tgtccctgcg tccggaggca 840

tgtagacccg cagctggtgg ggccgtgcat acccggggtc ttgacttcgc ctgcgatatc 900

tacatttggg cccctctggc tggtacttgc ggggtcctgc tgctttcact cgtgatcact 960

ctttactgta agcgcggtcg gaagaagctg ctgtacatct ttaagcaacc cttcatgagg 1020

cctgtgcaga ctactcaaga ggaggacggc tgttcatgcc ggttcccaga ggaggaggaa 1080

ggcggctgcg aactgcgcgt gaaattcagc cgcagcgcag atgctccagc ctaccagcag 1140

gggcagaacc agctctacaa cgaactcaat cttggtcgga gagaggagta cgacgtgctg 1200

gacaagcgga gaggacggga cccagaaatg ggcgggaagc cgcgcagaaa gaatccccaa 1260

gagggcctgt acaacgagct ccaaaaggat aagatggcag aagcctatag cgagattggt 1320

atgaaagggg aacgcagaag aggcaaaggc cacgacggac tgtaccaggg actcagcacc 1380

gccaccaagg acacctatga cgctcttcac atgcaggccc tgccgcctcg g 1431

<210> 130
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
<221> VARIANT
<222> (5)..(5)
<223> /replace="Lys"

<220>
<221> SITE
<222> (1)..(17)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 130
Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 131
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
<221> VARIANT
<222> (1)..(1)
<223> /replace="Glu"

<220>
<221> VARIANT
<222> (6)..(6)
<223> /replace="Leu"

<220>
<221> VARIANT
<222> (7)..(7)
<223> /replace="Arg"

<220>
<221> SITE
<222> (1)..(7)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 131
Asp Val Ser Asn Arg Pro Ser
1 5

<210> 132
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
<221> VARIANT

<222> (8)..(8)
<223> /replace="Ala"

<220>
<221> SITE
<222> (1)..(11)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 132
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1 5 10

<210> 133
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
<221> VARIANT
<222> (3)..(3)
<223> /replace="Lys"

<220>
<221> SITE
<222> (1)..(6)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 133
Ser Tyr Asp Gly Ser Asn
1 5

<210> 134
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
<221> VARIANT
<222> (1)..(1)
<223> /replace="Glu"

<220>
<221> SITE
<222> (1)..(3)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 134
Asp Val Ser
1

<210> 135
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
<221> VARIANT
<222> (6)..(6)
<223> /replace="Ala"

<220>
<221> SITE
<222> (1)..(8)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 135
Tyr Thr Ser Ser Ser Thr Leu Tyr
1 5

<210> 136
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
<221> VARIANT
<222> (4)..(4)
<223> /replace="Lys"

<220>
<221> SITE
<222> (1)..(8)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 136
Ile Ser Tyr Asp Gly Ser Asn Lys
1 5

<210> 137
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 137
Gly Phe Trp Met Ser
1 5

<210> 138
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 138
Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val Arg
1 5 10 15

Gly

<210> 139

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 139
Ala Leu Asp Tyr Tyr Gly Met Asp Val
1 5

<210> 140
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 140
Gly Phe Thr Phe Ser Gly Phe
1 5

<210> 141
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 141
Lys Gln Asp Gly Ser Glu
1 5

<210> 142
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 142
Gly Phe Thr Phe Ser Gly Phe Trp
1   5

<210> 143
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 143
Ile Lys Gln Asp Gly Ser Glu Lys
1   5

<210> 144
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 144
Ala Arg Ala Leu Asp Tyr Tyr Gly Met Asp Val
1   5   10

<210> 145
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 145
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Gly Phe
            20   25   30

```
Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val
    50                  55                  60


Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ala Leu Asp Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr
            100                 105                 110


Thr Val Thr Val Ser Ser
        115


<210> 146
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 146
gaagtgcaac tggtggagag cggtggaggg cttgtccagc ccggaggatc gctgcggctg       60

tcctgtgctg cgtccgggtt caccttctcc ggcttctgga tgtcctgggt cagacaggca      120

ccgggaaagg gcctcgaatg ggtggccaac atcaagcagg atggctccga gaagtactac      180

gtcgactccg tgagaggccg cttcaccatc tcccgggaca acgccaagaa ctcgctgtac      240

ctccaaatga atagcctcag ggcggaagat actgctgtgt attactgcgc acgcgccctt      300

gactactacg gcatggacgt ctggggccaa gggaccactg tgaccgtgtc tagc            354


<210> 147
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
```

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 147
Arg Ser Ser Gln Ser Leu Leu Asp Ser Asp Asp Gly Asn Thr Tyr Leu
1 5 10 15

Asp

<210> 148
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 148
Thr Leu Ser Tyr Arg Ala Ser
1 5

<210> 149
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 149
Thr Gln Arg Leu Glu Phe Pro Ser Ile Thr
1 5 10

<210> 150
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 150

Ser Gln Ser Leu Leu Asp Ser Asp Asp Gly Asn Thr Tyr
1   5   10

<210> 151
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 151
Thr Leu Ser
1

<210> 152
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 152
Arg Leu Glu Phe Pro Ser Ile
1   5

<210> 153
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 153
Gln Ser Leu Leu Asp Ser Asp Asp Gly Asn Thr Tyr
1   5   10

<210> 154
<211> 114
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 154
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Asp Ser
20 25 30

Asp Asp Gly Asn Thr Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln
35 40 45

Ser Pro Arg Leu Leu Ile Tyr Thr Leu Ser Tyr Arg Ala Ser Gly Val
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys
65 70 75 80

Ile Ser Arg Val Glu Ala Glu Asp Val Gly Leu Tyr Tyr Cys Thr Gln
85 90 95

Arg Leu Glu Phe Pro Ser Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu
100 105 110

Ile Lys

<210> 155
<211> 342
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 155
gatatcgtga tgacccagac tcccctgtcc ctgcctgtga ctcccggaga accagcctcc 60

atttcctgcc ggtcctccca gtccctgctg gacagcgacg acggcaacac ttacctggac 120

tggtacttgc agaagccggg ccaatcgcct cgcctgctga tctatacccct gtcataccgg 180

gcctcaggag tgcctgaccg cttctcggga tcagggagcg ggaccgattt caccctgaaa 240

atttcccgag tggaagccga ggacgtcgga ctgtactact gcacccagcg cctcgaattc 300

ccgtcgatta cgtttggaca gggtacccgg cttgagatca ag 342

<210> 156
<211> 252
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 156
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Gly Phe
20 25 30

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ala Leu Asp Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln
130 135 140

```
Thr Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser
145                 150                 155                 160


Cys Arg Ser Ser Gln Ser Leu Leu Asp Ser Asp Asp Gly Asn Thr Tyr
                165                 170                 175


Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Arg Leu Leu Ile
            180                 185                 190


Tyr Thr Leu Ser Tyr Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly
        195                 200                 205


Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala
    210                 215                 220


Glu Asp Val Gly Leu Tyr Tyr Cys Thr Gln Arg Leu Glu Phe Pro Ser
225                 230                 235                 240


Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
                245                 250
```

<210> 157
<211> 756
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 157
gaagtgcaac tggtggagag cggtggaggg cttgtccagc ccggaggatc gctgcggctg 60

tcctgtgctg cgtccgggtt caccttctcc ggcttctgga tgtcctgggt cagacaggca 120

ccgggaaagg gcctcgaatg ggtggccaac atcaagcagg atggctccga gaagtactac 180

gtcgactccg tgagaggccg cttcaccatc tcccgggaca acgccaagaa ctcgctgtac 240

ctccaaatga atagcctcag ggcggaagat actgctgtgt attactgcgc acgcgccctt 300

gactactacg gcatggacgt ctggggccaa gggaccactg tgaccgtgtc tagcggaggc 360

ggaggttcag ggggcggtgg atcaggcgga ggaggatcgg ggggtggtgg atcggatatc 420

gtgatgaccc agactcccct gtccctgcct gtgactcccg gagaaccagc ctccatttcc 480

tgccggtcct cccagtccct gctggacagc gacgacggca acacttacct ggactggtac 540

ttgcagaagc cgggccaatc gcctcgcctg ctgatctata ccctgtcata ccgggcctca 600

ggagtgcctg accgcttctc gggatcaggg agcgggaccg atttcaccct gaaaatttcc 660

cgagtggaag ccgaggacgt cggactgtac tactgcaccc agcgcctcga attcccgtcg 720

attacgtttg gacagggtac ccggcttgag atcaag 756

<210> 158
<211> 475
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 158
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Gly Phe
20 25 30

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val
50 55 60

Arg Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ala Leu Asp Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

```
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln
    130                 135                 140

Thr Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser
145                 150                 155                 160

Cys Arg Ser Ser Gln Ser Leu Leu Asp Ser Asp Asp Gly Asn Thr Tyr
                165                 170                 175

Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Arg Leu Leu Ile
            180                 185                 190

Tyr Thr Leu Ser Tyr Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly
        195                 200                 205

Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala
    210                 215                 220

Glu Asp Val Gly Leu Tyr Tyr Cys Thr Gln Arg Leu Glu Phe Pro Ser
225                 230                 235                 240

Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Thr Thr Thr Pro
                245                 250                 255

Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu
            260                 265                 270

Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His
        275                 280                 285

Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu
    290                 295                 300

Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr
305                 310                 315                 320

Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe
                325                 330                 335
```

```
Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg
            340                 345                 350

Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser
        355                 360                 365

Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr
    370                 375                 380

Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys
385                 390                 395                 400

Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn
                405                 410                 415

Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu
            420                 425                 430

Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly
        435                 440                 445

His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr
    450                 455                 460

Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
465                 470                 475
```

<210> 159
<211> 1425
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 159
gaagtgcaac tggtggagag cggtggaggg cttgtccagc ccggaggatc gctgcggctg 60

tcctgtgctg cgtccgggtt caccttctcc ggcttctgga tgtcctgggt cagacaggca 120

ccgggaaagg gcctcgaatg ggtggccaac atcaagcagg atggctccga gaagtactac 180

gtcgactccg tgagaggccg cttcaccatc tcccgggaca acgccaagaa ctcgctgtac 240

ctccaaatga atagcctcag ggcggaagat actgctgtgt attactgcgc acgcgccctt 300

gactactacg gcatggacgt ctggggccaa gggaccactg tgaccgtgtc tagcggaggc 360

ggaggttcag ggggcggtgg atcaggcgga ggaggatcgg ggggtggtgg atcggatatc 420

gtgatgaccc agactcccct gtccctgcct gtgactcccg gagaaccagc ctccatttcc 480

tgccggtcct cccagtccct gctggacagc gacgacggca acacttacct ggactggtac 540

ttgcagaagc cgggccaatc gcctcgcctg ctgatctata ccctgtcata ccgggcctca 600

ggagtgcctg accgcttctc gggatcaggg agcgggaccg atttcaccct gaaaatttcc 660

cgagtggaag ccgaggacgt cggactgtac tactgcaccc agcgcctcga attcccgtcg 720

attacgtttg gacagggtac ccggcttgag atcaagacca ctaccccagc accgaggcca 780

cccaccccgg ctcctaccat cgcctcccag cctctgtccc tgcgtccgga ggcatgtaga 840

cccgcagctg gtggggccgt gcatacccgg ggtcttgact tcgcctgcga tatctacatt 900

tgggcccctc tggctggtac ttgcggggtc ctgctgcttt cactcgtgat cactctttac 960

tgtaagcgcg gtcggaagaa gctgctgtac atctttaagc aacccttcat gaggcctgtg 1020

cagactactc aagaggagga cggctgttca tgccggttcc cagaggagga ggaaggcggc 1080

tgcgaactgc gcgtgaaatt cagccgcagc gcagatgctc cagcctacca gcaggggcag 1140

aaccagctct acaacgaact caatcttggt cggagagagg agtacgacgt gctggacaag 1200

cggagaggac gggacccaga aatgggcggg aagccgcgca gaaagaatcc ccaagagggc 1260

ctgtacaacg agctccaaaa ggataagatg gcagaagcct atagcgagat tggtatgaaa 1320

ggggaacgca gaagaggcaa aggccacgac ggactgtacc agggactcag caccgccacc 1380

aaggacacct atgacgctct tcacatgcag gccctgccgc ctcgg 1425

<210> 160
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 160
Ser Phe Arg Met Asn

1 5

<210> 161
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 161
Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 162
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 162
Trp Leu Ser Tyr Tyr Gly Met Asp Val
1 5

<210> 163
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 163
Gly Phe Thr Phe Ser Ser Phe
1 5

<210> 164
<211> 6

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 164
Ser Ser Ser Ser Ser Tyr
1 5

<210> 165
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 165
Gly Phe Thr Phe Ser Ser Phe Arg
1 5

<210> 166
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 166
Ile Ser Ser Ser Ser Ser Tyr Ile
1 5

<210> 167
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 167

Ala Arg Trp Leu Ser Tyr Tyr Gly Met Asp Val
1 5 10

<210> 168
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 168
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe
20 25 30

Arg Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Leu Ser Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser Ser
115

<210> 169
<211> 354
<212> DNA
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 169
gaagtgcaac tggtggagag cggtggaggg cttgtcaagc ccggaggatc gctgcggctg 60

tcctgtgctg cgtccgggtt caccttctcc tcgttccgca tgaactgggt cagacaggca 120

ccgggaaagg gcctcgaatg ggtgtcctca atctcatcgt cctcgtccta catctactac 180

gccgactccg tgaaaggccg cttcaccatc tcccgggaca acgccaagaa ctcgctgtac 240

ctccaaatga atagcctcag ggcggaagat actgctgtgt attactgcgc acgctggctt 300

tcctactacg gcatggacgt ctggggccaa gggaccactg tgaccgtgtc tagc 354

<210> 170
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 170
Thr Leu Ser Phe Arg Ala Ser
1 5

<210> 171
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 171
Met Gln Arg Ile Gly Phe Pro Ile Thr
1 5

<210> 172
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 172
Arg Ile Gly Phe Pro Ile
1 5

<210> 173
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 173
Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Thr Pro Gly
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu Asp Ser
20 25 30

Asp Asp Gly Asn Thr Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln
35 40 45

Ser Pro Gln Leu Leu Ile Tyr Thr Leu Ser Phe Arg Ala Ser Gly Val
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys
65 70 75 80

Ile Arg Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln
85 90 95

Arg Ile Gly Phe Pro Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile
100 105 110

Lys

<210> 174
<211> 339
<212> DNA

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 174
gatatcgtga tgacccagac tcccctgtcc ctgcctgtga ctcccggaga accagcctcc 60

atttcctgcc ggtcctccca gtccctgctg gacagcgacg acggcaacac ttacctggac 120

tggtacttgc agaagccggg ccaatcgcct cagctgctga tctataccct gtcattccgg 180

gcctcaggag tgcctgaccg cttctcggga tcagggagcg ggaccgattt caccctgaaa 240

attaggcgag tggaagccga ggacgtcgga gtgtactact gcatgcagcg catcggcttc 300

ccgattacgt ttggacaggg tacccggctt gagatcaag 339

<210> 175
<211> 251
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 175
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe
20 25 30

Arg Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

```
Ala Arg Trp Leu Ser Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr
            100                 105                 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln
    130                 135                 140

Thr Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser
145                 150                 155                 160

Cys Arg Ser Ser Gln Ser Leu Leu Asp Ser Asp Asp Gly Asn Thr Tyr
                165                 170                 175

Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile
            180                 185                 190

Tyr Thr Leu Ser Phe Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly
        195                 200                 205

Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Arg Arg Val Glu Ala
    210                 215                 220

Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Arg Ile Gly Phe Pro Ile
225                 230                 235                 240

Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
                245                 250
```

<210> 176
<211> 753
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 176
gaagtgcaac tggtggagag cggtggaggg cttgtcaagc ccggaggatc gctgcggctg 60

tcctgtgctg cgtccgggtt caccttctcc tcgttccgca tgaactgggt cagacaggca 120

ccgggaaagg gcctcgaatg ggtgtcctca atctcatcgt cctcgtccta catctactac 180

gccgactccg tgaaaggccg cttcaccatc tcccgggaca acgccaagaa ctcgctgtac 240

ctccaaatga atagcctcag ggcggaagat actgctgtgt attactgcgc acgctggctt 300

tcctactacg gcatggacgt ctggggccaa gggaccactg tgaccgtgtc tagcggaggc 360

ggaggttcag ggggcggtgg atcaggcgga ggaggatcgg ggggtggtgg atcggatatc 420

gtgatgaccc agactcccct gtccctgcct gtgactcccg gagaaccagc ctccatttcc 480

tgccggtcct cccagtccct gctggacagc gacgacggca acacttacct ggactggtac 540

ttgcagaagc cgggccaatc gcctcagctg ctgatctata ccctgtcatt ccgggcctca 600

ggagtgcctg accgcttctc gggatcaggg agcgggaccg atttcaccct gaaaattagg 660

cgagtggaag ccgaggacgt cggagtgtac tactgcatgc agcgcatcgg cttcccgatt 720

acgtttggac agggtacccg gcttgagatc aag 753

<210> 177
<211> 474
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 177
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe
20 25 30

Arg Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr

```
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Trp Leu Ser Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr
            100                 105                 110

Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln
    130                 135                 140

Thr Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser
145                 150                 155                 160

Cys Arg Ser Ser Gln Ser Leu Leu Asp Ser Asp Asp Gly Asn Thr Tyr
                165                 170                 175

Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile
            180                 185                 190

Tyr Thr Leu Ser Phe Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly
        195                 200                 205

Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Arg Arg Val Glu Ala
    210                 215                 220

Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Arg Ile Gly Phe Pro Ile
225                 230                 235                 240

Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Thr Thr Thr Pro Ala
                245                 250                 255

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
            260                 265                 270

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
        275                 280                 285
```

```
Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
    290                 295                 300

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
305                 310                 315                 320

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
                325                 330                 335

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
            340                 345                 350

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
        355                 360                 365

Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn
    370                 375                 380

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
385                 390                 395                 400

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
                405                 410                 415

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
            420                 425                 430

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
        435                 440                 445

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
    450                 455                 460

Ala Leu His Met Gln Ala Leu Pro Pro Arg
465                 470
```

<210> 178
<211> 1422
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 178
gaagtgcaac tggtggagag cggtggaggg cttgtcaagc ccggaggatc gctgcggctg 60

tcctgtgctg cgtccgggtt caccttctcc tcgttccgca tgaactgggt cagacaggca 120

ccgggaaagg gcctcgaatg ggtgtcctca atctcatcgt cctcgtccta catctactac 180

gccgactccg tgaaaggccg cttcaccatc tcccgggaca acgccaagaa ctcgctgtac 240

ctccaaatga atagcctcag ggcggaagat actgctgtgt attactgcgc acgctggctt 300

tcctactacg gcatggacgt ctggggccaa gggaccactg tgaccgtgtc tagcggaggc 360

ggaggttcag ggggcggtgg atcaggcgga ggaggatcgg ggggtggtgg atcggatatc 420

gtgatgaccc agactcccct gtccctgcct gtgactcccg gagaaccagc ctccatttcc 480

tgccggtcct cccagtccct gctggacagc gacgacggca acacttacct ggactggtac 540

ttgcagaagc cgggccaatc gcctcagctg ctgatctata ccctgtcatt ccgggcctca 600

ggagtgcctg accgcttctc gggatcaggg agcgggaccg atttcaccct gaaaattagg 660

cgagtggaag ccgaggacgt cggagtgtac tactgcatgc agcgcatcgg cttcccgatt 720

acgtttggac agggtacccg gcttgagatc aagaccacta ccccagcacc gaggccaccc 780

accccggctc ctaccatcgc ctcccagcct ctgtccctgc gtccggaggc atgtagaccc 840

gcagctggtg gggccgtgca tacccggggt cttgacttcg cctgcgatat ctacatttgg 900

gcccctctgg ctggtacttg cggggtcctg ctgctttcac tcgtgatcac tctttactgt 960

aagcgcggtc ggaagaagct gctgtacatc tttaagcaac ccttcatgag gcctgtgcag 1020

actactcaag aggaggacgg ctgttcatgc cggttcccag aggaggagga aggcggctgc 1080

gaactgcgcg tgaaattcag ccgcagcgca gatgctccag cctaccagca ggggcagaac 1140

cagctctaca acgaactcaa tcttggtcgg agagaggagt acgacgtgct ggacaagcgg 1200

agaggacggg acccagaaat gggcgggaag ccgcgcagaa agaatcccca agagggcctg 1260

tacaacgagc tccaaaagga taagatggca gaagcctata gcgagattgg tatgaaaggg 1320

gaacgcagaa gaggcaaagg ccacgacgga ctgtaccagg gactcagcac cgccaccaag 1380

gacacctatg acgctcttca catgcaggcc ctgccgcctc gg 1422

<210> 179
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
<221> VARIANT
<222> (1)..(1)
<223> /replace="Ser"

<220>
<221> VARIANT
<222> (3)..(3)
<223> /replace="Arg"

<220>
<221> VARIANT
<222> (5)..(5)
<223> /replace="Asn"

<220>
<221> SITE
<222> (1)..(5)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 179
Gly Phe Trp Met Ser
1 5

<210> 180
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
<221> VARIANT
<222> (1)..(1)
<223> /replace="Ser"

<220>
<221> VARIANT
<222> (3)..(3)
<223> /replace="Ser"

<220>
<221> VARIANT
<222> (4)..(4)
<223> /replace="Ser"

<220>
<221> VARIANT
<222> (5)..(5)
<223> /replace="Ser"

<220>
<221> VARIANT
<222> (6)..(6)
<223> /replace="Ser"

<220>
<221> VARIANT
<222> (8)..(8)
<223> /replace="Tyr"

<220>
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<222> (9)..(9)
<223> /replace="Ile"

<220>
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<222> (12)..(12)
<223> /replace="Ala"

<220>
<221> VARIANT
<222> (16)..(16)
<223> /replace="Lys"

<220>
<221> SITE
<222> (1)..(17)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 180
Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val Arg
1 5 10 15

Gly

<210> 181
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
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<222> (1)..(1)
<223> /replace="Trp"

<220>
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<222> (3)..(3)
<223> /replace="Ser"

<220>
<221> SITE
<222> (1)..(9)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 181
Ala Leu Asp Tyr Tyr Gly Met Asp Val
1 5

<210> 182
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
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<222> (4)..(4)
<223> /replace="Phe"

<220>
<221> SITE

<222> (1)..(7)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 182
Thr Leu Ser Tyr Arg Ala Ser
1 5

<210> 183
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
<221> VARIANT
<222> (1)..(1)
<223> /replace="Met"

<220>
<221> VARIANT
<222> (4)..(4)
<223> /replace="Ile"

<220>
<221> VARIANT
<222> (5)..(5)
<223> /replace="Gly"

<220>
<221> VARIANT
<222> (8)..(8)
<223> /replace=" "

<220>
<221> SITE
<222> (1)..(10)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 183
Thr Gln Arg Leu Glu Phe Pro Ser Ile Thr
1 5 10

<210> 184

<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
<221> VARIANT
<222> (6)..(6)
<223> /replace="Ser"

<220>
<221> SITE
<222> (1)..(7)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 184
Gly Phe Thr Phe Ser Gly Phe
1 5

<210> 185
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
<221> VARIANT
<222> (1)..(1)
<223> /replace="Ser"

<220>
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<222> (2)..(2)
<223> /replace="Ser"

<220>
<221> VARIANT
<222> (3)..(3)
<223> /replace="Ser"

<220>

<221> VARIANT
<222> (4)..(4)
<223> /replace="Ser"

<220>
<221> VARIANT
<222> (6)..(6)
<223> /replace="Tyr"

<220>
<221> SITE
<222> (1)..(6)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 185
Lys Gln Asp Gly Ser Glu
1 5

<210> 186
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
<221> VARIANT
<222> (2)..(2)
<223> /replace="Ile"

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<221> VARIANT
<222> (3)..(3)
<223> /replace="Gly"

<220>
<221> VARIANT
<222> (6)..(6)
<223> /replace=" "

<220>
<221> SITE
<222> (1)..(7)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 186
Arg Leu Glu Phe Pro Ser Ile
1   5

<210> 187
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<220>
<221> VARIANT
<222> (6)..(6)
<223> /replace="Ser"

<220>
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<222> (8)..(8)
<223> /replace="Arg"

<220>
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<222> (1)..(8)
<223> /note="Variant residues given in the sequence have no
      preference with respect to those in the annotations
      for variant positions"

<400> 187
Gly Phe Thr Phe Ser Gly Phe Trp
1   5

<210> 188
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<220>
<221> VARIANT
<222> (2)..(2)
<223> /replace="Ser"

<220>
<221> VARIANT
<222> (3)..(3)
<223> /replace="Ser"

<220>
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<222> (4)..(4)
<223> /replace="Ser"

<220>
<221> VARIANT
<222> (5)..(5)
<223> /replace="Ser"

<220>
<221> VARIANT
<222> (7)..(7)
<223> /replace="Tyr"

<220>
<221> VARIANT
<222> (8)..(8)
<223> /replace="Ile"

<220>
<221> SITE
<222> (1)..(8)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 188
Ile Lys Gln Asp Gly Ser Glu Lys
1   5

<210> 189
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<220>
<221> VARIANT
<222> (3)..(3)
<223> /replace="Trp"

<220>

<221> VARIANT
<222> (5)..(5)
<223> /replace="Ser"

<220>
<221> SITE
<222> (1)..(11)
<223> /note="Variant residues given in the sequence have no
preference with respect to those in the annotations
for variant positions"

<400> 189
Ala Arg Ala Leu Asp Tyr Tyr Gly Met Asp Val
1 5 10

<210> 190

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<210> 201

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<210> 202
<211> 69
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 202
Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala
1 5 10 15

Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly
20 25 30

Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile

35 40 45

Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Ser Leu Val
50 55 60

Ile Thr Leu Tyr Cys
65

<210> 203

<400> 203
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<210> 225
<211> 465
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 225
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

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Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35                  40                  45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu
        115                 120                 125

Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys
    130                 135                 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145                 150                 155                 160

Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser
                165                 170                 175

Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser Arg Val Thr Ile Ser
            180                 185                 190

Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr
        195                 200                 205

Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
    210                 215                 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
225                 230                 235                 240

Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255
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Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile
        275                 280                 285

Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser
    290                 295                 300

Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr
305                 310                 315                 320

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
                325                 330                 335

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
            340                 345                 350

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln
        355                 360                 365

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
    370                 375                 380

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
385                 390                 395                 400

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
                405                 410                 415

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
            420                 425                 430

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
        435                 440                 445

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
    450                 455                 460
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Arg
465

<210> 226

<400> 226
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<210> 250
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 250
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
            20   25   30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35   40   45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys
    50   55   60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65   70   75   80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85   90   95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
            100   105   110

Gly Thr Leu Val Thr Val Ser Ser
        115   120

<210> 251
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 251
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
            20   25   30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
        35   40   45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
    50   55   60

```
Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80


Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95


Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105


<210> 252
<211> 63
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      oligonucleotide"

<400> 252
atggccctcc ctgtcaccgc tctgttgctg ccgcttgctc tgctgctcca cgcagcgcga       60

ccg                                                                     63


<210> 253
<211> 747
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polynucleotide"

<400> 253
caggtacaat tgcaggagtc tggaggcggt gtggtgcaac ccggtcgcag cttgcgcctg       60

agttgtgctg cgtctggatt tacattttca tcttacggaa tgcattgggt acgccaggca      120

ccggggaaag gccttgaatg ggtggctgta atttcatacg atggttccaa caaatactat      180

gctgactcag tcaagggtcg atttacaatt agtcgggaca actccaagaa caccctttat      240

cttcaaatga attcccttag agcagaggat acggcggtct attactgtgg tggcagtggt      300

tatgcacttc atgatgatta ctatggcttg gatgtctggg ggcaagggac gcttgtaact      360

gtatcctctg gtggtggtgg tagtggtggg ggaggctccg gcggtggcgg ctctcaatct      420
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gctctgactc aaccagcaag cgtatcaggg tcaccgggac agagtattac cataagttgc 480

acggggacct ctagcgatgt agggggggtat aattatgtat cttggtatca acaacacccc 540

gggaaagccc ctaaattgat gatctacgac gtgagcaatc gacctagtgg cgtatcaaat 600

cgcttctctg gtagcaagag tgggaatacg gcgtccctta ctattagcgg attgcaagca 660

gaagatgagg ccgattacta ctgcagctcc tatactagct cttctacatt gtacgtcttt 720

gggagcggaa caaaagtaac agtactc 747

<210> 254
<211> 207
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 254
acaacaacac ctgccccgag accgcctaca ccagccccga ctattgccag ccagcctctg 60

agcctcaggc ctgaggcctg taggcccgca gcgggcggcg cagttcatac acggggcttg 120

gatttcgctt gtgatattta tatttgggct cctttggcgg ggacatgtgg cgtgctgctt 180

ctgtcacttg ttattacact gtactgt 207

<210> 255
<211> 126
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 255
aaacgcgggc gaaaaaaatt gctgtatatt tttaagcagc catttatgag gcccgttcag 60

acgacgcagg aggaggacgg ttgctcttgc aggttcccag aagaggaaga agggggctgt 120

gaattg 126

<210> 256
<211> 336

<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 256
cgggttaaat tttcaagatc cgcagacgct ccagcatacc aacagggaca aaaccaactc 60

tataacgagc tgaatcttgg aagaagggag gaatatgatg tgctggataa acggcgcggt 120

agagatccgg agatgggcgg aaaaccaagg cgaaaaaacc ctcaggaggg actctacaac 180

gaactgcaga aagacaaaat ggcggaggct tattccgaaa taggcatgaa gggcgagcgg 240

aggcgaggga aagggcacga cggactgtat caaggcctct caaccgcgac taaggatacg 300

tacgacgccc tgcacatgca ggccctgcct ccgaga 336

<210> 257
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 257
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Val
20 25 30

Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe
35 40 45

Thr Phe Ser Ser Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys
50 55 60

Gly Leu Glu Trp Val Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr
65 70 75 80

Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser

```
                85                  90                  95

Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Gly Gly Ser Gly Tyr Ala Leu His Asp Asp Tyr
        115                 120                 125

Tyr Gly Leu Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
    130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
145                 150                 155                 160

Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser
                165                 170                 175

Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn
            180                 185                 190

Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met
        195                 200                 205

Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe Ser
    210                 215                 220

Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln
225                 230                 235                 240

Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser
                245                 250                 255

Thr Leu Tyr Val Phe Gly Ser Gly Thr Lys Val Thr Val Leu Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300
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Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
            340                 345                 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
        355                 360                 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
    370                 375                 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
385                 390                 395                 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
                405                 410                 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
            420                 425                 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
        435                 440                 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
    450                 455                 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465                 470                 475                 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
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<210> 258
<211> 1479
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 258
atggccctcc ctgtcaccgc tctgttgctg ccgcttgctc tgctgctcca cgcagcgcga 60

ccgcaggtac aattgcagga gtctggaggc ggtgtggtgc aacccggtcg cagcttgcgc 120

ctgagttgtg ctgcgtctgg atttacattt tcatcttacg gaatgcattg ggtacgccag 180

gcaccgggga aaggccttga atgggtggct gtaatttcat acgatggttc caacaaatac 240

tatgctgact cagtcaaggg tcgatttaca attagtcggg acaactccaa gaacaccctt 300

tatcttcaaa tgaattccct tagagcagag gatacggcgg tctattactg tggtggcagt 360

ggttatgcac ttcatgatga ttactatggc ttggatgtct gggggcaagg gacgcttgta 420

actgtatcct ctggtggtgg tggtagtggt gggggaggct ccggcggtgg cggctctcaa 480

tctgctctga ctcaaccagc aagcgtatca gggtcaccgg gacagagtat taccataagt 540

tgcacgggga cctctagcga tgtaggggggg tataattatg tatcttggta tcaacaacac 600

cccgggaaag cccctaaatt gatgatctac gacgtgagca atcgacctag tggcgtatca 660

aatcgcttct ctggtagcaa gagtgggaat acggcgtccc ttactattag cggattgcaa 720

gcagaagatg aggccgatta ctactgcagc tcctatacta gctcttctac attgtacgtc 780

tttgggagcg gaacaaaagt aacagtactc acaacaacac ctgccccgag accgcctaca 840

ccagccccga ctattgccag ccagcctctg agcctcaggc ctgaggcctg taggcccgca 900

gcgggcggcg cagttcatac acggggcttg gatttcgctt gtgatattta tatttgggct 960

cctttggcgg ggacatgtgg cgtgctgctt ctgtcacttg ttattacact gtactgtaaa 1020

cgcgggcgaa aaaaattgct gtatattttt aagcagccat ttatgaggcc cgttcagacg 1080

acgcaggagg aggacggttg ctcttgcagg ttcccagaag aggaagaagg gggctgtgaa 1140

ttgcgggtta aattttcaag atccgcagac gctccagcat accaacaggg acaaaaccaa 1200

ctctataacg agctgaatct tggaagaagg gaggaatatg atgtgctgga taaacggcgc 1260

ggtagagatc cggagatggg cggaaaacca aggcgaaaaa accctcagga gggactctac 1320

aacgaactgc agaaagacaa aatggcggag gcttattccg aaataggcat gaagggcgag 1380

cggaggcgag ggaaagggca cgacggactg tatcaaggcc tctcaaccgc gactaaggat 1440

acgtacgacg ccctgcacat gcaggccctg cctccgaga 1479

<210> 259

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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
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Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Cys Leu Glu Trp Ile
35 40 45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys
50 55 60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

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Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
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Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
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Thr Phe Gly Cys Gly Thr Lys Leu Glu Ile Lys
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His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
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Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

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Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65                  70                  75                  80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
    130                 135                 140

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
145                 150                 155                 160

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser
        195                 200                 205

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
    210                 215                 220

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
225                 230                 235                 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
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        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
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Gln Ala Leu Pro Pro Arg
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cccgaaattg tgatgaccca gtcacccgcc actcttagcc tttcacccgg tgagcgcgca 120

accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta cacctttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcc aggtccaact ccaagaaagc ggaccgggtc ttgtgaagcc atcagaaact 480

ctttcactga cttgtactgt gagcggagtg tctctccccg attacggggt gtcttggatc 540

agacagccac cggggaaggg tctggaatgg attggagtga tttggggctc tgagactact 600

tactaccaat catccctcaa gtcacgcgtc accatctcaa aggacaactc taagaatcag 660

gtgtcactga aactgtcatc tgtgaccgca gccgacaccg ccgtgtacta ttgcgctaag 720

cattactatt atggcgggag ctacgcaatg gattactggg gacagggtac tctggtcacc 780

gtgtccagca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

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<213> Artificial Sequence

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<223> /note="Description of Artificial Sequence: Synthetic
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accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta cacctttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcc aggtccaact ccaagaaagc ggaccgggtc ttgtgaagcc atcagaaact 480

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agacagccac cggggaaggg tctggaatgg attggagtga tttggggctc tgagactact 600

tactaccaat catccctcaa gtcacgcgtc accatctcaa aggacaactc taagaatcag 660

gtgtcactga aactgtcatc tgtgaccgca gccgacaccg ccgtgtacta ttgcgctaag 720

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<220>
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ggacaggctc ctcgccttct gatctaccac accagccggc tccattctgg aatccctgcc 180

aggttcagcg gtagcggatc tgggaccgac tacaccctca ctatcagctc actgcagcca 240

gaggacttcg ctgtctattt ctgtcagcaa gggaacaccc tgccctacac ctttggacag 300

ggcaccaagc tcgagattaa aggtggaggt ggcagcggag gaggtgggtc cggcggtgga 360

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tcactgactt gtactgtgag cggagtgtct ctccccgatt acggggtgtc ttggatcaga 480

cagccaccgg ggaagggtct ggaatggatt ggagtgattt ggggctctga gactacttac 540

taccaatcat ccctcaagtc acgcgtcacc atctcaaagg acaactctaa gaatcaggtg 600

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ctgctgcttt cactcgtgat cactctttac tgtaagcgcg gtcggaagaa gctgctgtac 960

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cggagagagg agtacgacgt gctggacaag cggagaggac gggacccaga aatgggcggg 1200

aagccgcgca gaaagaatcc ccaagagggc ctgtacaacg agctccaaaa ggataagatg 1260

gcagaagcct atagcgagat tggtatgaaa ggggaacgca gaagaggcaa aggccacgac 1320

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<223> /note="Description of Artificial Sequence: Synthetic
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<400> 420
Ser Ala Ser Ser Ser Val Ser Tyr Met Asn
1 5 10

<210> 421
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 421
Asp Thr Ser Lys Leu Ala Ser
1 5

<210> 422
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 422
Gln Gln Trp Ser Ser Asn Pro Phe Thr
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<210> 423
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<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic
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<400> 423
Ser Ser Ser Val Ser Tyr
1 5

<210> 424

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<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 424
Asp Thr Ser
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<210> 425
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<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 425
Trp Ser Ser Asn Pro Phe
1 5

<210> 426
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<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 426
Ser Ser Val Ser Tyr
1 5

<210> 427
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
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<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

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1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Thr Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Phe Thr
85 90 95

Phe Gly Gln Gly Thr Lys Leu Gln Ile Thr
100 105

<210> 428
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 428
Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
1 5 10

<210> 429
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 429
Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Val Lys
1   5   10   15

Asp

<210> 430
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 430
Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr
1   5   10

<210> 431
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 431
Arg Tyr Thr Met His
1   5

<210> 432
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 432
Gly Tyr Thr Phe Thr Arg Tyr
1   5

<210> 433
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 433
Asn Pro Ser Arg Gly Tyr
1 5

<210> 434
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 434
Gly Tyr Thr Phe Thr Arg Tyr Thr
1 5

<210> 435
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 435
Ile Asn Pro Ser Arg Gly Tyr Thr
1 5

<210> 436
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 436
Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr
1   5   10

<210> 437
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 437
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1   5   10   15

Ser Leu Arg Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
            20   25   30

Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
        35   40   45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Val
    50   55   60

Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Ala Phe
65   70   75   80

Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val Tyr Phe Cys
                85   90   95

Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr Trp Gly Gln Gly
            100   105   110

Thr Pro Val Thr Val Ser Ser
        115

<210> 438
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 438
Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
1 5 10

<210> 439
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 439
Gly Thr Lys Phe Leu Ala Pro
1 5

<210> 440
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 440
Val Leu Trp Tyr Ser Asn Arg Trp Val
1 5

<210> 441
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 441
Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr
1 5 10

<210> 442
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 442
Gly Thr Lys
1

<210> 443
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 443
Trp Tyr Ser Asn Arg Trp
1 5

<210> 444
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 444
Thr Gly Ala Val Thr Ser Gly Asn Tyr
1 5

<210> 445
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 445
Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 446
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 446
Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Ser Gly
20 25 30

Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Val
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp Tyr Ser Asn
85 90 95

Arg Trp Val Phe Gly Cys Gly Thr Lys Leu Thr Val Leu
100 105

<210> 447
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 447
Gly Phe Thr Phe Asn Lys Tyr Ala Met Asn
1 5 10

<210> 448
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 448
Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
1 5 10 15

Val Lys Asp

<210> 449
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 449
His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr
1 5 10

<210> 450
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 450
Lys Tyr Ala Met Asn
1 5

<210> 451
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 451
Gly Phe Thr Phe Asn Lys Tyr
1 5

<210> 452
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 452
Arg Ser Lys Tyr Asn Asn Tyr Ala
1 5

<210> 453
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 453
Gly Phe Thr Phe Asn Lys Tyr Ala
1 5

<210> 454
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 454
Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr
1 5 10

<210> 455
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 455
Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr
1 5 10 15

<210> 456
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 456
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 457
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 457
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Lys Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu Trp Val
35 40 45

Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 458
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 458
Arg Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn
1 5 10

<210> 459
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 459
Gly Thr Asn Lys Arg Ala Pro
1 5

<210> 460
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 460
Ala Leu Trp Tyr Ser Asn Leu Trp Val
1 5

<210> 461
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 461
Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr
1 5 10

<210> 462
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 462
Gly Thr Asn
1

<210> 463
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 463
Trp Tyr Ser Asn Leu Trp
1 5

<210> 464
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 464
Thr Gly Ala Val Thr Thr Ser Asn Tyr
1 5

<210> 465
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 465
Gly Gly Thr
1

<210> 466
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 466
Ala Leu Trp Tyr Ser Asn Leu
1 5

<210> 467
<211> 109

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 467
Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Asp Lys Ala Ala Leu Thr Leu Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Phe Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 468
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 468
Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Asp Lys Ala Ala Leu Thr Leu Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Phe Cys Ala Leu Trp Tyr Ser Asn
85 90 95

Leu Trp Val Phe Gly Cys Gly Thr Lys Leu Thr Val Leu
100 105

<210> 469
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 469
Gly Phe Thr Phe Asn Thr Tyr Ala Met Asn
1 5 10

<210> 470
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 470
His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Phe Ala Tyr
1 5 10

<210> 471
<211> 5

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 471
Thr Tyr Ala Met Asn
1 5

<210> 472
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 472
Gly Phe Thr Phe Asn Thr Tyr
1 5

<210> 473
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 473
Gly Phe Thr Phe Asn Thr Tyr Ala
1 5

<210> 474
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 474

Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Phe Ala Tyr
1 5 10 15

<210> 475
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 475
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Ser Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 476
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 476
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Ser Gly Lys Cys Leu Glu Trp Val
35 40 45

Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 477
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 477
Arg Ser Ser Gln Ser Leu Val Arg Ser Glu Gly Thr Thr Tyr Phe Asn
1 5 10 15

<210> 478
<211> 7
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 478
Arg Val Ser Asn Arg Phe Ser
1 5

<210> 479
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 479
Leu Gln Ser Ser His Phe Pro Trp Thr
1 5

<210> 480
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 480
Ser Gln Ser Leu Val Arg Ser Glu Gly Thr Thr Tyr
1 5 10

<210> 481
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 481
Arg Val Ser

1

<210> 482
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 482
Ser Ser His Phe Pro Trp
1 5

<210> 483
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 483
Gln Ser Leu Val Arg Ser Glu Gly Thr Thr Tyr
1 5 10

<210> 484
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 484
Asp Ile Leu Val Thr Gln Thr Pro Val Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Gly His Val Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Arg Ser
20 25 30

Glu Gly Thr Thr Tyr Phe Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Arg Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Pro Glu Asp Leu Gly Val Tyr Tyr Cys Leu Gln Ser
85 90 95

Ser His Phe Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys
100 105 110

<210> 485
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 485
Gly Phe Thr Phe Ser Lys Gln Gly Met His
1 5 10

<210> 486
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 486
Met Ile Tyr Tyr Asp Ser Ser Lys Met Tyr Tyr Ala Asp Thr Val Lys
1 5 10 15

Gly

<210> 487
<211> 9

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 487
Phe Trp Trp Asp Leu Asp Phe Asp His
1 5

<210> 488
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 488
Lys Gln Gly Met His
1 5

<210> 489
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 489
Gly Phe Thr Phe Ser Lys Gln
1 5

<210> 490
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 490

Tyr Tyr Asp Ser Ser Lys
1 5

<210> 491
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 491
Gly Phe Thr Phe Ser Lys Gln Gly
1 5

<210> 492
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 492
Ile Tyr Tyr Asp Ser Ser Lys Met
1 5

<210> 493
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 493
Ala Ser Phe Trp Trp Asp Leu Asp Phe Asp His
1 5 10

<210> 494
<211> 118
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 494
Glu Val Lys Leu Val Glu Ser Gly Gly Asp Leu Val Gln Pro Gly Asp
1 5 10 15

Ser Leu Thr Leu Ser Cys Val Ala Ser Gly Phe Thr Phe Ser Lys Gln
20 25 30

Gly Met His Trp Ile Arg Gln Ala Pro Lys Lys Gly Leu Glu Trp Ile
35 40 45

Ala Met Ile Tyr Tyr Asp Ser Ser Lys Met Tyr Tyr Ala Asp Thr Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Glu Met Asn Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Ser Phe Trp Trp Asp Leu Asp Phe Asp His Trp Gly Gln Gly Val
100 105 110

Met Val Thr Val Ser Ser
115

<210> 495
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 495
Ser Ala Thr Ser Ser Val Ser Tyr Met His
1 5 10

<210> 496

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 496
Gln Gln Trp Ser Ser Asn Pro Leu Thr
1 5

<210> 497
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 497
Thr Ser Ser Val Ser Tyr
1 5

<210> 498
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 498
Trp Ser Ser Asn Pro Leu
1 5

<210> 499
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 499
Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1   5   10   15

Glu Lys Val Thr Met Thr Cys Ser Ala Thr Ser Ser Val Ser Tyr Met
            20   25   30

His Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr
        35   40   45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
    50   55   60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
65   70   75   80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr
                85   90   95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
            100   105

<210> 500
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 500
Gly Tyr Lys Phe Thr Ser Tyr Val Met His
1   5   10

<210> 501
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 501
Tyr Ile Asn Pro Tyr Asn Asp Val Thr Lys Tyr Asn Glu Lys Phe Lys
1   5   10   15

Gly

<210> 502
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 502
Gly Ser Tyr Tyr Asp Tyr Asp Gly Phe Val Tyr
1   5   10

<210> 503
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 503
Ser Tyr Val Met His
1   5

<210> 504
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 504
Gly Tyr Lys Phe Thr Ser Tyr
1   5

<210> 505
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 505
Asn Pro Tyr Asn Asp Val
1 5

<210> 506
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 506
Gly Tyr Lys Phe Thr Ser Tyr Val
1 5

<210> 507
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 507
Ile Asn Pro Tyr Asn Asp Val Thr
1 5

<210> 508
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 508
Ala Arg Gly Ser Tyr Tyr Asp Tyr Asp Gly Phe Val Tyr
1   5   10

<210> 509
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 509
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Lys Phe Thr Ser Tyr
            20   25   30

Val Met His Trp Val Lys Gln Lys Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45

Gly Tyr Ile Asn Pro Tyr Asn Asp Val Thr Lys Tyr Asn Glu Lys Phe
    50   55   60

Lys Gly Lys Ala Thr Leu Thr Ser Asp Lys Ser Ser Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val His Tyr Cys
                85   90   95

Ala Arg Gly Ser Tyr Tyr Asp Tyr Asp Gly Phe Val Tyr Trp Gly Gln
            100   105   110

Gly Thr Leu Val Thr Val Ser Ala
        115   120

<210> 510
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 510
His Ala Ser Gln Asn Ile Tyr Val Trp Leu Asn
1 5 10

<210> 511
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 511
Lys Ala Ser Asn Leu His Thr
1 5

<210> 512
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 512
Gln Gln Gly Gln Thr Tyr Pro Tyr Thr
1 5

<210> 513
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 513
Ser Gln Asn Ile Tyr Val Trp
1 5

<210> 514
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 514
Lys Ala Ser
1

<210> 515
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 515
Gly Gln Thr Tyr Pro Tyr
1 5

<210> 516
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 516
Gln Asn Ile Tyr Val Trp
1 5

<210> 517
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 517
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys His Ala Ser Gln Asn Ile Tyr Val Trp
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Lys Ala Ser Asn Leu His Thr Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Gln Thr Tyr Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 518
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 518
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys His Ala Ser Gln Asn Ile Tyr Val Trp
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

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Tyr Lys Ala Ser Asn Leu His Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Gln Thr Tyr Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205

Phe Asn Arg Gly Glu Cys
    210


<210> 519
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"
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<400> 519
Gly Tyr Thr Phe Thr Ser Tyr Tyr Ile His
1 5 10

<210> 520
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 520
Cys Ile Tyr Pro Gly Asn Val Asn Thr Asn Tyr Asn Glu Lys Phe Lys
1 5 10 15

Asp

<210> 521
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 521
Ser His Tyr Gly Leu Asp Trp Asn Phe Asp Val
1 5 10

<210> 522
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 522
Ser Tyr Tyr Ile His
1 5

<210> 523
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 523
Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> 524
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 524
Tyr Pro Gly Asn Val Asn
1 5

<210> 525
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 525
Gly Tyr Thr Phe Thr Ser Tyr Tyr
1 5

<210> 526
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 526
Ile Tyr Pro Gly Asn Val Asn Thr
1   5

<210> 527
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 527
Thr Arg Ser His Tyr Gly Leu Asp Trp Asn Phe Asp Val
1   5   10

<210> 528
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 528
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20   25   30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45

Gly Cys Ile Tyr Pro Gly Asn Val Asn Thr Asn Tyr Asn Glu Lys Phe
    50   55   60

Lys Asp Arg Ala Thr Leu Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
                85   90   95

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Thr Arg Ser His Tyr Gly Leu Asp Trp Asn Phe Asp Val Trp Gly Gln
            100                 105                 110


Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210> 529
<211> 223
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 529
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45


Gly Cys Ile Tyr Pro Gly Asn Val Asn Thr Asn Tyr Asn Glu Lys Phe
    50                  55                  60


Lys Asp Arg Ala Thr Leu Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95


Thr Arg Ser His Tyr Gly Leu Asp Trp Asn Phe Asp Val Trp Gly Gln
            100                 105                 110


Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125


Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
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    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
    210                 215                 220


<210> 530
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 530
Ser Gly Ser Ser Ser Asn Ile Val Ser Asn Tyr Val Asn
1               5                   10


<210> 531
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 531
Asp Asn Asn Lys Arg Pro Ser
1               5


<210> 532
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<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 532
Gln Ser Tyr Ala Ile Gly Ser Tyr Ser Val Val
1 5 10

<210> 533
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 533
Ser Ser Ser Asn Ile Val Ser Asn Tyr
1 5

<210> 534
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 534
Asp Asn Asn
1

<210> 535
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 535
Tyr Ala Ile Gly Ser Tyr Ser Val
1 5

<210> 536
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 536
Ser Ser Asn Ile Val Ser Asn Tyr
1 5

<210> 537
<211> 110
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 537
Asp Ile Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Val Ser Asn
20 25 30

Tyr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Asp Asn Asn Lys Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Ala Ile Gly Ser
85 90 95

Tyr Ser Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> 538
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 538
Gly Phe Thr Phe Ser Thr Tyr Gly Met Ser
1 5 10

<210> 539
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 539
Ser Ile Phe Tyr Thr Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 540
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 540
Ile Gly Tyr Ala Gly Asp Ser Lys Tyr Ala Ile
1 5 10

<210> 541
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 541
Thr Tyr Gly Met Ser
1 5

<210> 542
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 542
Gly Phe Thr Phe Ser Thr Tyr
1 5

<210> 543
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 543
Phe Tyr Thr Gly Ser Ser
1 5

<210> 544
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 544
Gly Phe Thr Phe Ser Thr Tyr Gly
1   5

<210> 545
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 545
Ile Phe Tyr Thr Gly Ser Ser Thr
1   5

<210> 546
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 546
Ala Arg Ile Gly Tyr Ala Gly Asp Ser Lys Tyr Ala Ile
1   5   10

<210> 547
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 547
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1   5   10   15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
            20   25   30

```
Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ser Ile Phe Tyr Thr Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ile Gly Tyr Ala Gly Asp Ser Lys Tyr Ala Ile Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser
        115                 120


<210> 548
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 548
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
            20                  25                  30


Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ser Ile Phe Tyr Thr Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80
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Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ile Gly Tyr Ala Gly Asp Ser Lys Tyr Ala Ile Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 549
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 549
Lys Ser Ser Gln Ser Leu Leu Ser Gly Ser Phe Asn Tyr Leu Thr
1 5 10 15

<210> 550
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 550
Tyr Ala Ser Thr Arg His Thr
1 5

<210> 551
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 551
His His His Tyr Asn Ala Pro Pro Thr
1   5

<210> 552
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 552
Ser Gln Ser Leu Leu Ser Gly Ser Phe Asn Tyr
1   5   10

<210> 553
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 553
Tyr Ala Ser
1

<210> 554
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 554
His Tyr Asn Ala Pro Pro
1   5

<210> 555
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 555
Gln Ser Leu Leu Ser Gly Ser Phe Asn Tyr
1 5 10

<210> 556
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 556
Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Ser Gly
20 25 30

Ser Phe Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Phe Tyr Ala Ser Thr Arg His Thr Gly Val Pro Asp
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys His His His Tyr
85 90 95

Asn Ala Pro Pro Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100 105 110

<210> 557
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 557
Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Leu Leu Ser Gly
20 25 30

Ser Phe Asn Tyr Leu Thr Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Phe Tyr Ala Ser Thr Arg His Thr Gly Val Pro Asp
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
65 70 75 80

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys His His His Tyr
85 90 95

Asn Ala Pro Pro Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys Arg
100 105 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
115 120 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
130 135 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145 150 155 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
165 170 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
180 185 190

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His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
        195                 200                 205


Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210> 558
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 558
Gly Phe Thr Phe Ser Asp Tyr Trp Met Asp
1               5                   10


<210> 559
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 559
Asn Ile Asp Glu Asp Gly Ser Ile Thr Glu Tyr Ser Pro Phe Val Lys
1               5                   10                  15


Gly



<210> 560
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 560
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Trp Gly Arg Phe Gly Phe Asp Ser
1   5

<210> 561
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 561
Asp Tyr Trp Met Asp
1   5

<210> 562
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 562
Gly Phe Thr Phe Ser Asp Tyr
1   5

<210> 563
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 563
Asp Glu Asp Gly Ser Ile
1   5

<210> 564
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 564
Gly Phe Thr Phe Ser Asp Tyr Trp
1 5

<210> 565
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 565
Ile Asp Glu Asp Gly Ser Ile Thr
1 5

<210> 566
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 566
Thr Arg Trp Gly Arg Phe Gly Phe Asp Ser
1 5 10

<210> 567
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 567
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
            20   25   30

Trp Met Asp Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Val Trp Val
        35   40   45

Ser Asn Ile Asp Glu Asp Gly Ser Ile Thr Glu Tyr Ser Pro Phe Val
    50   55   60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65   70   75   80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Thr Arg Trp Gly Arg Phe Gly Phe Asp Ser Trp Gly Gln Gly Thr Leu
            100   105   110

Val Thr Val Ser Ser
        115

<210> 568
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 568
Arg Ala Ser Gln Gly Ile Ser Arg Trp Leu Ala
1   5   10

<210> 569
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 569
Gln Gln Tyr Asn Thr Tyr Pro Arg Thr
1   5

<210> 570
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 570
Ser Gln Gly Ile Ser Arg Trp
1   5

<210> 571
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 571
Tyr Asn Thr Tyr Pro Arg
1   5

<210> 572
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 572
Gln Gly Ile Ser Arg Trp
1   5

<210> 573
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 573
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Arg Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Glu Lys Ala Pro Lys Ser Leu Ile
35 40 45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Thr Tyr Pro Arg
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 574
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 574
Gly Phe Thr Phe Ser Ser Tyr Asp Met His
1 5 10

<210> 575
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 575
Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 576
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 576
Gly Ser Gly Asn Trp Gly Phe Phe Asp Tyr
1 5 10

<210> 577
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 577
Ser Tyr Asp Met His
1 5

<210> 578
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 578
Trp Tyr Asp Gly Ser Asn
1   5

<210> 579
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 579
Gly Phe Thr Phe Ser Ser Tyr Asp
1   5

<210> 580
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 580
Ile Trp Tyr Asp Gly Ser Asn Lys
1   5

<210> 581
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 581
Ala Arg Gly Ser Gly Asn Trp Gly Phe Phe Asp Tyr
1   5   10

<210> 582
<211> 118
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 582
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Asp Met His Trp Val Arg Gln Ala Pro Gly Gly Leu Glu Trp Val Ala
35 40 45

Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg Gly Ser Gly Asn Trp Gly Phe Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 583
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 583
Ser Ala Ser Ser Ser Arg Ser Tyr Met Gln
1 5 10

<210> 584
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 584
His Gln Arg Ser Ser Tyr Thr
1 5

<210> 585
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 585
Ser Ser Ser Arg Ser Tyr
1 5

<210> 586
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 586
Arg Ser Ser Tyr
1

<210> 587
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 587
Ser Ser Arg Ser Tyr
1 5

<210> 588
<211> 104
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 588
Gln Ile Val Ser Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Arg Ser Tyr Met
20 25 30

Gln Trp Tyr Gln Gln Lys Pro Gly Thr Ser Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys His Gln Arg Ser Ser Tyr Thr Phe Gly
85 90 95

Gly Gly Thr Lys Leu Glu Ile Lys
100

<210> 589
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 589
Gly Tyr Ser Phe Thr Arg Tyr Trp Met His
1 5 10

<210> 590
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 590
Ala Ile Tyr Pro Gly Asn Ser Asp Thr Ser Tyr Asn Gln Lys Phe Glu
1 5 10 15

Gly

<210> 591
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 591
Asp Tyr Gly Tyr Tyr Phe Asp Phe
1 5

<210> 592
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 592
Arg Tyr Trp Met His
1 5

<210> 593
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 593
Gly Tyr Ser Phe Thr Arg Tyr
1 5

<210> 594
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 594
Tyr Pro Gly Asn Ser Asp
1 5

<210> 595
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 595
Gly Tyr Ser Phe Thr Arg Tyr Trp
1 5

<210> 596
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 596
Ile Tyr Pro Gly Asn Ser Asp Thr
1 5

<210> 597
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 597
Ser Arg Asp Tyr Gly Tyr Tyr Phe Asp Phe
1 5 10

<210> 598
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 598
Glu Val Gln Leu Gln Gln Ser Gly Thr Val Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Arg Tyr
20 25 30

Trp Met His Trp Ile Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Ser Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Glu Gly Lys Ala Lys Leu Thr Ala Val Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Thr His Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ser Arg Asp Tyr Gly Tyr Tyr Phe Asp Phe Trp Gly Gln Gly Thr Thr
100 105 110

Leu Thr Val Ser Ser
115

<210> 599
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 599
Lys Ala Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr Met Asn
1 5 10 15

<210> 600
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 600
Ala Ala Ser Asn Leu Glu Ser
1 5

<210> 601
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 601
Gln Gln Ser Asn Glu Asp Pro Tyr Thr

1 5

<210> 602
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 602
Ser Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr
1 5 10

<210> 603
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 603
Ser Asn Glu Asp Pro Tyr
1 5

<210> 604
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 604
Gln Ser Val Asp Tyr Asp Gly Asp Ser Tyr
1 5 10

<210> 605
<211> 111
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 605
Asp Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Arg Pro Gly Gln Ser Pro
35 40 45

Arg Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Val Pro Asp
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser
65 70 75 80

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln Ser Asn
85 90 95

Glu Asp Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

<210> 606
<211> 218
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 606
Asp Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ala Ser Gln Ser Val Asp Tyr Asp
20 25 30

Gly Asp Ser Tyr Met Asn Trp Tyr Gln Gln Arg Pro Gly Gln Ser Pro
35 40 45

```
Arg Leu Leu Ile Tyr Ala Ala Ser Asn Leu Glu Ser Gly Val Pro Asp
    50                  55                  60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser
65                  70                  75                  80

Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln Ser Asn
                85                  90                  95

Glu Asp Pro Tyr Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
            100                 105                 110

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln
        115                 120                 125

Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr
    130                 135                 140

Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser
145                 150                 155                 160

Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr
                165                 170                 175

Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
            180                 185                 190

His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro
        195                 200                 205

Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215
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<210> 607
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 607
Gly Tyr Ala Phe Thr Asn Tyr Leu Ile Glu
1 5 10

<210> 608
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 608
Val Ile Asn Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe Lys
1 5 10 15

Gly

<210> 609
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 609
Trp Arg Gly Asp Gly Tyr Tyr Ala Tyr Phe Asp Val
1 5 10

<210> 610
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 610
Asn Tyr Leu Ile Glu
1 5

<210> 611
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 611
Gly Tyr Ala Phe Thr Asn Tyr
1 5

<210> 612
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 612
Asn Pro Gly Ser Gly Gly
1 5

<210> 613
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 613
Gly Tyr Ala Phe Thr Asn Tyr Leu
1 5

<210> 614
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 614
Ile Asn Pro Gly Ser Gly Gly Thr
1 5

<210> 615
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 615
Ala Arg Trp Arg Gly Asp Gly Tyr Tyr Ala Tyr Phe Asp Val
1 5 10

<210> 616
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 616
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ala Phe Thr Asn Tyr
20 25 30

Leu Ile Glu Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Val Ile Asn Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

```
Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95


Ala Arg Trp Arg Gly Asp Gly Tyr Tyr Ala Tyr Phe Asp Val Trp Gly
            100                 105                 110


Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210> 617
<211> 224
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 617
Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1               5                   10                  15


Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ala Phe Thr Asn Tyr
            20                  25                  30


Leu Ile Glu Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
        35                  40                  45


Gly Val Ile Asn Pro Gly Ser Gly Gly Thr Asn Tyr Asn Glu Lys Phe
    50                  55                  60


Lys Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
                85                  90                  95


Ala Arg Trp Arg Gly Asp Gly Tyr Tyr Ala Tyr Phe Asp Val Trp Gly
            100                 105                 110


Gln Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
        115                 120                 125
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Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
    130                 135                 140


Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
145                 150                 155                 160


Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala
                165                 170                 175


Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
            180                 185                 190


Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His
        195                 200                 205


Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
    210                 215                 220


<210> 618
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 618
Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
1               5                   10


<210> 619
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 619
Asp Ala Ser Asn Arg Ala Thr
1               5
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<210> 620
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 620
Gln Gln Arg Ser Asn Trp Pro Pro Ala Leu Thr
1 5 10

<210> 621
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 621
Ser Gln Ser Val Ser Ser Tyr
1 5

<210> 622
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 622
Asp Ala Ser
1

<210> 623
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 623
Arg Ser Asn Trp Pro Pro Ala Leu
1 5

<210> 624
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 624
Gln Ser Val Ser Ser Tyr
1 5

<210> 625
<211> 109
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 625
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Pro

85 90 95

Ala Leu Thr Phe Cys Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 626
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 626
Gly Gly Ser Phe Ser Gly Tyr Tyr Trp Ser
1 5 10

<210> 627
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 627
Glu Ile Asn His Gly Gly Tyr Val Thr Tyr Asn Pro Ser Leu Glu Ser
1 5 10 15

<210> 628
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 628
Asp Tyr Gly Pro Gly Asn Tyr Asp Trp Tyr Phe Asp Leu
1 5 10

<210> 629
<211> 5

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 629
Gly Tyr Tyr Trp Ser
1 5

<210> 630
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 630
Gly Gly Ser Phe Ser Gly Tyr
1 5

<210> 631
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 631
Asn His Gly Gly Tyr
1 5

<210> 632
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 632

Gly Gly Ser Phe Ser Gly Tyr Tyr
1 5

<210> 633
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 633
Ile Asn His Gly Gly Tyr Val
1 5

<210> 634
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 634
Ala Arg Asp Tyr Gly Pro Gly Asn Tyr Asp Trp Tyr Phe Asp Leu
1 5 10 15

<210> 635
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 635
Gln Val Gln Leu Gln Gln Trp Gly Ala Gly Leu Leu Lys Pro Ser Glu
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Val Tyr Gly Gly Ser Phe Ser Gly Tyr
20 25 30

Tyr Trp Ser Trp Ile Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Ile

```
        35                  40                  45

Gly Glu Ile Asn His Gly Gly Tyr Val Thr Tyr Asn Pro Ser Leu Glu
    50                  55                  60

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
65                  70                  75                  80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85                  90                  95

Arg Asp Tyr Gly Pro Gly Asn Tyr Asp Trp Tyr Phe Asp Leu Trp Gly
            100                 105                 110

Arg Gly Thr Leu Val Thr Val Ser Ser
        115                 120
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<210> 636
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 636
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Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn
1               5                   10
```

<210> 637
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 637
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Tyr Thr Ser Arg Leu His Ser
1               5
```

<210> 638

<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 638
Ser Gln Asp Ile Ser Ser Tyr
1 5

<210> 639
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 639
Tyr Thr Ser
1

<210> 640
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 640
Gly Asn Thr Leu Pro Tyr
1 5

<210> 641
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 641
Gln Asp Ile Ser Ser Tyr
1   5

<210> 642
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 642
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Ile Ser Ser Tyr
            20   25   30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85   90   95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100   105

<210> 643
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 643
Gly Tyr Ser Ile Thr Ser Asp His Ala Trp Ser
1   5   10

<210> 644
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 644
Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu Lys Ser
1   5   10   15

<210> 645
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 645
Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr
1   5   10

<210> 646
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 646
Ser Asp His Ala Trp Ser
1   5

<210> 647
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 647
Gly Tyr Ser Ile Thr Ser Asp His
1 5

<210> 648
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 648
Ser Tyr Ser Gly Ile
1 5

<210> 649
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 649
Gly Tyr Ser Ile Thr Ser Asp His Ala
1 5

<210> 650
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 650
Ile Ser Tyr Ser Gly Ile Thr
1 5

<210> 651
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 651
Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr
1 5 10

<210> 652
<211> 119
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 652
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Tyr Ser Ile Thr Ser Asp
20 25 30

His Ala Trp Ser Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp
35 40 45

Ile Gly Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr Trp Gly Gln Gly
100 105 110

Ser Leu Val Thr Val Ser Ser
        115

<210> 653
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 653
Gln Gln Ser Tyr Ser Thr Pro Pro Ile Thr
1   5   10

<210> 654
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 654
Ser Tyr Ser Thr Pro Pro Ile
1   5

<210> 655
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 655
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1   5   10   15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr
            20   25   30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35   40   45

Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65   70   75   80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Ser Thr Pro Pro
                85   90   95

Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
            100   105

<210> 656
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 656
Gly Phe Thr Phe Ser Asp Tyr Tyr Met Thr
1   5   10

<210> 657
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 657
Tyr Ile Ser Ser Ser Gly Thr Asn Lys Tyr Asn Ala Asp Ser Val Lys
1   5   10   15

Gly

<210> 658
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 658
Asp Pro Pro Trp Gly Met Asp Val
1 5

<210> 659
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 659
Asp Tyr Tyr Met Thr
1 5

<210> 660
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 660
Ser Ser Ser Gly Thr Asn
1 5

<210> 661
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 661
Gly Phe Thr Phe Ser Asp Tyr Tyr
1 5

<210> 662
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 662
Ile Ser Ser Ser Gly Thr Asn Lys
1 5

<210> 663
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 663
Val Arg Asp Pro Pro Trp Gly Met Asp Val
1 5 10

<210> 664
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 664
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Tyr Met Thr Trp Ile Arg Gln Thr Pro Gly Lys Gly Leu Asp Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Thr Asn Lys Tyr Asn Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Val Arg Asp Pro Pro Trp Gly Met Asp Val Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser
115

<210> 665
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 665
Arg Ser Ser Gln Ser Leu Leu His Ser Ser Gly Asn Thr Tyr Leu Asn
1 5 10 15

<210> 666
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 666
Leu Val Ser Lys Leu Glu Ser
1 5

<210> 667
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 667
Met Gln Phe Thr His Tyr Pro Tyr Thr
1 5

<210> 668
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 668
Ser Gln Ser Leu Leu His Ser Ser Gly Asn Thr Tyr
1 5 10

<210> 669
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 669
Leu Val Ser
1

<210> 670
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 670
Phe Thr His Tyr Pro Tyr
1 5

<210> 671
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 671
Gln Ser Leu Leu His Ser Ser Gly Asn Thr Tyr
1 5 10

<210> 672
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 672
Asp Val Val Met Thr Gln Ser Pro Pro Ser Leu Leu Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Ser Gly Asn Thr Tyr Leu Asn Trp Leu Leu Gln Arg Pro Gly Gln Ser
35 40 45

Pro Gln Pro Leu Ile Tyr Leu Val Ser Lys Leu Glu Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Gly Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Phe
85 90 95

Thr His Tyr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 673
<211> 219
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 673
Asp Val Val Met Thr Gln Ser Pro Pro Ser Leu Leu Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Ser Gly Asn Thr Tyr Leu Asn Trp Leu Leu Gln Arg Pro Gly Gln Ser
35 40 45

Pro Gln Pro Leu Ile Tyr Leu Val Ser Lys Leu Glu Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Gly Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Phe
85 90 95

Thr His Tyr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe
130 135 140

```
Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln
145                 150                 155                 160


Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
                165                 170                 175


Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
            180                 185                 190


Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
        195                 200                 205


Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
    210                 215


<210> 674
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 674
Gly Tyr Ile Phe Thr Glu Tyr Tyr Met Tyr
1               5                   10


<210> 675
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 675
Arg Ile Asp Pro Glu Asp Gly Ser Ile Asp Tyr Val Glu Lys Phe Lys
1               5                   10                  15


Lys
```

<210> 676
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 676
Gly Lys Phe Asn Tyr Arg Phe Ala Tyr
1 5

<210> 677
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 677
Glu Tyr Tyr Met Tyr
1 5

<210> 678
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 678
Gly Tyr Ile Phe Thr Glu Tyr
1 5

<210> 679
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 679
Asp Pro Glu Asp Gly Ser
1 5

<210> 680
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 680
Gly Tyr Ile Phe Thr Glu Tyr Tyr
1 5

<210> 681
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 681
Ile Asp Pro Glu Asp Gly Ser Ile
1 5

<210> 682
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 682
Ala Arg Gly Lys Phe Asn Tyr Arg Phe Ala Tyr
1 5 10

<210> 683
<211> 118

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 683
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Gln Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Glu Tyr
20 25 30

Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Leu Val
35 40 45

Gly Arg Ile Asp Pro Glu Asp Gly Ser Ile Asp Tyr Val Glu Lys Phe
50 55 60

Lys Lys Lys Val Thr Leu Thr Ala Asp Thr Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Lys Phe Asn Tyr Arg Phe Ala Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 684
<211> 221
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 684
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Gln Arg Pro Gly Ala
1 5 10 15

```
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Glu Tyr
            20                  25                  30

Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Leu Val
        35                  40                  45

Gly Arg Ile Asp Pro Glu Asp Gly Ser Ile Asp Tyr Val Glu Lys Phe
    50                  55                  60

Lys Lys Lys Val Thr Leu Thr Ala Asp Thr Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Lys Phe Asn Tyr Arg Phe Ala Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
        115                 120                 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
    130                 135                 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145                 150                 155                 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
                165                 170                 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
            180                 185                 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
        195                 200                 205

Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys
    210                 215                 220
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<210> 685
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 685
atggccttac cagtgaccgc cttgctcctg ccgctggcct tgctgctcca cgccgccagg 60

ccggacatcc agatgacaca gactacatcc tccctgtctg cctctctggg agacagagtc 120

accatcagtt gcagggcaag tcaggacatt agtaaatatt taaattggta tcagcagaaa 180

ccagatggaa ctgttaaact cctgatctac catacatcaa gattacactc aggagtccca 240

tcaaggttca gtggcagtgg gtctggaaca gattattctc tcaccattag caacctggag 300

caagaagata ttgccactta cttttgccaa cagggtaata cgcttccgta cacgttcgga 360

gggggggacca agctggagat cacaggtggc ggtggctcgg gcggtggtgg gtcgggtggc 420

ggcggatctg aggtgaaact gcaggagtca ggacctggcc tggtggcgcc ctcacagagc 480

ctgtccgtca catgcactgt ctcaggggtc tcattacccg actatggtgt aagctggatt 540

cgccagcctc cacgaaaggg tctggagtgg ctgggagtaa tatggggtag tgaaaccaca 600

tactataatt cagctctcaa atccagactg accatcatca aggacaactc caagagccaa 660

gttttcttaa aaatgaacag tctgcaaact gatgacacag ccatttacta ctgtgccaaa 720

cattattact acggtggtag ctatgctatg gactactggg gccaaggaac ctcagtcacc 780

gtctcctcaa ccacgacgcc agcgccgcga ccaccaacac cggcgcccac catcgcgtcg 840

cagcccctgt ccctgcgccc agaggcgtgc cggccagcgg cgggggcgc agtgcacacg 900

agggggctgg acttcgcctg tgatatctac atctgggcgc ccttggccgg gacttgtggg 960

gtccttctcc tgtcactggt tatcaccctt tactgcaaac ggggcagaaa gaaactcctg 1020

tatatattca aacaaccatt tatgagacca gtacaaacta ctcaagagga agatggctgt 1080

agctgccgat ttccagaaga agaagaagga ggatgtgaac tgagagtgaa gttcagcagg 1140

agcgcagacg cccccgcgta caagcagggc cagaaccagc tctataacga gctcaatcta 1200

ggacgaagag aggagtacga tgttttggac aagagacgtg gccgggaccc tgagatgggg 1260

ggaaagccga gaaggaagaa ccctcaggaa ggcctgtaca atgaactgca gaaagataag 1320

atggcggagg cctacagtga gattgggatg aaaggcgagc gccggagggg caaggggcac 1380

gatggccttt accagggtct cagtacagcc accaaggaca cctacgacgc ccttcacatg 1440

caggccctgc cccctcgc 1458

<210> 686
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 686
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu
115 120 125

Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys
130 135 140

```
Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145                 150                 155                 160


Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser
                165                 170                 175


Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile
            180                 185                 190


Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln
        195                 200                 205


Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
    210                 215                 220


Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val
225                 230                 235                 240


Ser Ser
```

<210> 687
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 687
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Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser
1               5                   10                  15
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<210> 688
<211> 813
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 688
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaattg tgatgaccca gtcacccgcc actcttagcc tttcacccgg tgagcgcgca 120

accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta cacctttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcc aggtccaact ccaagaaagc ggaccgggtc ttgtgaagcc atcagaaact 480

ctttcactga cttgtactgt gagcggagtg tctctccccg attacggggt gtcttggatc 540

agacagccac cggggaaggg tctggaatgg attggagtga tttggggctc tgagactact 600

tactaccaat catccctcaa gtcacgcgtc accatctcaa aggacaactc taagaatcag 660

gtgtcactga aactgtcatc tgtgaccgca gccgacaccg ccgtgtacta ttgcgctaag 720

cattactatt atggcgggag ctacgcaatg gattactggg gacagggtac tctggtcacc 780

gtgtccagcc accaccatca tcaccatcac cat 813

<210> 689
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 689
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala

```
    50                  55                  60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65                  70                  75                  80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
    130                 135                 140

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
145                 150                 155                 160

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser
        195                 200                 205

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
    210                 215                 220

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
225                 230                 235                 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270
```

```
Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg
```

<210> 690
<211> 1458
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 690
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaattg tgatgaccca gtcacccgcc actcttagcc tttcacccgg tgagcgcgca 120

accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta cacctttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcc aggtccaact ccaagaaagc ggaccgggtc ttgtgaagcc atcagaaact 480

ctttcactga cttgtactgt gagcggagtg tctctccccg attacggggt gtcttggatc 540

agacagccac cggggaaggg tctggaatgg attggagtga tttggggctc tgagactact 600

tactaccaat catccctcaa gtcacgcgtc accatctcaa aggacaactc taagaatcag 660

gtgtcactga aactgtcatc tgtgaccgca gccgacaccg ccgtgtacta ttgcgctaag 720

cattactatt atggcgggag ctacgcaatg gattactggg gacagggtac tctggtcacc 780

gtgtccagca ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 840

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 900

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 960

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1020

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1080

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1140

agcgcagatg ctccagccta caagcagggg cagaaccagc tctacaacga actcaatctt 1200

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 1260

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 1320

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 1380

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 1440

caggccctgc cgcctcgg 1458

<210> 691
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<220>
<221> SITE
<222> (1)..(30)
<223> /note="This sequence may encompass 1-6 'Gly Gly Gly Gly Ser' repeating units"

<220>
<221> source
<223> /note="See specification as filed for detailed description of substitutions and preferred embodiments"

<400> 691
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
20 25 30

<210> 692
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 692
Arg Gly Asp Ser

1

<210> 693

<400> 693
000

<210> 694

<400> 694
000

<210> 695

<400> 695
000

<210> 696

<400> 696
000

<210> 697

<400> 697
000

<210> 698

<400> 698
000

<210> 699

<400> 699
000

<210> 700

<400> 700
000

<210> 701
<211> 227
<212> PRT

<213> Homo sapiens

<400> 701

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

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
            20                  25                  30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
        35                  40                  45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
    50                  55                  60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65                  70                  75                  80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
                85                  90                  95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
            100                 105                 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
        115                 120                 125

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
    130                 135                 140

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
145                 150                 155                 160

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
                165                 170                 175

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
            180                 185                 190

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
        195                 200                 205
```

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

Pro Gly Lys
225

<210> 702
<211> 227
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 702
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 Ala 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 Ala 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> 703
<211> 711
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 703
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Gln Arg Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Glu Tyr
            20                  25                  30


Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Leu Val
        35                  40                  45


Gly Arg Ile Asp Pro Glu Asp Gly Ser Ile Asp Tyr Val Glu Lys Phe
    50                  55                  60


Lys Lys Lys Val Thr Leu Thr Ala Asp Thr Ser Ser Ser Thr Ala Tyr
```

```
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Lys Phe Asn Tyr Arg Phe Ala Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
        115                 120                 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
    130                 135                 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145                 150                 155                 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
                165                 170                 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
            180                 185                 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
        195                 200                 205

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
    210                 215                 220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255

Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu Asp Pro
            260                 265                 270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285
```

```
Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val
    290                 295                 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu Lys Thr
                325                 330                 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                 390                 395                 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly
        435                 440                 445

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
    450                 455                 460

Gly Ser Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro
465                 470                 475                 480

Gly Arg Ser Leu Arg Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr
                485                 490                 495

Arg Tyr Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
```

```
            500                 505                 510

Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln
        515                 520                 525

Lys Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr
    530                 535                 540

Ala Phe Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val Tyr
545                 550                 555                 560

Phe Cys Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr Trp Gly
                565                 570                 575

Gln Gly Thr Pro Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
            580                 585                 590

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
        595                 600                 605

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
    610                 615                 620

Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr
625                 630                 635                 640

Gln Gln Thr Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
                645                 650                 655

Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
            660                 665                 670

Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
        675                 680                 685

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Phe Thr Phe Gly Gln
    690                 695                 700

Gly Thr Lys Leu Gln Ile Thr
705                 710
```

<210> 704
<211> 713
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 704
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Cys Ile Tyr Pro Gly Asn Val Asn Thr Asn Tyr Asn Glu Lys Phe
50 55 60

Lys Asp Arg Ala Thr Leu Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Thr Arg Ser His Tyr Gly Leu Asp Trp Asn Phe Asp Val Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

```
Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380
```

```
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    450                 455                 460

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val
465                 470                 475                 480

Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Lys Ala Ser Gly Tyr Thr
                485                 490                 495

Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly
            500                 505                 510

Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr
        515                 520                 525

Asn Gln Lys Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
    530                 535                 540

Asn Thr Ala Phe Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly
545                 550                 555                 560

Val Tyr Phe Cys Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr
                565                 570                 575

Trp Gly Gln Gly Thr Pro Val Thr Val Ser Ser Gly Gly Gly Gly Ser
            580                 585                 590

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
        595                 600                 605
```

```
Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
    610                 615                 620

Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met Asn
625                 630                 635                 640

Trp Tyr Gln Gln Thr Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
                645                 650                 655

Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
            660                 665                 670

Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp
        675                 680                 685

Ile Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Phe Thr Phe
    690                 695                 700

Gly Gln Gly Thr Lys Leu Gln Ile Thr
705                 710
```

<210> 705
<211> 226
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 705

```
Asp Ile Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1               5                   10                  15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Val Ser Asn
            20                  25                  30

Tyr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
        35                  40                  45

Ile Tyr Asp Asn Asn Lys Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
```

50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Ala Ile Gly Ser
85 90 95

Tyr Ser Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
100 105 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
115 120 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
130 135 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145 150 155 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
165 170 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
180 185 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
195 200 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
210 215 220

Glu Cys
225

<210> 706
<211> 713
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 706

```
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
            20                  25                  30


Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ser Ile Phe Tyr Thr Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ile Gly Tyr Ala Gly Asp Ser Lys Tyr Ala Ile Trp Gly Gln
            100                 105                 110


Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125


Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
    130                 135                 140


Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160


Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175


Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190


Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205
```

```
Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415
```

```
Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    450                 455                 460

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val
465                 470                 475                 480

Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Lys Ala Ser Gly Tyr Thr
                485                 490                 495

Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly
            500                 505                 510

Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr
        515                 520                 525

Asn Gln Lys Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
    530                 535                 540

Asn Thr Ala Phe Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly
545                 550                 555                 560

Val Tyr Phe Cys Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr
                565                 570                 575

Trp Gly Gln Gly Thr Pro Val Thr Val Ser Ser Gly Gly Gly Gly Ser
            580                 585                 590

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
        595                 600                 605

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
    610                 615                 620

Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met Asn
625                 630                 635                 640
```

```
Trp Tyr Gln Gln Thr Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
                645                 650                 655

Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
            660                 665                 670

Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp
        675                 680                 685

Ile Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Phe Thr Phe
    690                 695                 700

Gly Gln Gly Thr Lys Leu Gln Ile Thr
705                 710
```

<210> 707
<211> 720
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 707

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Gln Arg Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Glu Tyr
            20                  25                  30

Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Leu Val
        35                  40                  45

Gly Arg Ile Asp Pro Glu Asp Gly Ser Ile Asp Tyr Val Glu Lys Phe
    50                  55                  60

Lys Lys Lys Val Thr Leu Thr Ala Asp Thr Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
```

```
                85                  90                  95

Ala Arg Gly Lys Phe Asn Tyr Arg Phe Ala Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
        115                 120                 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
    130                 135                 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145                 150                 155                 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
                165                 170                 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
            180                 185                 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
        195                 200                 205

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
    210                 215                 220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255

Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu Asp Pro
            260                 265                 270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val
    290                 295                 300
```

```
Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu Lys Thr
                325                 330                 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                 390                 395                 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly
        435                 440                 445

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
    450                 455                 460

Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro
465                 470                 475                 480

Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn
                485                 490                 495

Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Cys Leu Glu
            500                 505                 510

Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr
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        515                 520                 525

Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys
    530                 535                 540

Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala
545                 550                 555                 560

Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Ile Ser
                565                 570                 575

Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly
            580                 585                 590

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
        595                 600                 605

Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser
    610                 615                 620

Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val
625                 630                 635                 640

Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly Gln Ala
                645                 650                 655

Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly Thr Pro
            660                 665                 670

Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu
        675                 680                 685

Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val Leu Trp
    690                 695                 700

Tyr Ser Asn Arg Trp Val Phe Gly Cys Gly Thr Lys Leu Thr Val Leu
705                 710                 715                 720

<210> 708
<211> 715
<212> PRT
```

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 708
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Gln Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Glu Tyr
20 25 30

Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Leu Val
35 40 45

Gly Arg Ile Asp Pro Glu Asp Gly Ser Ile Asp Tyr Val Glu Lys Phe
50 55 60

Lys Lys Lys Val Thr Leu Thr Ala Asp Thr Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Lys Phe Asn Tyr Arg Phe Ala Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
115 120 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
130 135 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145 150 155 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
165 170 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
180 185 190

```
Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
        195                 200                 205

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
    210                 215                 220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255

Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu Asp Pro
            260                 265                 270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val
    290                 295                 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu Lys Thr
                325                 330                 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                 390                 395                 400
```

```
Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly
        435                 440                 445

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
    450                 455                 460

Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro
465                 470                 475                 480

Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn
                485                 490                 495

Thr Tyr Ala Met Asn Trp Val Arg Gln Ala Ser Gly Lys Cys Leu Glu
            500                 505                 510

Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr
        515                 520                 525

Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys
    530                 535                 540

Ser Thr Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala
545                 550                 555                 560

Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser
                565                 570                 575

Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly
            580                 585                 590

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ala
        595                 600                 605

Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val
    610                 615                 620
```

```
Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr
625                 630                 635                 640

Ala Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile
                645                 650                 655

Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg Phe Ser Gly
            660                 665                 670

Ser Leu Leu Gly Asp Lys Ala Ala Leu Thr Leu Ser Gly Ala Gln Pro
        675                 680                 685

Glu Asp Glu Ala Glu Tyr Phe Cys Ala Leu Trp Tyr Ser Asn Leu Trp
    690                 695                 700

Val Phe Gly Cys Gly Thr Lys Leu Thr Val Leu
705                 710                 715


<210> 709
<211> 722
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 709
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Cys Ile Tyr Pro Gly Asn Val Asn Thr Asn Tyr Asn Glu Lys Phe
    50                  55                  60

Lys Asp Arg Ala Thr Leu Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr
```

```
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95

Thr Arg Ser His Tyr Gly Leu Asp Trp Asn Phe Asp Val Trp Gly Gln
            100                 105                 110

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285
```

```
Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    450                 455                 460

Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
465                 470                 475                 480

Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr
                485                 490                 495

Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Cys
```

```
            500                 505                 510

Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr
        515                 520                 525

Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp
    530                 535                 540

Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp
545                 550                 555                 560

Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr
                565                 570                 575

Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
            580                 585                 590

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
        595                 600                 605

Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu Thr
    610                 615                 620

Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly
625                 630                 635                 640

Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro Gly
                645                 650                 655

Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro Gly
            660                 665                 670

Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu
        675                 680                 685

Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys Val
    690                 695                 700

Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Cys Gly Thr Lys Leu Thr
705                 710                 715                 720
```

Val Leu

<210> 710
<211> 717
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 710
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Cys Ile Tyr Pro Gly Asn Val Asn Thr Asn Tyr Asn Glu Lys Phe
50 55 60

Lys Asp Arg Ala Thr Leu Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Thr Arg Ser His Tyr Gly Leu Asp Trp Asn Phe Asp Val Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

```
Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365
```

```
Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    450                 455                 460

Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
465                 470                 475                 480

Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr
                485                 490                 495

Phe Asn Thr Tyr Ala Met Asn Trp Val Arg Gln Ala Ser Gly Lys Cys
            500                 505                 510

Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr
        515                 520                 525

Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp
    530                 535                 540

Ser Lys Ser Thr Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp
545                 550                 555                 560

Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr
                565                 570                 575

Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
            580                 585                 590
```

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
595 600 605

Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly
610 615 620

Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr Ser
625 630 635 640

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly
645 650 655

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg Phe
660 665 670

Ser Gly Ser Leu Leu Gly Asp Lys Ala Ala Leu Thr Leu Ser Gly Ala
675 680 685

Gln Pro Glu Asp Glu Ala Glu Tyr Phe Cys Ala Leu Trp Tyr Ser Asn
690 695 700

Leu Trp Val Phe Gly Cys Gly Thr Lys Leu Thr Val Leu
705 710 715

<210> 711
<211> 713
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 711
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile

```
        35                  40                  45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Val
    50                  55                  60

Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Ala Phe
65                  70                  75                  80

Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val Tyr Phe Cys
                85                  90                  95

Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Pro Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln
                165                 170                 175

Thr Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Leu
            180                 185                 190

Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Trp Ser Ser Asn Pro Phe Thr Phe Gly Gln Gly Thr
225                 230                 235                 240

Lys Leu Gln Ile Thr Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
                245                 250                 255
```

```
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser
            260                 265                 270

Gly Ala Glu Val Gln Arg Pro Gly Ala Ser Val Lys Val Ser Cys Lys
        275                 280                 285

Ala Ser Gly Tyr Ile Phe Thr Glu Tyr Tyr Met Tyr Trp Val Arg Gln
    290                 295                 300

Ala Pro Gly Gln Gly Leu Glu Leu Val Gly Arg Ile Asp Pro Glu Asp
305                 310                 315                 320

Gly Ser Ile Asp Tyr Val Glu Lys Phe Lys Lys Lys Val Thr Leu Thr
                325                 330                 335

Ala Asp Thr Ser Ser Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Thr
            340                 345                 350

Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala Arg Gly Lys Phe Asn Tyr
        355                 360                 365

Arg Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala
    370                 375                 380

Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser
385                 390                 395                 400

Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe
                405                 410                 415

Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
            420                 425                 430

Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu
        435                 440                 445

Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr
    450                 455                 460

Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg
```

```
465                 470                 475                 480

Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro
                485                 490                 495

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
            500                 505                 510

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
        515                 520                 525

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
    530                 535                 540

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
545                 550                 555                 560

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
                565                 570                 575

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
            580                 585                 590

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
        595                 600                 605

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met
    610                 615                 620

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
625                 630                 635                 640

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
                645                 650                 655

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
            660                 665                 670

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
        675                 680                 685
```

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
690 695 700

Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710

<210> 712
<211> 715
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 712
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Val
50 55 60

Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Ala Phe
65 70 75 80

Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val Tyr Phe Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Pro Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
130 135 140

```
Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln
                165                 170                 175

Thr Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Leu
            180                 185                 190

Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Trp Ser Ser Asn Pro Phe Thr Phe Gly Gln Gly Thr
225                 230                 235                 240

Lys Leu Gln Ile Thr Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
                245                 250                 255

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser
            260                 265                 270

Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys
        275                 280                 285

Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Tyr Ile His Trp Val Arg Gln
    290                 295                 300

Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly Cys Ile Tyr Pro Gly Asn
305                 310                 315                 320

Val Asn Thr Asn Tyr Asn Glu Lys Phe Lys Asp Arg Ala Thr Leu Thr
                325                 330                 335

Val Asp Thr Ser Ile Ser Thr Ala Tyr Met Glu Leu Ser Arg Leu Arg
            340                 345                 350
```

```
Ser Asp Asp Thr Ala Val Tyr Phe Cys Thr Arg Ser His Tyr Gly Leu
        355                 360                 365

Asp Trp Asn Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser
    370                 375                 380

Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser
385                 390                 395                 400

Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp
                405                 410                 415

Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr
            420                 425                 430

Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr
        435                 440                 445

Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
    450                 455                 460

Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp
465                 470                 475                 480

Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro
                485                 490                 495

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
            500                 505                 510

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
        515                 520                 525

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
    530                 535                 540

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
545                 550                 555                 560

Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
                565                 570                 575
```

```
Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
            580                 585                 590

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
        595                 600                 605

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu
    610                 615                 620

Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
625                 630                 635                 640

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
                645                 650                 655

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
            660                 665                 670

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
        675                 680                 685

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
    690                 695                 700

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705                 710                 715
```

<210> 713
<211> 711
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 713

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Gln Arg Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Glu Tyr
```

```
            20                  25                  30

Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Leu Val
        35                  40                  45

Gly Arg Ile Asp Pro Glu Asp Gly Ser Ile Asp Tyr Val Glu Lys Phe
    50                  55                  60

Lys Lys Lys Val Thr Leu Thr Ala Asp Thr Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Lys Phe Asn Tyr Arg Phe Ala Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
        115                 120                 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
    130                 135                 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145                 150                 155                 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
                165                 170                 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
            180                 185                 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
        195                 200                 205

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
    210                 215                 220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240
```

```
Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            260                 265                 270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    290                 295                 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
            340                 345                 350

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys
        355                 360                 365

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
    370                 375                 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385                 390                 395                 400

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
                405                 410                 415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
            420                 425                 430

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly
        435                 440                 445

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
```

```
    450                 455                 460

Gly Ser Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro
465                 470                 475                 480

Gly Arg Ser Leu Arg Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr
                485                 490                 495

Arg Tyr Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu
            500                 505                 510

Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln
        515                 520                 525

Lys Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr
    530                 535                 540

Ala Phe Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val Tyr
545                 550                 555                 560

Phe Cys Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr Trp Gly
                565                 570                 575

Gln Gly Thr Pro Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
            580                 585                 590

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln
        595                 600                 605

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val
    610                 615                 620

Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr
625                 630                 635                 640

Gln Gln Thr Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser
                645                 650                 655

Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
            660                 665                 670
```

Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala
675 680 685

Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Phe Thr Phe Gly Gln
690 695 700

Gly Thr Lys Leu Gln Ile Thr
705 710

<210> 714
<211> 713
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 714
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Cys Ile Tyr Pro Gly Asn Val Asn Thr Asn Tyr Asn Glu Lys Phe
50 55 60

Lys Asp Arg Ala Thr Leu Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

Thr Arg Ser His Tyr Gly Leu Asp Trp Asn Phe Asp Val Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

```
Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
                325                 330                 335
```

```
Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
    450                 455                 460

Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val
465                 470                 475                 480

Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Lys Ala Ser Gly Tyr Thr
                485                 490                 495

Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly
            500                 505                 510

Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr
        515                 520                 525

Asn Gln Lys Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
    530                 535                 540

Asn Thr Ala Phe Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly
545                 550                 555                 560
```

```
Val Tyr Phe Cys Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr
                565                 570                 575

Trp Gly Gln Gly Thr Pro Val Thr Val Ser Ser Gly Gly Gly Gly Ser
            580                 585                 590

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
        595                 600                 605

Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp
    610                 615                 620

Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met Asn
625                 630                 635                 640

Trp Tyr Gln Gln Thr Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp
                645                 650                 655

Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
            660                 665                 670

Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp
        675                 680                 685

Ile Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Phe Thr Phe
    690                 695                 700

Gly Gln Gly Thr Lys Leu Gln Ile Thr
705                 710
```

<210> 715
<211> 723
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 715
```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Gln Arg Pro Gly Ala
```

```
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Glu Tyr
            20                  25                  30

Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Leu Val
        35                  40                  45

Gly Arg Ile Asp Pro Glu Asp Gly Ser Ile Asp Tyr Val Glu Lys Phe
    50                  55                  60

Lys Lys Lys Val Thr Leu Thr Ala Asp Thr Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Gly Lys Phe Asn Tyr Arg Phe Ala Tyr Trp Gly Gln Gly Thr
            100                 105                 110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
        115                 120                 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
    130                 135                 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145                 150                 155                 160

Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
                165                 170                 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
            180                 185                 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
        195                 200                 205

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Gly Gly Gly
    210                 215                 220
```

```
Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser Gly Gly
225                 230                 235                 240


Gly Val Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Lys Ala Ser
                245                 250                 255


Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln Ala Pro
            260                 265                 270


Gly Lys Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg Gly Tyr
        275                 280                 285


Thr Asn Tyr Asn Gln Lys Val Lys Asp Arg Phe Thr Ile Ser Arg Asp
    290                 295                 300


Asn Ser Lys Asn Thr Ala Phe Leu Gln Met Asp Ser Leu Arg Pro Glu
305                 310                 315                 320


Asp Thr Gly Val Tyr Phe Cys Ala Arg Tyr Tyr Asp Asp His Tyr Ser
                325                 330                 335


Leu Asp Tyr Trp Gly Gln Gly Thr Pro Val Thr Val Ser Ser Gly Gly
            340                 345                 350


Gly Gly Ser Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
        355                 360                 365


Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser
    370                 375                 380


Val Gly Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser
385                 390                 395                 400


Tyr Met Asn Trp Tyr Gln Gln Thr Pro Gly Lys Ala Pro Lys Arg Trp
                405                 410                 415


Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser
            420                 425                 430


Gly Ser Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln
```

```
        435                 440                 445

Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro
    450                 455                 460

Phe Thr Phe Gly Gln Gly Thr Lys Leu Gln Ile Thr Gly Gly Gly Gly
465                 470                 475                 480

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
                485                 490                 495

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
            500                 505                 510

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
        515                 520                 525

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
    530                 535                 540

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
545                 550                 555                 560

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
                565                 570                 575

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
            580                 585                 590

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
        595                 600                 605

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
    610                 615                 620

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
625                 630                 635                 640

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
                645                 650                 655
```

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
660 665 670

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
675 680 685

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
690 695 700

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
705 710 715 720

Pro Gly Lys

<210> 716
<211> 725
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 716
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Cys Ile Tyr Pro Gly Asn Val Asn Thr Asn Tyr Asn Glu Lys Phe
50 55 60

Lys Asp Arg Ala Thr Leu Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
85 90 95

```
Thr Arg Ser His Tyr Gly Leu Asp Trp Asn Phe Asp Val Trp Gly Gln
            100                 105                 110

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Gly
    210                 215                 220

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Val Gln Ser
225                 230                 235                 240

Gly Gly Gly Val Val Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Lys
                245                 250                 255

Ala Ser Gly Tyr Thr Phe Thr Arg Tyr Thr Met His Trp Val Arg Gln
            260                 265                 270

Ala Pro Gly Lys Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Ser Arg
        275                 280                 285

Gly Tyr Thr Asn Tyr Asn Gln Lys Val Lys Asp Arg Phe Thr Ile Ser
    290                 295                 300
```

```
Arg Asp Asn Ser Lys Asn Thr Ala Phe Leu Gln Met Asp Ser Leu Arg
305                 310                 315                 320

Pro Glu Asp Thr Gly Val Tyr Phe Cys Ala Arg Tyr Tyr Asp Asp His
                325                 330                 335

Tyr Ser Leu Asp Tyr Trp Gly Gln Gly Thr Pro Val Thr Val Ser Ser
            340                 345                 350

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
        355                 360                 365

Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser
    370                 375                 380

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser
385                 390                 395                 400

Val Ser Tyr Met Asn Trp Tyr Gln Gln Thr Pro Gly Lys Ala Pro Lys
                405                 410                 415

Arg Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg
            420                 425                 430

Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Phe Thr Ile Ser Ser
        435                 440                 445

Leu Gln Pro Glu Asp Ile Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser
    450                 455                 460

Asn Pro Phe Thr Phe Gly Gln Gly Thr Lys Leu Gln Ile Thr Gly Gly
465                 470                 475                 480

Gly Gly Ser Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
                485                 490                 495

Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
            500                 505                 510

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
        515                 520                 525
```

```
Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
    530                 535                 540

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
545                 550                 555                 560

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
                565                 570                 575

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
            580                 585                 590

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
        595                 600                 605

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
    610                 615                 620

Gln Val Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln
625                 630                 635                 640

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
                645                 650                 655

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
            660                 665                 670

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
        675                 680                 685

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
    690                 695                 700

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
705                 710                 715                 720

Leu Ser Pro Gly Lys
                725
```

<210> 717
<211> 716
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 717
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Val
50 55 60

Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Ala Phe
65 70 75 80

Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val Tyr Phe Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Pro Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
130 135 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145 150 155 160

Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln
165 170 175

```
Thr Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Leu
            180                 185                 190

Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Trp Ser Ser Asn Pro Phe Thr Phe Gly Gln Gly Thr
225                 230                 235                 240

Lys Leu Gln Ile Thr Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys
                245                 250                 255

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
            260                 265                 270

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
        275                 280                 285

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
    290                 295                 300

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
305                 310                 315                 320

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
                325                 330                 335

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
            340                 345                 350

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
        355                 360                 365

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
    370                 375                 380

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
```

```
385                 390                 395                 400

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
                405                 410                 415

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
            420                 425                 430

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
        435                 440                 445

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
    450                 455                 460

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly Gly Ser
465                 470                 475                 480

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
                485                 490                 495

Val Gln Leu Val Gln Ser Gly Ala Glu Val Gln Arg Pro Gly Ala Ser
            500                 505                 510

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Glu Tyr Tyr
        515                 520                 525

Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Leu Val Gly
    530                 535                 540

Arg Ile Asp Pro Glu Asp Gly Ser Ile Asp Tyr Val Glu Lys Phe Lys
545                 550                 555                 560

Lys Lys Val Thr Leu Thr Ala Asp Thr Ser Ser Ser Thr Ala Tyr Met
                565                 570                 575

Glu Leu Ser Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala
            580                 585                 590

Arg Gly Lys Phe Asn Tyr Arg Phe Ala Tyr Trp Gly Gln Gly Thr Leu
        595                 600                 605
```

```
Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu
    610                 615                 620


Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys
625                 630                 635                 640


Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser
                645                 650                 655


Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
            660                 665                 670


Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser
        675                 680                 685


Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn
    690                 695                 700


Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
705                 710                 715


<210> 718
<211> 718
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 718
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
            20                  25                  30


Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45


Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Val
    50                  55                  60
```

```
Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Ala Phe
65                  70                  75                  80

Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val Tyr Phe Cys
                85                  90                  95

Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Pro Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln
                165                 170                 175

Thr Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Leu
            180                 185                 190

Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Trp Ser Ser Asn Pro Phe Thr Phe Gly Gln Gly Thr
225                 230                 235                 240

Lys Leu Gln Ile Thr Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys
                245                 250                 255

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
            260                 265                 270
```

```
Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
        275                 280                 285

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
    290                 295                 300

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
305                 310                 315                 320

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
                325                 330                 335

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
            340                 345                 350

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
        355                 360                 365

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser
    370                 375                 380

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys
385                 390                 395                 400

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
                405                 410                 415

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
            420                 425                 430

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
        435                 440                 445

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
    450                 455                 460

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly Gly Ser
465                 470                 475                 480

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
                485                 490                 495
```

```
Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser
            500                 505                 510

Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr Tyr
        515                 520                 525

Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile Gly
    530                 535                 540

Cys Ile Tyr Pro Gly Asn Val Asn Thr Asn Tyr Asn Glu Lys Phe Lys
545                 550                 555                 560

Asp Arg Ala Thr Leu Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr Met
                565                 570                 575

Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys Thr
            580                 585                 590

Arg Ser His Tyr Gly Leu Asp Trp Asn Phe Asp Val Trp Gly Gln Gly
        595                 600                 605

Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
    610                 615                 620

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu
625                 630                 635                 640

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp
                645                 650                 655

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu
            660                 665                 670

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser
        675                 680                 685

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro
    690                 695                 700
```

Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys
705 710 715

<210> 719
<211> 448
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 719
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Gln Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Glu Tyr
20 25 30

Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Leu Val
35 40 45

Gly Arg Ile Asp Pro Glu Asp Gly Ser Ile Asp Tyr Val Glu Lys Phe
50 55 60

Lys Lys Lys Val Thr Leu Thr Ala Asp Thr Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Lys Phe Asn Tyr Arg Phe Ala Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro
115 120 125

Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly
130 135 140

Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn
145 150 155 160

```
Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln
                165                 170                 175

Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser
            180                 185                 190

Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser
        195                 200                 205

Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr
    210                 215                 220

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
225                 230                 235                 240

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
                245                 250                 255

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
            260                 265                 270

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
        275                 280                 285

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
    290                 295                 300

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
305                 310                 315                 320

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
                325                 330                 335

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu
            340                 345                 350

Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Ser Cys
        355                 360                 365

Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
```

370 375 380

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
385 390 395 400

Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser
405 410 415

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
420 425 430

Leu His Asn Arg Phe Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 720
<211> 477
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 720
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Val
50 55 60

Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Ala Phe
65 70 75 80

Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val Tyr Phe Cys
85 90 95

```
Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Pro Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln
                165                 170                 175

Thr Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Leu
            180                 185                 190

Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Trp Ser Ser Asn Pro Phe Thr Phe Gly Gln Gly Thr
225                 230                 235                 240

Lys Leu Gln Ile Thr Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys
                245                 250                 255

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
            260                 265                 270

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
        275                 280                 285

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
    290                 295                 300

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
305                 310                 315                 320
```

```
Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
               325                 330                 335

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
            340                 345                 350

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
        355                 360                 365

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Cys
    370                 375                 380

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys
385                 390                 395                 400

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
               405                 410                 415

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
            420                 425                 430

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
        435                 440                 445

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
    450                 455                 460

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
465                 470                 475


<210> 721
<211> 450
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 721
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
```

```
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Cys Ile Tyr Pro Gly Asn Val Asn Thr Asn Tyr Asn Glu Lys Phe
    50                  55                  60

Lys Asp Arg Ala Thr Leu Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95

Thr Arg Ser His Tyr Gly Leu Asp Trp Asn Phe Asp Val Trp Gly Gln
            100                 105                 110

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
    210                 215                 220
```

```
Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
225                 230                 235                 240


Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255


Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
            260                 265                 270


Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285


Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
    290                 295                 300


Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320


Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
                325                 330                 335


Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys
            340                 345                 350


Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365


Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380


Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400


Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp
                405                 410                 415


Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430


Glu Ala Leu His Asn Arg Phe Thr Gln Lys Ser Leu Ser Leu Ser Pro
```

435 440 445

Gly Lys
450

<210> 722
<211> 227
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 722
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
20 25 30

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
115 120 125

Cys Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser
130 135 140

```
Leu Ser Cys Ala 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 Val 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 Arg Phe Thr Gln Lys Ser Leu Ser Leu Ser
    210                 215                 220


Pro Gly Lys
225


<210> 723
<211> 534
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 723
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
            20                  25                  30


Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45


Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Val
    50                  55                  60


Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Ala Phe
65                  70                  75                  80
```

```
Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val Tyr Phe Cys
                85                  90                  95

Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr Trp Gly Gln Gly
            100                 105                 110

Thr Pro Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
    130                 135                 140

Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln
                165                 170                 175

Thr Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Leu
            180                 185                 190

Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Trp Ser Ser Asn Pro Phe Thr Phe Gly Gln Gly Thr
225                 230                 235                 240

Lys Leu Gln Ile Thr Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys
                245                 250                 255

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
            260                 265                 270

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
        275                 280                 285

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
```

```
    290                 295                 300

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
305                 310                 315                 320

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
                325                 330                 335

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
            340                 345                 350

Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
        355                 360                 365

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Cys
    370                 375                 380

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys
385                 390                 395                 400

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
                405                 410                 415

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
            420                 425                 430

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
        435                 440                 445

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
    450                 455                 460

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly Gly Gly
465                 470                 475                 480

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Glu Asp Pro Cys
                485                 490                 495

Ala Cys Glu Ser Leu Val Lys Phe Gln Ala Lys Val Glu Gly Leu Leu
            500                 505                 510
```

```
Gln Ala Leu Thr Arg Lys Leu Glu Ala Val Ser Lys Arg Leu Ala Ile
        515                 520                 525


Leu Glu Asn Thr Val Val
    530


<210> 724
<211> 529
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 724
Gln Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
            20                  25                  30


Thr Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
        35                  40                  45


Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Val
    50                  55                  60


Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Ala Phe
65                  70                  75                  80


Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val Tyr Phe Cys
                85                  90                  95


Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr Trp Gly Gln Gly
            100                 105                 110


Thr Pro Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        115                 120                 125


Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr
    130                 135                 140
```

```
Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile
145                 150                 155                 160

Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met Asn Trp Tyr Gln Gln
                165                 170                 175

Thr Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys Leu
            180                 185                 190

Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
        195                 200                 205

Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp Ile Ala Thr Tyr
    210                 215                 220

Tyr Cys Gln Gln Trp Ser Ser Asn Pro Phe Thr Phe Gly Gln Gly Thr
225                 230                 235                 240

Lys Leu Gln Ile Thr Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys
                245                 250                 255

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
            260                 265                 270

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
        275                 280                 285

Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys
    290                 295                 300

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
305                 310                 315                 320

Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu
                325                 330                 335

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
            340                 345                 350
```

```
Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys
        355                 360                 365

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Cys
    370                 375                 380

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys
385                 390                 395                 400

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
                405                 410                 415

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
            420                 425                 430

Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
        435                 440                 445

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
    450                 455                 460

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Gly Gly Gly Gly
465                 470                 475                 480

Ser Asp Leu Gly Pro Gln Met Leu Arg Glu Leu Gln Glu Thr Asn Ala
                485                 490                 495

Ala Leu Gln Asp Val Arg Glu Leu Leu Arg Gln Gln Val Arg Glu Ile
            500                 505                 510

Thr Phe Leu Lys Asn Thr Val Met Glu Cys Asp Ala Cys Gly Met Gln
        515                 520                 525

Gln
```

<210> 725
<211> 419
<212> PRT
<213> Homo sapiens

<400> 725

```
Met His Leu Leu Gly Phe Phe Ser Val Ala Cys Ser Leu Leu Ala Ala
1               5                  10                  15

Ala Leu Leu Pro Gly Pro Arg Glu Ala Pro Ala Ala Ala Ala Ala Phe
            20                  25                  30

Glu Ser Gly Leu Asp Leu Ser Asp Ala Glu Pro Asp Ala Gly Glu Ala
        35                  40                  45

Thr Ala Tyr Ala Ser Lys Asp Leu Glu Glu Gln Leu Arg Ser Val Ser
    50                  55                  60

Ser Val Asp Glu Leu Met Thr Val Leu Tyr Pro Glu Tyr Trp Lys Met
65                  70                  75                  80

Tyr Lys Cys Gln Leu Arg Lys Gly Gly Trp Gln His Asn Arg Glu Gln
                85                  90                  95

Ala Asn Leu Asn Ser Arg Thr Glu Glu Thr Ile Lys Phe Ala Ala Ala
            100                 105                 110

His Tyr Asn Thr Glu Ile Leu Lys Ser Ile Asp Asn Glu Trp Arg Lys
        115                 120                 125

Thr Gln Cys Met Pro Arg Glu Val Cys Ile Asp Val Gly Lys Glu Phe
    130                 135                 140

Gly Val Ala Thr Asn Thr Phe Phe Lys Pro Pro Cys Val Ser Val Tyr
145                 150                 155                 160

Arg Cys Gly Gly Cys Cys Asn Ser Glu Gly Leu Gln Cys Met Asn Thr
                165                 170                 175

Ser Thr Ser Tyr Leu Ser Lys Thr Leu Phe Glu Ile Thr Val Pro Leu
            180                 185                 190

Ser Gln Gly Pro Lys Pro Val Thr Ile Ser Phe Ala Asn His Thr Ser
        195                 200                 205

Cys Arg Cys Met Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser Ile
    210                 215                 220
```

```
Ile Arg Arg Ser Leu Pro Ala Thr Leu Pro Gln Cys Gln Ala Ala Asn
225                 230                 235                 240

Lys Thr Cys Pro Thr Asn Tyr Met Trp Asn Asn His Ile Cys Arg Cys
                245                 250                 255

Leu Ala Gln Glu Asp Phe Met Phe Ser Ser Asp Ala Gly Asp Asp Ser
            260                 265                 270

Thr Asp Gly Phe His Asp Ile Cys Gly Pro Asn Lys Glu Leu Asp Glu
        275                 280                 285

Glu Thr Cys Gln Cys Val Cys Arg Ala Gly Leu Arg Pro Ala Ser Cys
    290                 295                 300

Gly Pro His Lys Glu Leu Asp Arg Asn Ser Cys Gln Cys Val Cys Lys
305                 310                 315                 320

Asn Lys Leu Phe Pro Ser Gln Cys Gly Ala Asn Arg Glu Phe Asp Glu
                325                 330                 335

Asn Thr Cys Gln Cys Val Cys Lys Arg Thr Cys Pro Arg Asn Gln Pro
            340                 345                 350

Leu Asn Pro Gly Lys Cys Ala Cys Glu Cys Thr Glu Ser Pro Gln Lys
        355                 360                 365

Cys Leu Leu Lys Gly Lys Lys Phe His His Gln Thr Cys Ser Cys Tyr
    370                 375                 380

Arg Arg Pro Cys Thr Asn Arg Gln Lys Ala Cys Glu Pro Gly Phe Ser
385                 390                 395                 400

Tyr Ser Glu Glu Val Cys Arg Cys Val Pro Ser Tyr Trp Lys Arg Pro
                405                 410                 415

Gln Met Ser
```

<210> 726
<211> 719
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 726
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Phe Tyr Thr Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ile Gly Tyr Ala Gly Asp Ser Lys Tyr Ala Ile Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

```
Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
```

385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
450 455 460

Gly Gly Gly Gly Ser Glu Val Lys Leu Val Glu Ser Gly Gly Asp Leu
465 470 475 480

Val Gln Pro Gly Asp Ser Leu Thr Leu Ser Cys Val Ala Ser Gly Phe
485 490 495

Thr Phe Ser Lys Gln Gly Met His Trp Ile Arg Gln Ala Pro Lys Lys
500 505 510

Gly Leu Glu Trp Ile Ala Met Ile Tyr Tyr Asp Ser Ser Lys Met Tyr
515 520 525

Tyr Ala Asp Thr Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
530 535 540

Lys Asn Thr Leu Tyr Leu Glu Met Asn Ser Leu Arg Ser Glu Asp Thr
545 550 555 560

Ala Met Tyr Tyr Cys Ala Ser Phe Trp Trp Asp Leu Asp Phe Asp His
565 570 575

Trp Gly Gln Gly Val Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser
580 585 590

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
595 600 605

Ile Leu Val Thr Gln Thr Pro Val Ser Leu Pro Val Ser Leu Gly Gly
610 615 620

His Val Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Arg Ser Glu
625 630 635 640

Gly Thr Thr Tyr Phe Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro
645 650 655

Gln Leu Leu Ile Tyr Arg Val Ser Asn Arg Phe Ser Gly Val Pro Asp
660 665 670

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser
675 680 685

Arg Val Glu Pro Glu Asp Leu Gly Val Tyr Tyr Cys Leu Gln Ser Ser
690 695 700

His Phe Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys
705 710 715

<210> 727
<211> 204
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 727
Phe Glu Ser Gly Leu Asp Leu Ser Asp Ala Glu Pro Asp Ala Gly Glu
1 5 10 15

Ala Thr Ala Tyr Ala Ser Lys Asp Leu Glu Glu Gln Leu Arg Ser Val
20 25 30

Ser Ser Val Asp Glu Leu Met Thr Val Leu Tyr Pro Glu Tyr Trp Lys
35 40 45

Met Tyr Lys Cys Gln Leu Arg Lys Gly Gly Trp Gln His Asn Arg Glu
50 55 60

```
Gln Ala Asn Leu Asn Ser Arg Thr Glu Glu Thr Ile Lys Phe Ala Ala
65                  70                  75                  80


Ala His Tyr Asn Thr Glu Ile Leu Lys Ser Ile Asp Asn Glu Trp Arg
                85                  90                  95


Lys Thr Gln Cys Met Pro Arg Glu Val Cys Ile Asp Val Gly Lys Glu
            100                 105                 110


Phe Gly Val Ala Thr Asn Thr Phe Phe Lys Pro Pro Cys Val Ser Val
        115                 120                 125


Tyr Arg Cys Gly Gly Cys Cys Asn Ser Glu Gly Leu Gln Cys Met Asn
    130                 135                 140


Thr Ser Thr Ser Tyr Leu Ser Lys Thr Leu Phe Glu Ile Thr Val Pro
145                 150                 155                 160


Leu Ser Gln Gly Pro Lys Pro Val Thr Ile Ser Phe Ala Asn His Thr
                165                 170                 175


Ser Cys Arg Cys Met Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser
            180                 185                 190


Ile Ile Arg Arg Gly Ser His His His His His His
        195                 200


<210> 728
<211> 226
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 728
Asp Ile Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1               5                   10                  15


Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Val Ser Asn
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            20                  25                  30

Tyr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
        35                  40                  45

Ile Tyr Asp Asn Asn Lys Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
    50                  55                  60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln
65                  70                  75                  80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Ala Ile Gly Ser
                85                  90                  95

Tyr Ser Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
                165                 170                 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
            180                 185                 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
        195                 200                 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
    210                 215                 220

Glu Cys
225
```

<210> 729
<211> 196
<212> PRT
<213> Homo sapiens

<400> 729
Phe Glu Ser Gly Leu Asp Leu Ser Asp Ala Glu Pro Asp Ala Gly Glu
1   5   10   15

Ala Thr Ala Tyr Ala Ser Lys Asp Leu Glu Glu Gln Leu Arg Ser Val
            20   25   30

Ser Ser Val Asp Glu Leu Met Thr Val Leu Tyr Pro Glu Tyr Trp Lys
        35   40   45

Met Tyr Lys Cys Gln Leu Arg Lys Gly Gly Trp Gln His Asn Arg Glu
    50   55   60

Gln Ala Asn Leu Asn Ser Arg Thr Glu Glu Thr Ile Lys Phe Ala Ala
65   70   75   80

Ala His Tyr Asn Thr Glu Ile Leu Lys Ser Ile Asp Asn Glu Trp Arg
                85   90   95

Lys Thr Gln Cys Met Pro Arg Glu Val Cys Ile Asp Val Gly Lys Glu
            100   105   110

Phe Gly Val Ala Thr Asn Thr Phe Phe Lys Pro Pro Cys Val Ser Val
        115   120   125

Tyr Arg Cys Gly Gly Cys Cys Asn Ser Glu Gly Leu Gln Cys Met Asn
    130   135   140

Thr Ser Thr Ser Tyr Leu Ser Lys Thr Leu Phe Glu Ile Thr Val Pro
145   150   155   160

Leu Ser Gln Gly Pro Lys Pro Val Thr Ile Ser Phe Ala Asn His Thr
                165   170   175

Ser Cys Arg Cys Met Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser
            180   185   190

Ile Ile Arg Arg
195

<210> 730
<211> 216
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 730
Asp Ile Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Val Ser Asn
20 25 30

Tyr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Asp Asn Asn Lys Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Ala Ile Gly Ser
85 90 95

Tyr Ser Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
100 105 110

Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser Ser Glu Glu
115 120 125

Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser Asp Phe Tyr
130 135 140

Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser Pro Val Lys
145 150 155 160

Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn Asn Lys Tyr
165 170 175

Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp Lys Ser His
180 185 190

Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr Val Glu Lys
195 200 205

Thr Val Ala Pro Thr Glu Cys Ser
210 215

<210> 731
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 731
Ala His Tyr Asn Thr Glu Ile Leu Lys Ser Ile Asp Asn Glu Trp Arg
1 5 10 15

Lys Thr Gln Cys Met Pro Arg Glu Val Cys Ile Asp Val Gly Lys Glu
20 25 30

Phe Gly Val Ala Thr Asn Thr Phe Phe Lys Pro Pro Cys Val Ser Val
35 40 45

Tyr Arg Cys Gly Gly Cys Cys Asn Ser Glu Gly Leu Gln Cys Met Asn
50 55 60

Thr Ser Thr Ser Tyr Leu Ser Lys Thr Leu Phe Glu Ile Thr Val Pro
65 70 75 80

Leu Ser Gln Gly Pro Lys Pro Val Thr Ile Ser Phe Ala Asn His Thr
85 90 95

Ser Cys Arg Cys Met Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser

100 105 110

Ile Ile Arg Arg Gly Ser His His His His His His
115 120

<210> 732
<211> 116
<212> PRT
<213> Homo sapiens

<400> 732
Ala His Tyr Asn Thr Glu Ile Leu Lys Ser Ile Asp Asn Glu Trp Arg
1 5 10 15

Lys Thr Gln Cys Met Pro Arg Glu Val Cys Ile Asp Val Gly Lys Glu
20 25 30

Phe Gly Val Ala Thr Asn Thr Phe Phe Lys Pro Pro Cys Val Ser Val
35 40 45

Tyr Arg Cys Gly Gly Cys Cys Asn Ser Glu Gly Leu Gln Cys Met Asn
50 55 60

Thr Ser Thr Ser Tyr Leu Ser Lys Thr Leu Phe Glu Ile Thr Val Pro
65 70 75 80

Leu Ser Gln Gly Pro Lys Pro Val Thr Ile Ser Phe Ala Asn His Thr
85 90 95

Ser Cys Arg Cys Met Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser
100 105 110

Ile Ile Arg Arg
115

<210> 733
<211> 133
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 733
Thr Glu Glu Thr Ile Lys Phe Ala Ala Ala His Tyr Asn Thr Glu Ile
1   5   10   15

Leu Lys Ser Ile Asp Asn Glu Trp Arg Lys Thr Gln Cys Met Pro Arg
            20   25   30

Glu Val Cys Ile Asp Val Gly Lys Glu Phe Gly Val Ala Thr Asn Thr
        35   40   45

Phe Phe Lys Pro Pro Cys Val Ser Val Tyr Arg Cys Gly Gly Cys Cys
    50   55   60

Asn Ser Glu Gly Leu Gln Cys Met Asn Thr Ser Thr Ser Tyr Leu Ser
65   70   75   80

Lys Thr Leu Phe Glu Ile Thr Val Pro Leu Ser Gln Gly Pro Lys Pro
                85   90   95

Val Thr Ile Ser Phe Ala Asn His Thr Ser Cys Arg Cys Met Ser Lys
            100   105   110

Leu Asp Val Tyr Arg Gln Val His Ser Ile Ile Arg Arg Gly Ser His
        115   120   125

His His His His His
    130

<210> 734
<211> 125
<212> PRT
<213> Homo sapiens

<400> 734
Thr Glu Glu Thr Ile Lys Phe Ala Ala Ala His Tyr Asn Thr Glu Ile
1   5   10   15

Leu Lys Ser Ile Asp Asn Glu Trp Arg Lys Thr Gln Cys Met Pro Arg
            20   25   30

Glu Val Cys Ile Asp Val Gly Lys Glu Phe Gly Val Ala Thr Asn Thr
        35   40   45

```
Phe Phe Lys Pro Pro Cys Val Ser Val Tyr Arg Cys Gly Gly Cys Cys
    50                  55                  60

Asn Ser Glu Gly Leu Gln Cys Met Asn Thr Ser Thr Ser Tyr Leu Ser
65                  70                  75                  80

Lys Thr Leu Phe Glu Ile Thr Val Pro Leu Ser Gln Gly Pro Lys Pro
                85                  90                  95

Val Thr Ile Ser Phe Ala Asn His Thr Ser Cys Arg Cys Met Ser Lys
            100                 105                 110

Leu Asp Val Tyr Arg Gln Val His Ser Ile Ile Arg Arg
        115                 120                 125
```

<210> 735
<211> 133
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 735

```
Thr Glu Glu Thr Ile Lys Phe Ala Ala Ala His Tyr Asn Thr Glu Ile
1               5                   10                  15

Leu Lys Ser Ile Asp Asn Glu Trp Arg Lys Thr Gln Cys Met Pro Arg
            20                  25                  30

Glu Val Ala Ile Asp Val Gly Lys Glu Phe Gly Val Ala Thr Asn Thr
        35                  40                  45

Phe Phe Lys Pro Pro Cys Val Ser Val Tyr Arg Cys Gly Gly Cys Cys
    50                  55                  60

Asn Ser Glu Gly Leu Gln Cys Met Asn Thr Ser Thr Ser Tyr Leu Ser
65                  70                  75                  80

Lys Thr Leu Phe Glu Ile Thr Val Pro Leu Ser Gln Gly Pro Lys Pro
```

```
                85                  90                  95

Val Thr Ile Ser Phe Ala Asn His Thr Ser Cys Arg Cys Met Ser Lys
            100                 105                 110

Leu Asp Val Tyr Arg Gln Val His Ser Ile Ile Arg Arg Gly Ser His
        115                 120                 125

His His His His His
    130
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<210> 736
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 736

```
Thr Glu Glu Thr Ile Lys Phe Ala Ala Ala His Tyr Asn Thr Glu Ile
1               5                   10                  15

Leu Lys Ser Ile Asp Asn Glu Trp Arg Lys Thr Gln Cys Met Pro Arg
            20                  25                  30

Glu Val Ala Ile Asp Val Gly Lys Glu Phe Gly Val Ala Thr Asn Thr
        35                  40                  45

Phe Phe Lys Pro Pro Cys Val Ser Val Tyr Arg Cys Gly Gly Cys Cys
    50                  55                  60

Asn Ser Glu Gly Leu Gln Cys Met Asn Thr Ser Thr Ser Tyr Leu Ser
65                  70                  75                  80

Lys Thr Leu Phe Glu Ile Thr Val Pro Leu Ser Gln Gly Pro Lys Pro
                85                  90                  95

Val Thr Ile Ser Phe Ala Asn His Thr Ser Cys Arg Cys Met Ser Lys
            100                 105                 110
```

Leu Asp Val Tyr Arg Gln Val His Ser Ile Ile Arg Arg
115 120 125

<210> 737
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 737
Ala His Tyr Asn Thr Glu Ile Leu Lys Ser Ile Asp Asn Glu Trp Arg
1 5 10 15

Lys Thr Gln Cys Met Pro Arg Glu Val Ala Ile Asp Val Gly Lys Glu
20 25 30

Phe Gly Val Ala Thr Asn Thr Phe Phe Lys Pro Pro Cys Val Ser Val
35 40 45

Tyr Arg Cys Gly Gly Cys Cys Asn Ser Glu Gly Leu Gln Cys Met Asn
50 55 60

Thr Ser Thr Ser Tyr Leu Ser Lys Thr Leu Phe Glu Ile Thr Val Pro
65 70 75 80

Leu Ser Gln Gly Pro Lys Pro Val Thr Ile Ser Phe Ala Asn His Thr
85 90 95

Ser Cys Arg Cys Met Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser
100 105 110

Ile Ile Arg Arg Gly Ser His His His His His His
115 120

<210> 738
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 738
Ala His Tyr Asn Thr Glu Ile Leu Lys Ser Ile Asp Asn Glu Trp Arg
1 5 10 15

Lys Thr Gln Cys Met Pro Arg Glu Val Ala Ile Asp Val Gly Lys Glu
20 25 30

Phe Gly Val Ala Thr Asn Thr Phe Phe Lys Pro Pro Cys Val Ser Val
35 40 45

Tyr Arg Cys Gly Gly Cys Cys Asn Ser Glu Gly Leu Gln Cys Met Asn
50 55 60

Thr Ser Thr Ser Tyr Leu Ser Lys Thr Leu Phe Glu Ile Thr Val Pro
65 70 75 80

Leu Ser Gln Gly Pro Lys Pro Val Thr Ile Ser Phe Ala Asn His Thr
85 90 95

Ser Cys Arg Cys Met Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser
100 105 110

Ile Ile Arg Arg
115

<210> 739
<211> 80
<212> PRT
<213> Homo sapiens

<400> 739
Phe Glu Ser Gly Leu Asp Leu Ser Asp Ala Glu Pro Asp Ala Gly Glu
1 5 10 15

Ala Thr Ala Tyr Ala Ser Lys Asp Leu Glu Glu Gln Leu Arg Ser Val
20 25 30

Ser Ser Val Asp Glu Leu Met Thr Val Leu Tyr Pro Glu Tyr Trp Lys
35 40 45

```
Met Tyr Lys Cys Gln Leu Arg Lys Gly Gly Trp Gln His Asn Arg Glu
    50                  55                  60


Gln Ala Asn Leu Asn Ser Arg Thr Glu Glu Thr Ile Lys Phe Ala Ala
65                  70                  75                  80


<210> 740
<211> 9
<212> PRT
<213> Homo sapiens

<400> 740
Thr Glu Glu Thr Ile Lys Phe Ala Ala
1               5


<210> 741
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"


<220>
<221> VARIANT
<222> (26)..(26)
<223> /replace="Ala"

<400> 741
Ala His Tyr Asn Thr Glu Ile Leu Lys Ser Ile Asp Asn Glu Trp Arg
1               5                   10                  15


Lys Thr Gln Cys Met Pro Arg Glu Val Cys Ile Asp Val Gly Lys Glu
            20                  25                  30


Phe Gly Val Ala Thr Asn Thr Phe Phe Lys Pro Pro Cys Val Ser Val
        35                  40                  45


Tyr Arg Cys Gly Gly Cys Cys Asn Ser Glu Gly Leu Gln Cys Met Asn
    50                  55                  60


Thr Ser Thr Ser Tyr Leu Ser Lys Thr Leu Phe Glu Ile Thr Val Pro
65                  70                  75                  80
```

```
Leu Ser Gln Gly Pro Lys Pro Val Thr Ile Ser Phe Ala Asn His Thr
                85                  90                  95

Ser Cys Arg Cys Met Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser
            100                 105                 110

Ile Ile Arg Arg
        115
```

<210> 742
<211> 116
<212> PRT
<213> Homo sapiens

<400> 742

```
Ala His Tyr Asn Thr Glu Ile Leu Lys Ser Ile Asp Asn Glu Trp Arg
1               5                   10                  15

Lys Thr Gln Cys Met Pro Arg Glu Val Cys Ile Asp Val Gly Lys Glu
            20                  25                  30

Phe Gly Val Ala Thr Asn Thr Phe Phe Lys Pro Pro Cys Val Ser Val
        35                  40                  45

Tyr Arg Cys Gly Gly Cys Cys Asn Ser Glu Gly Leu Gln Cys Met Asn
    50                  55                  60

Thr Ser Thr Ser Tyr Leu Ser Lys Thr Leu Phe Glu Ile Thr Val Pro
65                  70                  75                  80

Leu Ser Gln Gly Pro Lys Pro Val Thr Ile Ser Phe Ala Asn His Thr
                85                  90                  95

Ser Cys Arg Cys Met Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser
            100                 105                 110

Ile Ile Arg Arg
        115
```

<210> 743
<211> 116
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 743
Ala His Tyr Asn Thr Glu Ile Leu Lys Ser Ile Asp Asn Glu Trp Arg
1 5 10 15

Lys Thr Gln Cys Met Pro Arg Glu Val Ala Ile Asp Val Gly Lys Glu
20 25 30

Phe Gly Val Ala Thr Asn Thr Phe Phe Lys Pro Pro Cys Val Ser Val
35 40 45

Tyr Arg Cys Gly Gly Cys Cys Asn Ser Glu Gly Leu Gln Cys Met Asn
50 55 60

Thr Ser Thr Ser Tyr Leu Ser Lys Thr Leu Phe Glu Ile Thr Val Pro
65 70 75 80

Leu Ser Gln Gly Pro Lys Pro Val Thr Ile Ser Phe Ala Asn His Thr
85 90 95

Ser Cys Arg Cys Met Ser Lys Leu Asp Val Tyr Arg Gln Val His Ser
100 105 110

Ile Ile Arg Arg
115

<210> 744
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 744
Gly Asp Ser Met Leu Ser Asn Ser Asp Thr Trp Asn
1 5 10

<210> 745
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 745
Ser Asn Ser Asp Thr Trp Asn
1 5

<210> 746
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 746
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val
1 5 10 15

Arg Gly

<210> 747
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 747
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val
1 5 10 15

Arg Gly

<210> 748
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 748
Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 749
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 749
Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 750
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 750
Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
1 5 10

<210> 751
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 751
Asp Val Ser Asn Arg Pro Ser
1 5

<210> 752
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 752
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1 5 10

<210> 753
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 753
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Met Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
50 55 60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65 70 75 80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
85 90 95

```
Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
            100                 105                 110


Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly
        115                 120                 125


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ser
    130                 135                 140


Ala Leu Thr Gln Pro Ala Ser Ala Ser Gly Ser Pro Gly Gln Ser Val
145                 150                 155                 160


Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr
                165                 170                 175


Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile
            180                 185                 190


Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly
        195                 200                 205


Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala
    210                 215                 220


Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr
225                 230                 235                 240


Leu Tyr Val Phe Gly Thr Gly Thr Gln Leu Thr Val Leu
                245                 250


<210> 754
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 754
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
```

1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Met Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
50 55 60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65 70 75 80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
85 90 95

Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
100 105 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120 125

<210> 755
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 755
Gln Ser Ala Leu Thr Gln Pro Ala Ser Ala Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Gln Leu Thr Val Leu
100 105 110

<210> 756
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 756
Leu Glu Glu Lys Lys Gly Asn Tyr Val Val Thr Asp His
1 5 10

<210> 757
<211> 465
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 757
Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
35 40 45

```
Tyr His Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65                  70                  75                  80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Lys Leu Gln Glu
        115                 120                 125

Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser Leu Ser Val Thr Cys
    130                 135                 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145                 150                 155                 160

Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly Val Ile Trp Gly Ser
                165                 170                 175

Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser Arg Leu Thr Ile Ile
            180                 185                 190

Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys Met Asn Ser Leu Gln
        195                 200                 205

Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
    210                 215                 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val
225                 230                 235                 240

Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270
```

```
Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile
        275                 280                 285

Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser
    290                 295                 300

Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr
305                 310                 315                 320

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
                325                 330                 335

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
            340                 345                 350

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
        355                 360                 365

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
    370                 375                 380

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
385                 390                 395                 400

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
                405                 410                 415

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
            420                 425                 430

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
        435                 440                 445

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
    450                 455                 460

Arg
465
```

<210> 758
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 758
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
100 105 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu
115 120 125

Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys
130 135 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145 150 155 160

Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser
165 170 175

Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser Arg Val Thr Ile Ser
180 185 190

Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr
195 200 205

Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
210 215 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
225 230 235 240

Ser Ser

<210> 759
<211> 465
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 759
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr
85 90 95

```
Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser
            100                 105                 110

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu
        115                 120                 125

Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys
    130                 135                 140

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
145                 150                 155                 160

Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser
                165                 170                 175

Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser Arg Val Thr Ile Ser
            180                 185                 190

Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr
        195                 200                 205

Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
    210                 215                 220

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
225                 230                 235                 240

Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr
                245                 250                 255

Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala
            260                 265                 270

Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile
        275                 280                 285

Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser
    290                 295                 300
```

```
Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr
305                 310                 315                 320

Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu
                325                 330                 335

Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu
            340                 345                 350

Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Lys Gln
        355                 360                 365

Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu
    370                 375                 380

Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly
385                 390                 395                 400

Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln
                405                 410                 415

Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu
            420                 425                 430

Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr
        435                 440                 445

Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro
    450                 455                 460

Arg
465
```

<210> 760
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 760
Asp Tyr Gly Val Ser
1 5

<210> 761
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 761
Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser
1 5 10 15

<210> 762
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 762
His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr
1 5 10

<210> 763
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 763
Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn
1 5 10

<210> 764
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 764
His Thr Ser Arg Leu His Ser
1 5

<210> 765
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 765
Gln Gln Gly Asn Thr Leu Pro Tyr Thr
1 5

<210> 766
<211> 486
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 766
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu
20 25 30

Ser Ala Ser Leu Gly Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr
50 55 60

Val Lys Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Val Pro

```
65                  70                  75                  80

Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile
                85                  90                  95

Ser Asn Leu Glu Gln Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Thr
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu
    130                 135                 140

Val Lys Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln Ser
145                 150                 155                 160

Leu Ser Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser
        195                 200                 205

Arg Leu Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu Lys
    210                 215                 220

Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Ile Tyr Tyr Cys Ala Lys
225                 230                 235                 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Ser Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285
```

```
Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Lys Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg
                485
```

<210> 767

<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 767
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10

<210> 768
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 768
Gly Gly Gly Gly Ser
1 5

<210> 769
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 769
Asn Tyr Asn Leu His
1 5

<210> 770
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 770
Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1   5   10   15

Gly

<210> 771
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 771
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1   5   10

<210> 772
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 772
Gly Tyr Thr Phe Thr Asn Tyr
1   5

<210> 773
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 773
Tyr Pro Gly Asn Tyr Asp
1   5

<210> 774
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 774
Gly Tyr Thr Phe Thr Asn Tyr Asn
1 5

<210> 775
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 775
Ile Tyr Pro Gly Asn Tyr Asp Thr
1 5

<210> 776
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 776
Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10 15

<210> 777
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 777
Gly Tyr Thr Phe Thr Asn Tyr Asn Leu His
1   5   10

<210> 778
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 778
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20   25   30

Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe
    50   55   60

Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85   90   95

Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val Trp
            100   105   110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 779
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 779
caagtccaac tcgtccagtc cggtgcagaa gtcaagaaac ctggagcatc cgtgaaagtg 60

tcttgcaaag cctccggcta caccttcacc aactacaacc tccattgggt cagacaggcc 120

cccggacaag gactcgaatg gatgggagcg atctacccgg gaaactacga caccagctac 180

aaccagaagt tcaagggccg cgtgactatg accgccgata agagcacctc caccgcctac 240

atggaactgt cctcgctgag gtccgaggac actgcggtgt actactgcgc ccgcgtggac 300

ttcggacact cacggtattg gtacttcgac gtctggggac agggcactac cgtgaccgtg 360

tcgagc 366

<210> 780
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 780
Arg Ala Thr Ser Ser Val Ser Ser Met Asn
1 5 10

<210> 781
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 781
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 782
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 782
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 783
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 783
Thr Ser Ser Val Ser Ser
1 5

<210> 784
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 784
Ala Thr Ser
1

<210> 785
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 785
Trp Thr Phe Asn Pro Pro

1 5

<210> 786
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 786
Ser Ser Val Ser Ser
1 5

<210> 787
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 787
Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Thr Ser Ser Val Ser Ser Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile His
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr
85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys

100 105

<210> 788
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 788
gatatccagc tgactcagtc cccgtcattc ctgtccgcct ccgtgggaga cagagtgacc 60

atcacctgtc gggccacttc ctccgtgtca agcatgaact ggtatcagca gaagcccggg 120

aaggccccaa agccgctgat tcacgcgacg tccaacctgg cttccggcgt gccgagccgg 180

ttctccggct cggggagcgg gactgagtac accctgacta tttcctcgct tcaacccgag 240

gactttgcta cctactactg ccaacagtgg accttcaatc ctccgacatt cggacagggt 300

accaagttgg aaatcaag 318

<210> 789
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 789
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

```
Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Thr Ser Ser Val Ser Ser Met Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile His Ala Thr
            180                 185                 190

Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr Phe Gly
225                 230                 235                 240

Gln Gly Thr Lys Leu Glu Ile Lys
                245
```

<210> 790
<211> 744
<212> DNA
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 790
caagtccaac tcgtccagtc cggtgcagaa gtcaagaaac ctggagcatc cgtgaaagtg 60

tcttgcaaag cctccggcta caccttcacc aactacaacc tccattgggt cagacaggcc 120

cccggacaag gactcgaatg gatgggagcg atctacccgg gaaactacga caccagctac 180

aaccagaagt tcaagggccg cgtgactatg accgccgata agagcacctc caccgcctac 240

atggaactgt cctcgctgag gtccgaggac actgcggtgt actactgcgc ccgcgtggac 300

ttcggacact cacggtattg gtacttcgac gtctggggac agggcactac cgtgaccgtg 360

tcgagcggcg gaggaggttc gggaggggggc ggatcagggg gcggcggcag cggtggaggg 420

ggctcggata tccagctgac tcagtccccg tcattcctgt ccgcctccgt gggagacaga 480

gtgaccatca cctgtcgggc cacttcctcc gtgtcaagca tgaactggta tcagcagaag 540

cccgggaagg ccccaaagcc gctgattcac gcgacgtcca acctggcttc cggcgtgccg 600

agccggttct ccggctcggg gagcgggact gagtacaccc tgactatttc ctcgcttcaa 660

cccgaggact ttgctaccta ctactgccaa cagtggacct tcaatcctcc gacattcgga 720

cagggtacca agttggaaat caag 744

<210> 791
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 791
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

```
Thr Phe Thr Asn Tyr Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser
                85                  90                  95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp
        115                 120                 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala
                165                 170                 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Thr Ser Ser Val
            180                 185                 190

Ser Ser Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro
        195                 200                 205

Leu Ile His Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr
```

```
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465                 470                 475                 480
```

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 792
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 792
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtcc aactcgtcca gtccggtgca gaagtcaaga aacctggagc atccgtgaaa 120

gtgtcttgca aagcctccgg ctacaccttc accaactaca acctccattg ggtcagacag 180

gcccccggac aaggactcga atggatggga gcgatctacc cgggaaacta cgacaccagc 240

tacaaccaga agttcaaggg ccgcgtgact atgaccgccg ataagagcac ctccaccgcc 300

tacatggaac tgtcctcgct gaggtccgag gacactgcgg tgtactactg cgcccgcgtg 360

gacttcggac actcacggta ttggtacttc gacgtctggg gacagggcac taccgtgacc 420

gtgtcgagcg gcggaggagg ttcgggaggg ggcggatcag ggggcggcgg cagcggtgga 480

gggggctcgg atatccagct gactcagtcc ccgtcattcc tgtccgcctc cgtgggagac 540

agagtgacca tcacctgtcg ggccacttcc tccgtgtcaa gcatgaactg gtatcagcag 600

aagcccggga aggccccaaa gccgctgatt cacgcgacgt ccaacctggc ttccggcgtg 660

ccgagccggt tctccggctc ggggagcggg actgagtaca ccctgactat ttcctcgctt 720

caacccgagg actttgctac ctactactgc caacagtgga ccttcaatcc tccgacattc 780

ggacagggta ccaagttgga aatcaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccct 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctacc agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 793
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 793
Ser Tyr Asn Met His
1 5

<210> 794
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 794
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe Lys
1 5 10 15

Gly

<210> 795
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 795
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 796
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 796
Tyr Pro Gly Asn Gly Asp
1 5

<210> 797
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 797
Gly Tyr Thr Phe Thr Ser Tyr Asn
1 5

<210> 798
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 798
Ile Tyr Pro Gly Asn Gly Asp Thr
1 5

<210> 799

<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 799
Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10 15

<210> 800
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 800
Gly Tyr Thr Phe Thr Ser Tyr Asn Met His
1 5 10

<210> 801
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 801
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 802
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 802
caagtgcagc tcgtccagtc cggtgcagaa gtcaagaaac ccggtgcttc agtgaaagtg 60

tcctgcaagg cctccggtta caccttcacc tcctacaaca tgcactgggt ccgccaagcc 120

ccgggccagg gactcgaatg gatgggagcc atctaccctg gcaacgggga cacctcatac 180

aaccctaagt tcaagggcag agtgaccatg actgcggaca agtccactag aacagcgtac 240

atggagctga gcagcctgcg gtccgaggat actgccgtgt actactgcgc ccgctcctac 300

ttctacggaa gctcgtcgtg gtacttcgat gtctggggac agggcaccac tgtgactgtg 360

tcctcc 366

<210> 803
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 803
Arg Ala Ser Ser Ser Val Ser Ser Met His
1   5   10

<210> 804
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 804
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1   5

<210> 805
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 805
Ser Ser Ser Val Ser Ser
1   5

<210> 806
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 806
Trp Ile Phe Asn Pro Pro
1   5

<210> 807
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 807
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Ser Ser Val Ser Ser Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro Leu Ile Phe
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
65 70 75 80

Asp Ala Ala Val Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 808
<211> 318
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 808
gaaattgtgc tgactcagag ccccgccacc ctgagcttgt cccccgggga aagggcaacg 60

ctgtcatgcc gcgcctcgtc atccgtgtcc tccatgcatt ggtaccagca gaagccggga 120

caggcccctc ggccgctgat cttcgccacc tccaatctcg cttccggcat tccggcccgg 180

ttctcgggaa gcgggtcggg gaccgactat accctgacca tctctagcct tgaacctgag 240

gacgccgcgg tgtactattg tcaacagtgg atctttaacc ccccaacctt cggtggaggc 300

accaaagtgg agattaag 318

<210> 809
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 809
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
130 135 140

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
145 150 155 160

```
Ala Thr Leu Ser Cys Arg Ala Ser Ser Ser Val Ser Ser Met His Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro Leu Ile Phe Ala Thr
            180                 185                 190

Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Ala
    210                 215                 220

Ala Val Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr Phe Gly
225                 230                 235                 240

Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 810
<211> 744
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 810

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caagtgcagc tcgtccagtc cggtgcagaa gtcaagaaac ccggtgcttc agtgaaagtg       60

tcctgcaagg cctccggtta caccttcacc tcctacaaca tgcactgggt ccgccaagcc      120

ccgggccagg gactcgaatg gatgggagcc atctaccctg gcaacgggga cacctcatac      180

aaccctaagt tcaagggcag agtgaccatg actgcggaca agtccactag aacagcgtac      240

atggagctga gcagcctgcg gtccgaggat actgccgtgt actactgcgc ccgctcctac      300

ttctacggaa gctcgtcgtg gtacttcgat gtctggggac agggcaccac tgtgactgtg      360

tcctccggtg gcggaggctc gggcggaggc ggaagcggcg gcgggggatc gggaggagga      420

gggtccgaaa ttgtgctgac tcagagcccc gccaccctga gcttgtcccc cggggaaagg      480

gcaacgctgt catgccgcgc ctcgtcatcc gtgtcctcca tgcattggta ccagcagaag      540
```

ccgggacagg cccctcggcc gctgatcttc gccacctcca atctcgcttc cggcattccg 600

gcccggttct cgggaagcgg gtcggggacc gactataccc tgaccatctc tagccttgaa 660

cctgaggacg ccgcggtgta ctattgtcaa cagtggatct ttaacccccc aaccttcggt 720

ggaggcacca aagtggagat taag 744

<210> 811
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 811
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser
65 70 75 80

Tyr Asn Pro Lys Phe Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser
85 90 95

Thr Arg Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp
115 120 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly

```
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu
                165                 170                 175

Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Ser Ser Val
            180                 185                 190

Ser Ser Met His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro
        195                 200                 205

Leu Ile Phe Ala Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240

Glu Pro Glu Asp Ala Ala Val Tyr Tyr Cys Gln Gln Trp Ile Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350
```

```
Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365


Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380


Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385                 390                 395                 400


Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415


Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430


Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445


Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460


Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465                 470                 475                 480


Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 812
<211> 1476
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 812
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccaagtgc agctcgtcca gtccggtgca gaagtcaaga aacccggtgc ttcagtgaaa 120

gtgtcctgca aggcctccgg ttacaccttc acctcctaca acatgcactg ggtccgccaa 180

gccccgggcc agggactcga atggatggga gccatctacc ctggcaacgg ggacacctca 240

tacaacccta agttcaaggg cagagtgacc atgactgcgg acaagtccac tagaacagcg 300

tacatggagc tgagcagcct gcggtccgag gatactgccg tgtactactg cgcccgctcc 360

tacttctacg gaagctcgtc gtggtacttc gatgtctggg gacagggcac cactgtgact 420

gtgtcctccg gtggcggagg ctcgggcgga ggcggaagcg gcggcggggg atcgggagga 480

ggagggtccg aaattgtgct gactcagagc cccgccaccc tgagcttgtc ccccggggaa 540

agggcaacgc tgtcatgccg cgcctcgtca tccgtgtcct ccatgcattg gtaccagcag 600

aagccgggac aggcccctcg gccgctgatc ttcgccacct ccaatctcgc ttccggcatt 660

ccggcccggt tctcgggaag cgggtcgggg accgactata ccctgaccat ctctagcctt 720

gaacctgagg acgccgcggt gtactattgt caacagtgga tctttaaccc cccaaccttc 780

ggtggaggca ccaaagtgga gattaagacc actaccccag caccgaggcc acccaccccg 840

gctcctacca tcgcctccca gcctctgtcc ctgcgtccgg aggcatgtag acccgcagct 900

ggtggggccg tgcatacccg gggtcttgac ttcgcctgcg atatctacat ttgggccccc 960

ctggctggta cttgcggggt cctgctgctt tcactcgtga tcactcttta ctgtaagcgc 1020

ggtcggaaga agctgctgta catctttaag caacccttca tgaggcctgt gcagactact 1080

caagaggagg acggctgttc atgccggttc ccagaggagg aggaaggcgg ctgcgaactg 1140

cgcgtgaaat tcagccgcag cgcagatgct ccagcctacc agcaggggca gaaccagctc 1200

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 1260

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 1320

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 1380

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 1440

tatgacgctc ttcacatgca ggccctgccg cctcgg 1476

<210> 813
<211> 2238
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 813
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaaattg tgatgaccca gtcacccgcc actcttagcc tttcacccgg tgagcgcgca 120

accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta cacctttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcc aggtccaact ccaagaaagc ggaccgggtc ttgtgaagcc atcagaaact 480

ctttcactga cttgtactgt gagcggagtg tctctccccg attacggggt gtcttggatc 540

agacagccac cggggaaggg tctggaatgg attggagtga tttggggctc tgagactact 600

tactaccaat catccctcaa gtcacgcgtc accatctcaa aggacaactc taagaatcag 660

gtgtcactga aactgtcatc tgtgaccgca gccgacaccg ccgtgtacta ttgcgctaag 720

cattactatt atggcgggag ctacgcaatg gattactggg gacagggtac tctggtcacc 780

gtgtccagct tggcagaagc cgccgcgaaa gaagtgcagc ttcaacaatc aggaccagga 840

ctcgtcaaac catcacagac cctctccctc acatgtgcca tctccgggga ctccatgttg 900

agcaattccg acacttggaa ttggattaga caaagcccgt cccggggtct ggaatggttg 960

ggacgcacct accaccggtc tacttggtac gacgactacg cgtcatccgt gcggggaaga 1020

gtgtccatca acgtggacac ctccaagaac cagtacagcc tgcagcttaa tgccgtgact 1080

cctgaggata cgggcgtcta ctactgcgcc cgcgtccgcc tgcaagacgg gaacagctgg 1140

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ggatcgggtg gcgggggttc gggggggcggc ggctctcagt ccgctcttac ccaaccggcc 1260

tcagcctcgg ggagccccgg ccagagcgtg accatttcct gcaccggcac ttcatccgac 1320

gtgggcggct acaactacgt gtcctggtac caacagcacc cgggaaaggc ccccaagctc 1380

atgatctacg acgtgtccaa caggccctcg ggagtgtcca accggttctc gggttcgaaa 1440

tcgggaaaca cagccagcct gaccatcagc ggactgcagg ctgaagatga agccgactac 1500

tactgctcct cctacacctc gtcatccacg ctctacgtgt tcggcactgg aactcagctg 1560

actgtgctga ccactacccc agcaccgagg ccacccaccc cggctcctac catcgcctcc 1620

cagcctctgt ccctgcgtcc ggaggcatgt agacccgcag ctggtggggc cgtgcatacc 1680

cggggtcttg acttcgcctg cgatatctac atttgggccc ctctggctgg tacttgcggg 1740

gtcctgctgc tttcactcgt gatcactctt tactgtaagc gcggtcggaa gaagctgctg 1800

tacatcttta agcaaccctt catgaggcct gtgcagacta ctcaagagga ggacggctgt 1860

tcatgccggt tcccagagga ggaggaaggc ggctgcgaac tgcgcgtgaa attcagccgc 1920

agcgcagatg ctccagccta ccagcagggg cagaaccagc tctacaacga actcaatctt 1980

ggtcggagag aggagtacga cgtgctggac aagcggagag gacgggaccc agaaatgggc 2040

gggaagccgc gcagaaagaa tccccaagag ggcctgtaca acgagctcca aaaggataag 2100

atggcagaag cctatagcga gattggtatg aaaggggaac gcagaagagg caaaggccac 2160

gacggactgt accagggact cagcaccgcc accaaggaca cctatgacgc tcttcacatg 2220

caggccctgc cgcctcgg 2238

<210> 814
<211> 746
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 814
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65 70 75 80

```
Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
                85                  90                  95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
    130                 135                 140

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
145                 150                 155                 160

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser
        195                 200                 205

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
    210                 215                 220

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
225                 230                 235                 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Leu Val Thr Val Ser Ser Leu Ala Glu Ala Ala Ala Lys Glu Val
            260                 265                 270

Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln Thr Leu
        275                 280                 285
```

```
Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Met Leu Ser Asn Ser Asp
    290                 295                 300

Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu Trp Leu
305                 310                 315                 320

Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser
                325                 330                 335

Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn Gln Tyr
            340                 345                 350

Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val Tyr Tyr
        355                 360                 365

Cys Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe
    370                 375                 380

Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly
385                 390                 395                 400

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ser Ala Leu
                405                 410                 415

Thr Gln Pro Ala Ser Ala Ser Gly Ser Pro Gly Gln Ser Val Thr Ile
            420                 425                 430

Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
        435                 440                 445

Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Asp
    450                 455                 460

Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly Ser Lys
465                 470                 475                 480

Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp
                485                 490                 495

Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr
            500                 505                 510
```

```
Val Phe Gly Thr Gly Thr Gln Leu Thr Val Leu Thr Thr Thr Pro Ala
        515                 520                 525

Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser
    530                 535                 540

Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr
545                 550                 555                 560

Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala
                565                 570                 575

Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys
            580                 585                 590

Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met
        595                 600                 605

Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe
    610                 615                 620

Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg
625                 630                 635                 640

Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn
                645                 650                 655

Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg
            660                 665                 670

Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro
        675                 680                 685

Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala
    690                 695                 700

Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His
705                 710                 715                 720
```

Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp
725 730 735

Ala Leu His Met Gln Ala Leu Pro Pro Arg
740 745

<210> 815
<211> 2232
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 815
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

cccgaagtgc agcttcaaca atcaggacca ggactcgtca aaccatcaca gaccctctcc 120

ctcacatgtg ccatctccgg ggactccatg ttgagcaatt ccgacacttg gaattggatt 180

agacaaagcc cgtcccgggg tctggaatgg ttgggacgca cctaccaccg gtctacttgg 240

tacgacgact acgcgtcatc cgtgcgggga agagtgtcca tcaacgtgga cacctccaag 300

aaccagtaca gcctgcagct taatgccgtg actcctgagg atacgggcgt ctactactgc 360

gcccgcgtcc gcctgcaaga cgggaacagc tggagcgatg cattcgatgt ctggggccag 420

ggaactatgg tcaccgtgtc gtctgggggc ggtggatcgg gtggcggggg ttcgggggggc 480

ggcggctctc agtccgctct tacccaaccg gcctcagcct cggggagccc cggccagagc 540

gtgaccattt cctgcaccgg cacttcatcc gacgtgggcg gctacaacta cgtgtcctgg 600

taccaacagc acccgggaaa ggcccccaag ctcatgatct acgacgtgtc caacaggccc 660

tcgggagtgt ccaaccggtt ctcgggttcg aaatcgggaa acacagccag cctgaccatc 720

agcggactgc aggctgaaga tgaagccgac tactactgct cctcctacac ctcgtcatcc 780

acgctctacg tgttcggcac tggaactcag ctgactgtgc tgggaggggg agggagtgaa 840

attgtgatga cccagtcacc cgccactctt agcctttcac ccggtgagcg cgcaaccctg 900

tcttgcagag cctcccaaga catctcaaaa taccttaatt ggtatcaaca gaagcccgga 960

caggctcctc gccttctgat ctaccacacc agccggctcc attctggaat ccctgccagg 1020

ttcagcggta gcggatctgg gaccgactac accctcacta tcagctcact gcagccagag 1080

gacttcgctg tctatttctg tcagcaaggg aacaccctgc cctacacctt tggacagggc 1140

accaagctcg agattaaagg tggaggtggc agcggaggag gtgggtccgg cggtggagga 1200

agccaggtcc aactccaaga aagcggaccg ggtcttgtga agccatcaga aactctttca 1260

ctgacttgta ctgtgagcgg agtgtctctc cccgattacg gggtgtcttg gatcagacag 1320

ccaccgggga agggtctgga atggattgga gtgatttggg gctctgagac tacttactac 1380

caatcatccc tcaagtcacg cgtcaccatc tcaaaggaca actctaagaa tcaggtgtca 1440

ctgaaactgt catctgtgac cgcagccgac accgccgtgt actattgcgc taagcattac 1500

tattatggcg ggagctacgc aatggattac tggggacagg gtactctggt caccgtgtcc 1560

agcaccacta ccccagcacc gaggccaccc accccggctc ctaccatcgc ctcccagcct 1620

ctgtccctgc gtccggaggc atgtagaccc gcagctggtg gggccgtgca tacccggggt 1680

cttgacttcg cctgcgatat ctacatttgg gcccctctgg ctggtacttg cggggtcctg 1740

ctgctttcac tcgtgatcac tctttactgt aagcgcggtc ggaagaagct gctgtacatc 1800

tttaagcaac ccttcatgag gcctgtgcag actactcaag aggaggacgg ctgttcatgc 1860

cggttcccag aggaggagga aggcggctgc gaactgcgcg tgaaattcag ccgcagcgca 1920

gatgctccag cctaccagca ggggcagaac cagctctaca acgaactcaa tcttggtcgg 1980

agagaggagt acgacgtgct ggacaagcgg agaggacggg acccagaaat gggcgggaag 2040

ccgcgcagaa agaatcccca agagggcctg tacaacgagc tccaaaagga taagatggca 2100

gaagcctata gcgagattgg tatgaaaggg gaacgcagaa gaggcaaagg ccacgacgga 2160

ctgtaccagg gactcagcac cgccaccaag gacacctatg acgctcttca catgcaggcc 2220

ctgccgcctc gg 2232

<210> 816
<211> 744
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 816
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu

```
1               5                   10                  15

His Ala Ala Arg Pro Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu
            20                  25                  30

Val Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp
        35                  40                  45

Ser Met Leu Ser Asn Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro
    50                  55                  60

Ser Arg Gly Leu Glu Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp
65                  70                  75                  80

Tyr Asp Asp Tyr Ala Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val
                85                  90                  95

Asp Thr Ser Lys Asn Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro
            100                 105                 110

Glu Asp Thr Gly Val Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly
        115                 120                 125

Asn Ser Trp Ser Asp Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val
    130                 135                 140

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Gln Ser Ala Leu Thr Gln Pro Ala Ser Ala Ser Gly Ser
                165                 170                 175

Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val
            180                 185                 190

Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala
        195                 200                 205

Pro Lys Leu Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser
    210                 215                 220
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Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile
225                 230                 235                 240

Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr
                245                 250                 255

Thr Ser Ser Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Gln Leu Thr
            260                 265                 270

Val Leu Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala
        275                 280                 285

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
    290                 295                 300

Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
305                 310                 315                 320

Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly
                325                 330                 335

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu
            340                 345                 350

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln
        355                 360                 365

Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu
    370                 375                 380

Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
385                 390                 395                 400

Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser
                405                 410                 415

Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp
            420                 425                 430

Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
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        435                 440                 445

Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu
    450                 455                 460

Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser
465                 470                 475                 480

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                485                 490                 495

Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly
            500                 505                 510

Gln Gly Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg
        515                 520                 525

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
    530                 535                 540

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
545                 550                 555                 560

Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
                565                 570                 575

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg
            580                 585                 590

Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro
        595                 600                 605

Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu
    610                 615                 620

Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala
625                 630                 635                 640

Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
                645                 650                 655
```

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
660 665 670

Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
675 680 685

Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
690 695 700

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
705 710 715 720

Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
725 730 735

His Met Gln Ala Leu Pro Pro Arg
740

<210> 817
<211> 2202
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 817
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccccagtccg ctcttaccca accggcctca gcctcgggga gccccggcca gagcgtgacc 120

atttcctgca ccggcacttc atccgacgtg ggcggctaca actacgtgtc ctggtaccaa 180

cagcacccgg gaaaggcccc caagctcatg atctacgacg tgtccaacag gccctcggga 240

gtgtccaacc ggttctcggg ttcgaaatcg ggaaacacag ccagcctgac catcagcgga 300

ctgcaggctg aagatgaagc cgactactac tgctcctcct acacctcgtc atccacgctc 360

tacgtgttcg gcactggaac tcagctgact gtgctgggcg gaggaggctc cgaagtgcag 420

cttcaacaat caggaccagg actcgtcaaa ccatcacaga ccctctccct cacatgtgcc 480

atctccgggg actccatgtt gagcaattcc gacacttgga attggattag acaaagcccg 540

tcccggggtc tggaatggtt gggacgcacc taccaccggt ctacttggta cgacgactac 600

gcgtcatccg tgcggggaag agtgtccatc aacgtggaca cctccaagaa ccagtacagc 660

ctgcagctta atgccgtgac tcctgaggat acgggcgtct actactgcgc ccgcgtccgc 720

ctgcaagacg ggaacagctg gagcgatgca ttcgatgtct ggggccaggg aactatggtc 780

accgtgtcgt ctggaggggg agggagtgaa attgtgatga cccagtcacc cgccactctt 840

agcctttcac ccggtgagcg cgcaaccctg tcttgcagag cctcccaaga catctcaaaa 900

taccttaatt ggtatcaaca gaagcccgga caggctcctc gccttctgat ctaccacacc 960

agccggctcc attctggaat ccctgccagg ttcagcggta gcggatctgg gaccgactac 1020

accctcacta tcagctcact gcagccagag gacttcgctg tctatttctg tcagcaaggg 1080

aacaccctgc cctacacctt tggacagggc accaagctcg agattaaagg tggaggtggc 1140

agcggaggag gtgggtccgg cggtggagga agccaggtcc aactccaaga aagcggaccg 1200

ggtcttgtga agccatcaga aactctttca ctgacttgta ctgtgagcgg agtgtctctc 1260

cccgattacg gggtgtcttg gatcagacag ccaccgggga agggtctgga atggattgga 1320

gtgatttggg gctctgagac tacttactac caatcatccc tcaagtcacg cgtcaccatc 1380

tcaaaggaca actctaagaa tcaggtgtca ctgaaactgt catctgtgac cgcagccgac 1440

accgccgtgt actattgcgc taagcattac tattatggcg ggagctacgc aatggattac 1500

tggggacagg gtactctggt caccgtgtcc agcaccacta ccccagcacc gaggccaccc 1560

accccggctc ctaccatcgc ctcccagcct ctgtccctgc gtccggaggc atgtagaccc 1620

gcagctggtg gggccgtgca tacccggggt cttgacttcg cctgcgatat ctacatttgg 1680

gcccctctgg ctggtacttg cggggtcctg ctgctttcac tcgtgatcac tctttactgt 1740

aagcgcggtc ggaagaagct gctgtacatc tttaagcaac ccttcatgag gcctgtgcag 1800

actactcaag aggaggacgg ctgttcatgc cggttcccag aggaggagga aggcggctgc 1860

gaactgcgcg tgaaattcag ccgcagcgca gatgctccag cctaccagca ggggcagaac 1920

cagctctaca acgaactcaa tcttggtcgg agagaggagt acgacgtgct ggacaagcgg 1980

agaggacggg acccagaaat gggcgggaag ccgcgcagaa agaatcccca agagggcctg 2040

tacaacgagc tccaaaagga taagatggca gaagcctata gcgagattgg tatgaaaggg 2100

gaacgcagaa gaggcaaagg ccacgacgga ctgtaccagg gactcagcac cgccaccaag 2160

gacacctatg acgctcttca catgcaggcc ctgccgcctc gg 2202

<210> 818
<211> 734
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 818
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Ser Ala Leu Thr Gln Pro Ala Ser Ala Ser
20 25 30

Gly Ser Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser
35 40 45

Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly
50 55 60

Lys Ala Pro Lys Leu Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly
65 70 75 80

Val Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu
85 90 95

Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser
100 105 110

Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Gln
115 120 125

Leu Thr Val Leu Gly Gly Gly Gly Ser Glu Val Gln Leu Gln Gln Ser
130 135 140

Gly Pro Gly Leu Val Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys Ala
145 150 155 160

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Ile Ser Gly Asp Ser Met Leu Ser Asn Ser Asp Thr Trp Asn Trp Ile
                165                 170                 175

Arg Gln Ser Pro Ser Arg Gly Leu Glu Trp Leu Gly Arg Thr Tyr His
            180                 185                 190

Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val Arg Gly Arg Val
        195                 200                 205

Ser Ile Asn Val Asp Thr Ser Lys Asn Gln Tyr Ser Leu Gln Leu Asn
    210                 215                 220

Ala Val Thr Pro Glu Asp Thr Gly Val Tyr Tyr Cys Ala Arg Val Arg
225                 230                 235                 240

Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val Trp Gly Gln
                245                 250                 255

Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Glu Ile Val
            260                 265                 270

Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
        275                 280                 285

Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp
    290                 295                 300

Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr
305                 310                 315                 320

Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser
                325                 330                 335

Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
            340                 345                 350

Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly
        355                 360                 365

Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly
    370                 375                 380
```

```
Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Pro
385                 390                 395                 400

Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser
                405                 410                 415

Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro
            420                 425                 430

Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr
        435                 440                 445

Tyr Tyr Gln Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn
    450                 455                 460

Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp
465                 470                 475                 480

Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr
                485                 490                 495

Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Thr
            500                 505                 510

Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser
        515                 520                 525

Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly
    530                 535                 540

Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp
545                 550                 555                 560

Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile
                565                 570                 575

Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys
            580                 585                 590
```

```
Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys
        595                 600                 605

Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val
    610                 615                 620

Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn
625                 630                 635                 640

Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val
                645                 650                 655

Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg
            660                 665                 670

Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys
        675                 680                 685

Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg
    690                 695                 700

Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys
705                 710                 715                 720

Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                725                 730
```

<210> 819
<211> 2232
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 819
atggccctgc ccgtgactgc gctcctgctt ccgttggccc tgctcctgca tgccgccaga 60

cctcagtccg ctctgactca gccggcctca gcttcggggt cccctggtca aagcgtcact 120

atttcctgta ccggaacctc atcagacgtg ggcggctaca ttacgtgtc ctggtaccaa 180

cagcaccccg gaaaggctcc taagcttatg atctacgacg tgtccaaccg gccgtcagga 240

gtgtccaaca gattctccgg ctccaagagc ggaaacactg ccagcttgac cattagcggc 300

ttgcaggccg aggacgaagc cgactactac tgctctagct acacatcctc gtctaccctc 360

tacgtgtttg gaacggggac ccagctgact gtgctcgggg gtggaggatc agaggtgcaa 420

ctccagcagt ccggtcctgg cctcgtgaaa ccgtcccaaa ccctgtccct gacttgcgcc 480

atctcgggcg actccatgct gtccaattcc gacacctgga actggattag acaatcgcct 540

agccggggac tcgaatggct gggccggacc taccaccggt ccacgtggta tgacgactac 600

gcaagctccg tccggggaag ggtgtccatt aacgtcgata cctccaagaa ccagtacagc 660

cttcagctga acgctgtgac ccccgaggat accggcgtct actactgtgc aagagtgcga 720

ttgcaggatg gaaactcgtg gtcggacgca ttcgatgtct ggggacaggg aactatggtg 780

accgtgtcct cgggcggagg cgggagcgga ggaggaggct ctggcggagg aggaagcgag 840

attgtcatga ctcagtcccc ggccacactc tccctgtcac ccggagaaag agcaaccctg 900

agctgcaggg cgtcccagga catctcgaag tacctgaact ggtaccagca gaagcctgga 960

caagcacccc gcctcctgat ctaccacacc tcgcggctgc attcgggaat ccccgccaga 1020

ttctcaggga gcggatcagg aaccgactac accctgacta tctcgagcct gcaaccagag 1080

gatttcgccg tgtacttctg ccagcaagga aacaccctgc cctacacctt tggacaggga 1140

accaagctcg agattaaggg gggtggtgga tcgggagggg gtggatcagg aggaggcggc 1200

tcacaagtcc agctgcaaga atccggtccg ggacttgtga agccgtccga aaccctgtca 1260

ctgacttgca ctgtgtccgg ggtgtcattg cccgactacg gcgtgagctg gattcggcag 1320

ccccctggaa agggattgga atggatcggc gtgatctggg gttcggaaac tacctactat 1380

cagtcctcac tgaagtcccg cgtgaccatc agcaaggata attccaaaaa ccaagtgtct 1440

ctgaagctct ccagcgtcac tgccgccgat actgccgtgt actactgcgc caagcactac 1500

tattacggcg gttcgtacgc catggactac tggggccaag ggacactcgt gaccgtgtca 1560

tccaccacta ccccagcacc gaggccaccc accccggctc ctaccatcgc ctcccagcct 1620

ctgtccctgc gtccggaggc atgtagaccc gcagctggtg gggccgtgca tacccggggt 1680

cttgacttcg cctgcgatat ctacatttgg gcccctctgg ctggtacttg cggggtcctg 1740

ctgctttcac tcgtgatcac tctttactgt aagcgcggtc ggaagaagct gctgtacatc 1800

tttaagcaac ccttcatgag gcctgtgcag actactcaag aggaggacgg ctgttcatgc 1860

cggttcccag aggaggagga aggcggctgc gaactgcgcg tgaaattcag ccgcagcgca 1920

gatgctccag cctaccagca ggggcagaac cagctctaca acgaactcaa tcttggtcgg 1980

agagaggagt acgacgtgct ggacaagcgg agaggacggg acccagaaat gggcgggaag 2040

ccgcgcagaa agaatcccca agagggcctg tacaacgagc tccaaaagga taagatggca 2100

gaagcctata gcgagattgg tatgaaaggg gaacgcagaa gaggcaaagg ccacgacgga 2160

ctgtaccagg gactcagcac cgccaccaag gacacctatg acgctcttca catgcaggcc 2220

ctgccgcctc gg 2232

<210> 820
<211> 744
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 820
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Ser Ala Leu Thr Gln Pro Ala Ser Ala Ser
20 25 30

Gly Ser Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser
35 40 45

Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly
50 55 60

Lys Ala Pro Lys Leu Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly
65 70 75 80

Val Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu
85 90 95

Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser
100 105 110

```
Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Gln
        115                 120                 125

Leu Thr Val Leu Gly Gly Gly Gly Ser Glu Val Gln Leu Gln Gln Ser
    130                 135                 140

Gly Pro Gly Leu Val Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys Ala
145                 150                 155                 160

Ile Ser Gly Asp Ser Met Leu Ser Asn Ser Asp Thr Trp Asn Trp Ile
                165                 170                 175

Arg Gln Ser Pro Ser Arg Gly Leu Glu Trp Leu Gly Arg Thr Tyr His
            180                 185                 190

Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val Arg Gly Arg Val
        195                 200                 205

Ser Ile Asn Val Asp Thr Ser Lys Asn Gln Tyr Ser Leu Gln Leu Asn
    210                 215                 220

Ala Val Thr Pro Glu Asp Thr Gly Val Tyr Tyr Cys Ala Arg Val Arg
225                 230                 235                 240

Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val Trp Gly Gln
                245                 250                 255

Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
            260                 265                 270

Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala
        275                 280                 285

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
    290                 295                 300

Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
305                 310                 315                 320

Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly
```

```
                325                 330                 335

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu
            340                 345                 350

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln
        355                 360                 365

Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu
    370                 375                 380

Ile Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
385                 390                 395                 400

Ser Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser
                405                 410                 415

Glu Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp
            420                 425                 430

Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
        435                 440                 445

Ile Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu
    450                 455                 460

Lys Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser
465                 470                 475                 480

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
                485                 490                 495

Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly
            500                 505                 510

Gln Gly Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg
        515                 520                 525

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
    530                 535                 540
```

```
Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
545                 550                 555                 560

Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
                565                 570                 575

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg
            580                 585                 590

Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro
        595                 600                 605

Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu
    610                 615                 620

Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala
625                 630                 635                 640

Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
                645                 650                 655

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
            660                 665                 670

Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
        675                 680                 685

Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
    690                 695                 700

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
705                 710                 715                 720

Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
                725                 730                 735

His Met Gln Ala Leu Pro Pro Arg
            740
```

<210> 821

<211> 2232
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 821
atggccctgc ccgtgactgc gctcctgctt ccgttggccc tgctcctgca tgccgccaga 60

cctcagtccg ctctgactca gccggcctca gcttcggggt cccctggtca aagcgtcact 120

atttcctgta ccggaacctc atcagacgtg ggcggctaca ttacgtgtc ctggtaccaa 180

cagcaccccg gaaaggctcc taagcttatg atctacgacg tgtccaaccg gccgtcagga 240

gtgtccaaca gattctccgg ctccaagagc ggaaacactg ccagcttgac cattagcggc 300

ttgcaggccg aggacgaagc cgactactac tgctctagct acacatcctc gtctaccctc 360

tacgtgtttg gaacggggac ccagctgact gtgctcgggg gtggaggatc agaggtgcaa 420

ctccagcagt ccggtcctgg cctcgtgaaa ccgtcccaaa ccctgtccct gacttgcgcc 480

atctcgggcg actccatgct gtccaattcc gacacctgga actggattag acaatcgcct 540

agccggggac tcgaatggct gggccggacc taccaccggt ccacgtggta tgacgactac 600

gcaagctccg tccggggaag ggtgtccatt aacgtcgata cctccaagaa ccagtacagc 660

cttcagctga acgctgtgac ccccgaggat accggcgtct actactgtgc aagagtgcga 720

ttgcaggatg gaaactcgtg gtcggacgca ttcgatgtct ggggacaggg aactatggtc 780

actgtgtcct ccggcggtgg aggctcgggg gggggcggct caggaggagg cggctcacaa 840

gtccagctgc aagaatccgg tccgggactt gtgaagccgt ccgaaaccct gtcactgact 900

tgcactgtgt ccggggtgtc attgcccgac tacggcgtga gctggattcg gcagcccccct 960

ggaaagggat tggaatggat cggcgtgatc tggggttcgg aaactaccta ctatcagtcc 1020

tcactgaagt cccgcgtgac catcagcaag gataattcca aaaaccaagt gtctctgaag 1080

ctctccagcg tcactgccgc cgatactgcc gtgtactact gcgccaagca ctactattac 1140

ggcggttcgt acgccatgga ctactgggga caaggcactc ttgtgactgt gtcaagcggc 1200

ggtggaggga gcggtggggg cggttcagga ggaggcggat cagagatcgt gatgacccaa 1260

tccccagcca ccctgtccct cagccctgga gaaagagcca ccctgagctg ccgggcctcc 1320

caggatatca gcaagtactt gaactggtac caacaaaagc cggggcaggc gccccggctc 1380

ctgatctacc acacctcgcg cctccactca ggtatccccg ccagattctc agggagcggc 1440

tccggtactg actacaccct gactatttcc tcactgcagc cagaggactt tgccgtgtac 1500

ttctgccagc agggaaacac tctgccgtac accttcgggc agggaacgaa gcttgaaatt 1560

aagaccacta ccccagcacc gaggccaccc accccggctc ctaccatcgc ctcccagcct 1620

ctgtccctgc gtccggaggc atgtagaccc gcagctggtg gggccgtgca tacccggggt 1680

cttgacttcg cctgcgatat ctacatttgg gcccctctgg ctggtacttg cggggtcctg 1740

ctgctttcac tcgtgatcac tctttactgt aagcgcggtc ggaagaagct gctgtacatc 1800

tttaagcaac ccttcatgag gcctgtgcag actactcaag aggaggacgg ctgttcatgc 1860

cggttcccag aggaggagga aggcggctgc gaactgcgcg tgaaattcag ccgcagcgca 1920

gatgctccag cctaccagca ggggcagaac cagctctaca acgaactcaa tcttggtcgg 1980

agagaggagt acgacgtgct ggacaagcgg agaggacggg acccagaaat gggcgggaag 2040

ccgcgcagaa agaatcccca agagggcctg tacaacgagc tccaaaagga taagatggca 2100

gaagcctata gcgagattgg tatgaaaggg gaacgcagaa gaggcaaagg ccacgacgga 2160

ctgtaccagg gactcagcac cgccaccaag gacacctatg acgctcttca catgcaggcc 2220

ctgccgcctc gg 2232

<210> 822
<211> 744
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 822
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Ser Ala Leu Thr Gln Pro Ala Ser Ala Ser
20 25 30

Gly Ser Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser
35 40 45

```
Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly
    50                  55                  60

Lys Ala Pro Lys Leu Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly
65                  70                  75                  80

Val Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu
                85                  90                  95

Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser
            100                 105                 110

Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Gln
        115                 120                 125

Leu Thr Val Leu Gly Gly Gly Gly Ser Glu Val Gln Leu Gln Gln Ser
    130                 135                 140

Gly Pro Gly Leu Val Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys Ala
145                 150                 155                 160

Ile Ser Gly Asp Ser Met Leu Ser Asn Ser Asp Thr Trp Asn Trp Ile
                165                 170                 175

Arg Gln Ser Pro Ser Arg Gly Leu Glu Trp Leu Gly Arg Thr Tyr His
            180                 185                 190

Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val Arg Gly Arg Val
        195                 200                 205

Ser Ile Asn Val Asp Thr Ser Lys Asn Gln Tyr Ser Leu Gln Leu Asn
    210                 215                 220

Ala Val Thr Pro Glu Asp Thr Gly Val Tyr Tyr Cys Ala Arg Val Arg
225                 230                 235                 240

Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val Trp Gly Gln
                245                 250                 255
```

```
Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
            260                 265                 270

Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu Ser Gly Pro
        275                 280                 285

Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys Thr Val Ser
    290                 295                 300

Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg Gln Pro Pro
305                 310                 315                 320

Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser Glu Thr Thr
                325                 330                 335

Tyr Tyr Gln Ser Ser Leu Lys Ser Arg Val Thr Ile Ser Lys Asp Asn
            340                 345                 350

Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp
        355                 360                 365

Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly Gly Ser Tyr
    370                 375                 380

Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly
385                 390                 395                 400

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
                405                 410                 415

Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
            420                 425                 430

Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn
        435                 440                 445

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His
    450                 455                 460

Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly
465                 470                 475                 480
```

```
Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
                485                 490                 495

Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe
            500                 505                 510

Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr Pro Ala Pro Arg
        515                 520                 525

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
    530                 535                 540

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
545                 550                 555                 560

Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
                565                 570                 575

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg
            580                 585                 590

Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro
        595                 600                 605

Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu
    610                 615                 620

Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala
625                 630                 635                 640

Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
                645                 650                 655

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
            660                 665                 670

Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
        675                 680                 685
```

```
Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
    690                 695                 700

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
705                 710                 715                 720

Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
                725                 730                 735

His Met Gln Ala Leu Pro Pro Arg
            740
```

<210> 823
<211> 2985
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 823

```
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg       60

cccgaagtgc agctgcagca gtcagggcct ggcctggtca agccgtcgca gaccctctcc      120

ctgacatgcg ccattagcgg ggactccatg ctgagcaact cggacacctg gaactggatt      180

cggcagtccc cttcccgggg actcgagtgg ctcggacgca cctaccatcg gagcacttgg      240

tacgacgact acgcctcctc cgtgagaggt cgcgtgtcga tcaacgtgga tacctcgaag      300

aaccagtata gcttgcaact gaacgccgtg acccctgagg ataccggagt gtactattgt      360

gcgagagtca ggctgcaaga cggaaactcc tggtccgacg catttgatgt ctggggacag      420

ggtactatgg tcacggtgtc atctggaggc ggaggatcgc aaagcgccct gactcagccg      480

gcttcggcta gcggttcacc ggggcagtcc gtgactatct cctgcaccgg gacttcctcc      540

gacgtgggag gctacaatta cgtgtcctgg taccagcaac accccggcaa agccccaaag      600

ctgatgatct acgacgtcag caacagaccc agcggagtgt ccaaccggtt cagcggctcc      660

aagtccggca acaccgcctc cctgaccatc agcgggcttc aggccgaaga tgaggcggat      720

tactactgct cctcgtacac ctcaagctca actctgtacg tgttcggcac cggtactcag      780

ctcaccgtgc tgaccactac cccagcaccg aggccaccca ccccggctcc taccatcgcc      840
```

tcccagcctc tgtccctgcg tccggaggca tgtagacccg cagctggtgg ggccgtgcat 900

acccggggtc ttgacttcgc ctgcgatatc tacatttggg cccctctggc tggtacttgc 960

ggggtcctgc tgctttcact cgtgatcact ctttactgta agcgcggtcg gaagaagctg 1020

ctgtacatct ttaagcaacc cttcatgagg cctgtgcaga ctactcaaga ggaggacggc 1080

tgttcatgcc ggttcccaga ggaggaggaa ggcggctgcg aactgcgcgt gaaattcagc 1140

cgcagcgcag atgctccagc ctaccagcag gggcagaacc agctctacaa cgaactcaat 1200

cttggtcgga gagaggagta cgacgtgctg gacaagcgga gaggacggga cccagaaatg 1260

ggcgggaagc cgcgcagaaa gaatccccaa gagggcctgt acaacgagct ccaaaaggat 1320

aagatggcag aagcctatag cgagattggt atgaaagggg aacgcagaag aggcaaaggc 1380

cacgacggac tgtaccaggg actcagcacc gccaccaagg acacctatga cgctcttcac 1440

atgcaggccc tgccgcctcg gggaagcgga gctactaact tcagcctgct gaagcaggct 1500

ggagacgtgg aggagaaccc tggacctatg gccttaccag tgaccgcctt gctcctgccg 1560

ctggccttgc tgctccacgc cgccaggccg gaaattgtga tgacccagtc acccgccact 1620

cttagccttt cacccggtga gcgcgcaacc ctgtcttgca gagcctccca agacatctca 1680

aaatacctta attggtatca acagaagccc ggacaggctc ctcgccttct gatctaccac 1740

accagccggc tccattctgg aatccctgcc aggttcagcg gtagcggatc tgggaccgac 1800

tacaccctca ctatcagctc actgcagcca gaggacttcg ctgtctattt ctgtcagcaa 1860

gggaacaccc tgccctacac ctttggacag ggcaccaagc tcgagattaa aggtggaggt 1920

ggcagcggag gaggtgggtc cggcggtgga ggaagccagg tccaactcca agaaagcgga 1980

ccgggtcttg tgaagccatc agaaactctt tcactgactt gtactgtgag cggagtgtct 2040

ctccccgatt acggggtgtc ttggatcaga cagccaccgg ggaagggtct ggaatggatt 2100

ggagtgattt ggggctctga gactacttac taccaatcat ccctcaagtc acgcgtcacc 2160

atctcaaagg acaactctaa gaatcaggtg tcactgaaac tgtcatctgt gaccgcagcc 2220

gacaccgccg tgtactattg cgctaagcat tactattatg gcgggagcta cgcaatggat 2280

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tgggcgccct tggccgggac ttgtggggtc cttctcctgt cactggttat cacccttac 2520

tgcaaacggg gcagaaagaa actcctgtat atattcaaac aaccatttat gagaccagta 2580

caaactactc aagaggaaga tggctgtagc tgccgatttc cagaagaaga agaaggagga 2640

tgtgaactga gagtgaagtt cagcaggagc gcagacgccc ccgcgtacca gcagggccag 2700

aaccagctct ataacgagct caatctagga cgaagagagg agtacgatgt tttggacaag 2760

agacgtggcc gggaccctga gatgggggga aagccgagaa ggaagaaccc tcaggaaggc 2820

ctgtacaatg aactgcagaa agataagatg gcggaggcct acagtgagat tgggatgaaa 2880

ggcgagcgcc ggaggggcaa ggggcacgat ggcctttacc agggtctcag tacagccacc 2940

aaggacacct acgacgccct tcacatgcag gccctgcccc ctcgc 2985

<210> 824
<211> 995
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 824
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu
20 25 30

Val Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp
35 40 45

Ser Met Leu Ser Asn Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro
50 55 60

Ser Arg Gly Leu Glu Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp
65 70 75 80

Tyr Asp Asp Tyr Ala Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val
85 90 95

```
Asp Thr Ser Lys Asn Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro
            100                 105                 110

Glu Asp Thr Gly Val Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly
        115                 120                 125

Asn Ser Trp Ser Asp Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val
    130                 135                 140

Thr Val Ser Ser Gly Gly Gly Gly Ser Gln Ser Ala Leu Thr Gln Pro
145                 150                 155                 160

Ala Ser Ala Ser Gly Ser Pro Gly Gln Ser Val Thr Ile Ser Cys Thr
                165                 170                 175

Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln
            180                 185                 190

Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Asp Val Ser Asn
        195                 200                 205

Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn
    210                 215                 220

Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp
225                 230                 235                 240

Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val Phe Gly
                245                 250                 255

Thr Gly Thr Gln Leu Thr Val Leu Thr Thr Thr Pro Ala Pro Arg Pro
            260                 265                 270

Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
        275                 280                 285

Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
    290                 295                 300

Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
```

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305                 310                 315                 320

Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly
                325                 330                 335

Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val
            340                 345                 350

Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu
        355                 360                 365

Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp
    370                 375                 380

Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
385                 390                 395                 400

Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
                405                 410                 415

Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
            420                 425                 430

Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
        435                 440                 445

Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
    450                 455                 460

Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
465                 470                 475                 480

Met Gln Ala Leu Pro Pro Arg Gly Ser Gly Ala Thr Asn Phe Ser Leu
                485                 490                 495

Leu Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Ala Leu
            500                 505                 510

Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu His Ala Ala
        515                 520                 525
```

```
Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser
    530                 535                 540

Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser
545                 550                 555                 560

Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu
                565                 570                 575

Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro Ala Arg Phe
            580                 585                 590

Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu
        595                 600                 605

Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu
    610                 615                 620

Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly
625                 630                 635                 640

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu
                645                 650                 655

Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu
            660                 665                 670

Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp
        675                 680                 685

Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp
    690                 695                 700

Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser Arg Val Thr
705                 710                 715                 720

Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser
                725                 730                 735

Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr
```

```
            740                 745                 750

Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val
        755                 760                 765

Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
    770                 775                 780

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
785                 790                 795                 800

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
                805                 810                 815

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
            820                 825                 830

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
        835                 840                 845

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
    850                 855                 860

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
865                 870                 875                 880

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
                885                 890                 895

Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
            900                 905                 910

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
        915                 920                 925

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
    930                 935                 940

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
945                 950                 955                 960
```

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
965 970 975

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
980 985 990

Pro Pro Arg
995

<210> 825
<211> 508
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 825
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu
20 25 30

Val Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp
35 40 45

Ser Met Leu Ser Asn Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro
50 55 60

Ser Arg Gly Leu Glu Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp
65 70 75 80

Tyr Asp Asp Tyr Ala Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val
85 90 95

Asp Thr Ser Lys Asn Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro
100 105 110

Glu Asp Thr Gly Val Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly
115 120 125

```
Asn Ser Trp Ser Asp Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val
    130                 135                 140

Thr Val Ser Ser Gly Gly Gly Gly Ser Gln Ser Ala Leu Thr Gln Pro
145                 150                 155                 160

Ala Ser Ala Ser Gly Ser Pro Gly Gln Ser Val Thr Ile Ser Cys Thr
                165                 170                 175

Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln
            180                 185                 190

Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Asp Val Ser Asn
        195                 200                 205

Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn
    210                 215                 220

Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp
225                 230                 235                 240

Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val Phe Gly
                245                 250                 255

Thr Gly Thr Gln Leu Thr Val Leu Thr Thr Thr Pro Ala Pro Arg Pro
            260                 265                 270

Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
        275                 280                 285

Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
    290                 295                 300

Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
305                 310                 315                 320

Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly
                325                 330                 335
```

```
Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val
            340                 345                 350

Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu
        355                 360                 365

Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp
    370                 375                 380

Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
385                 390                 395                 400

Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
                405                 410                 415

Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
            420                 425                 430

Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
        435                 440                 445

Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
    450                 455                 460

Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
465                 470                 475                 480

Met Gln Ala Leu Pro Pro Arg Gly Ser Gly Ala Thr Asn Phe Ser Leu
                485                 490                 495

Leu Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly
            500                 505
```

<210> 826
<211> 487
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 826
Pro Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu
1   5   10   15

Leu His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr
            20   25   30

Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser
        35   40   45

Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln
    50   55   60

Ala Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile
65   70   75   80

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr
                85   90   95

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln
            100   105   110

Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile
        115   120   125

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    130   135   140

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
145   150   155   160

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
                165   170   175

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
            180   185   190

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys
        195   200   205

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu

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    210                 215                 220

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
225                 230                 235                 240

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
                245                 250                 255

Gly Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro
            260                 265                 270

Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro
        275                 280                 285

Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu
    290                 295                 300

Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys
305                 310                 315                 320

Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly
                325                 330                 335

Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val
            340                 345                 350

Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu
        355                 360                 365

Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp
    370                 375                 380

Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn
385                 390                 395                 400

Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg
                405                 410                 415

Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly
            420                 425                 430
```

Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu
435 440 445

Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu
450 455 460

Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His
465 470 475 480

Met Gln Ala Leu Pro Pro Arg
485

<210> 827
<211> 2985
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 827
atggccttac cagtgaccgc cttgctcctg ccgctggcct tgctgctcca cgccgccagg 60

ccggaaattg tgatgaccca gtcacccgcc actcttagcc tttcacccgg tgagcgcgca 120

accctgtctt gcagagcctc ccaagacatc tcaaaatacc ttaattggta tcaacagaag 180

cccggacagg ctcctcgcct tctgatctac cacaccagcc ggctccattc tggaatccct 240

gccaggttca gcggtagcgg atctgggacc gactacaccc tcactatcag ctcactgcag 300

ccagaggact tcgctgtcta tttctgtcag caagggaaca ccctgcccta cacctttgga 360

cagggcacca agctcgagat taaaggtgga ggtggcagcg gaggaggtgg gtccggcggt 420

ggaggaagcc aggtccaact ccaagaaagc ggaccgggtc ttgtgaagcc atcagaaact 480

ctttcactga cttgtactgt gagcggagtg tctctccccg attacggggt gtcttggatc 540

agacagccac cggggaaggg tctggaatgg attggagtga tttggggctc tgagactact 600

tactaccaat catccctcaa gtcacgcgtc accatctcaa aggacaactc taagaatcag 660

gtgtcactga aactgtcatc tgtgaccgca gccgacaccg ccgtgtacta ttgcgctaag 720

cattactatt atggcgggag ctacgcaatg gattactggg gacagggtac tctggtcacc 780

gtgtccagca ccacgacgcc agcgccgcga ccaccaacac cggcgcccac catcgcgtcg 840

cagcccctgt ccctgcgccc agaggcgtgc cggccagcgg cgggggcgc agtgcacacg 900

agggggctgg acttcgcctg tgatatctac atctgggcgc ccttggccgg gacttgtggg 960

gtccttctcc tgtcactggt tatcaccctt tactgcaaac ggggcagaaa gaaactcctg 1020

tatatattca aacaaccatt tatgagacca gtacaaacta ctcaagagga agatggctgt 1080

agctgccgat ttccagaaga agaagaagga ggatgtgaac tgagagtgaa gttcagcagg 1140

agcgcagacg cccccgcgta ccagcagggc cagaaccagc tctataacga gctcaatcta 1200

ggacgaagag aggagtacga tgttttggac aagagacgtg gccgggaccc tgagatgggg 1260

ggaaagccga gaaggaagaa ccctcaggaa ggcctgtaca atgaactgca gaaagataag 1320

atggcggagg cctacagtga gattgggatg aaaggcgagc gccggagggg caaggggcac 1380

gatggccttt accagggtct cagtacagcc accaaggaca cctacgacgc ccttcacatg 1440

caggccctgc cccctcgcgg aagcggagct actaacttca gcctgctgaa gcaggctgga 1500

gacgtggagg agaaccctgg acctatggcc ctccctgtca ccgccctgct gcttccgctg 1560

gctcttctgc tccacgccgc tcggcccgaa gtgcagctgc agcagtcagg gcctggcctg 1620

gtcaagccgt cgcagaccct ctccctgaca tgcgccatta gcggggactc catgctgagc 1680

aactcggaca cctggaactg gattcggcag tccccttccc ggggactcga gtggctcgga 1740

cgcacctacc atcggagcac ttggtacgac gactacgcct cctccgtgag aggtcgcgtg 1800

tcgatcaacg tggatacctc gaagaaccag tatagcttgc aactgaacgc cgtgacccct 1860

gaggataccg gagtgtacta ttgtgcgaga gtcaggctgc aagacggaaa ctcctggtcc 1920

gacgcatttg atgtctgggg acagggtact atggtcacgg tgtcatctgg aggcggagga 1980

tcgcaaagcg ccctgactca gccggcttcg gctagcggtt caccggggca gtccgtgact 2040

atctcctgca ccgggacttc ctccgacgtg ggaggctaca attacgtgtc ctggtaccag 2100

caacaccccg gcaaagcccc aaagctgatg atctacgacg tcagcaacag acccagcgga 2160

gtgtccaacc ggttcagcgg ctccaagtcc ggcaacaccg cctccctgac catcagcggg 2220

cttcaggccg aagatgaggc ggattactac tgctcctcgt acacctcaag ctcaactctg 2280

tacgtgttcg gcaccggtac tcagctcacc gtgctgacca ctaccccagc accgaggcca 2340

cccaccccgg ctcctaccat cgcctcccag cctctgtccc tgcgtccgga ggcatgtaga 2400

cccgcagctg gtggggccgt gcatacccgg ggtcttgact tcgcctgcga tatctacatt 2460

tgggcccctc tggctggtac ttgcggggtc ctgctgcttt cactcgtgat cactctttac 2520

tgtaagcgcg gtcggaagaa gctgctgtac atctttaagc aacccttcat gaggcctgtg 2580

cagactactc aagaggagga cggctgttca tgccggttcc cagaggagga ggaaggcggc 2640

tgcgaactgc gcgtgaaatt cagccgcagc gcagatgctc cagcctacca gcaggggcag 2700

aaccagctct acaacgaact caatcttggt cggagagagg agtacgacgt gctggacaag 2760

cggagaggac gggacccaga aatgggcggg aagccgcgca gaaagaatcc ccaagagggc 2820

ctgtacaacg agctccaaaa ggataagatg gcagaagcct atagcgagat tggtatgaaa 2880

ggggaacgca gaagaggcaa aggccacgac ggactgtacc agggactcag caccgccacc 2940

aaggacacct atgacgctct tcacatgcag gccctgccgc ctcgg 2985

<210> 828
<211> 995
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 828
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
85 90 95

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Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
            100                 105                 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
    130                 135                 140

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
145                 150                 155                 160

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser
        195                 200                 205

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
    210                 215                 220

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
225                 230                 235                 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300
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Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335

Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu
                485                 490                 495

Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly Pro Met Ala Leu Pro
            500                 505                 510

Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu His Ala Ala Arg
        515                 520                 525
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Pro Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser
    530                 535                 540

Gln Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Met Leu Ser
545                 550                 555                 560

Asn Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu
                565                 570                 575

Glu Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr
            580                 585                 590

Ala Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys
        595                 600                 605

Asn Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly
    610                 615                 620

Val Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser
625                 630                 635                 640

Asp Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
                645                 650                 655

Gly Gly Gly Gly Ser Gln Ser Ala Leu Thr Gln Pro Ala Ser Ala Ser
            660                 665                 670

Gly Ser Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser
        675                 680                 685

Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly
    690                 695                 700

Lys Ala Pro Lys Leu Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly
705                 710                 715                 720

Val Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu
                725                 730                 735
```

```
Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser
            740                 745                 750

Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Gln
        755                 760                 765

Leu Thr Val Leu Thr Thr Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala
    770                 775                 780

Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg
785                 790                 795                 800

Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp Phe Ala Cys
                805                 810                 815

Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly Val Leu Leu
            820                 825                 830

Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu
        835                 840                 845

Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln Thr Thr Gln
    850                 855                 860

Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly
865                 870                 875                 880

Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr
                885                 890                 895

Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg
            900                 905                 910

Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met
        915                 920                 925

Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu
    930                 935                 940

Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys
945                 950                 955                 960
```

Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr Gln Gly Leu
965 970 975

Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met Gln Ala Leu
980 985 990

Pro Pro Arg
995

<210> 829
<211> 507
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 829
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu
20 25 30

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
35 40 45

Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala
50 55 60

Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile Pro
65 70 75 80

Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile
85 90 95

Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Gly
100 105 110

Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys

```
        115                 120                 125

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln
    130                 135                 140

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
145                 150                 155                 160

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
                165                 170                 175

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
            180                 185                 190

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser
        195                 200                 205

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
    210                 215                 220

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
225                 230                 235                 240

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
                245                 250                 255

Thr Leu Val Thr Val Ser Ser Thr Thr Thr Pro Ala Pro Arg Pro Pro
            260                 265                 270

Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg Pro Glu
        275                 280                 285

Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly Leu Asp
    290                 295                 300

Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr Cys Gly
305                 310                 315                 320

Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg Gly Arg
                325                 330                 335
```

```
Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro Val Gln
            340                 345                 350

Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu Glu Glu
        355                 360                 365

Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala Asp Ala
    370                 375                 380

Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu Asn Leu
385                 390                 395                 400

Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly Arg Asp
                405                 410                 415

Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu
            420                 425                 430

Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile
        435                 440                 445

Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly Leu Tyr
    450                 455                 460

Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu His Met
465                 470                 475                 480

Gln Ala Leu Pro Pro Arg Gly Ser Gly Ala Thr Asn Phe Ser Leu Leu
                485                 490                 495

Lys Gln Ala Gly Asp Val Glu Glu Asn Pro Gly
            500                 505
```

<210> 830
<211> 488
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 830
Pro Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu
1   5   10   15

Leu His Ala Ala Arg Pro Glu Val Gln Leu Gln Gln Ser Gly Pro Gly
            20   25   30

Leu Val Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly
        35   40   45

Asp Ser Met Leu Ser Asn Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser
    50   55   60

Pro Ser Arg Gly Leu Glu Trp Leu Gly Arg Thr Tyr His Arg Ser Thr
65   70   75   80

Trp Tyr Asp Asp Tyr Ala Ser Ser Val Arg Gly Arg Val Ser Ile Asn
                85   90   95

Val Asp Thr Ser Lys Asn Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr
            100   105   110

Pro Glu Asp Thr Gly Val Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp
        115   120   125

Gly Asn Ser Trp Ser Asp Ala Phe Asp Val Trp Gly Gln Gly Thr Met
    130   135   140

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gln Ser Ala Leu Thr Gln
145   150   155   160

Pro Ala Ser Ala Ser Gly Ser Pro Gly Gln Ser Val Thr Ile Ser Cys
                165   170   175

Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr
            180   185   190

Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Asp Val Ser
        195   200   205

```
Asn Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly
    210                 215                 220

Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala
225                 230                 235                 240

Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val Phe
                245                 250                 255

Gly Thr Gly Thr Gln Leu Thr Val Leu Thr Thr Thr Pro Ala Pro Arg
            260                 265                 270

Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro Leu Ser Leu Arg
        275                 280                 285

Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val His Thr Arg Gly
    290                 295                 300

Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro Leu Ala Gly Thr
305                 310                 315                 320

Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu Tyr Cys Lys Arg
                325                 330                 335

Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro Phe Met Arg Pro
            340                 345                 350

Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys Arg Phe Pro Glu
        355                 360                 365

Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe Ser Arg Ser Ala
    370                 375                 380

Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu Tyr Asn Glu Leu
385                 390                 395                 400

Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp Lys Arg Arg Gly
                405                 410                 415

Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys Asn Pro Gln Glu
            420                 425                 430
```

Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala Glu Ala Tyr Ser
435 440 445

Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys Gly His Asp Gly
450 455 460

Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr Tyr Asp Ala Leu
465 470 475 480

His Met Gln Ala Leu Pro Pro Arg
485

<210> 831
<211> 2985
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 831
atggcacttc ccgtcaccgc cctgctgctc ccactcgccc tccttctgca cgccgcccgc 60

cccgaagtgc agctgcagca gtcaggaccg ggcctggtca aaccttcgca gactctgtcc 120

ctgacttgcg ctataagcgg ggactccatg ctgagcaatt cggacacttg gaactggatt 180

cgccaaagcc ccagccgggg tctggaatgg ctgggaagga cctaccatcg ctctacttgg 240

tacgacgact acgccagctc cgtgcgagga cgcgtgtcca tcaacgtgga cacctccaag 300

aaccagtact cgcttcaact caacgcagtg acccctgaag ataccggagt ctactattgc 360

gcccgcgtgc ggctccagga cgggaactcc tggtcggacg ctttcgatgt ctggggacag 420

ggcactatgg tcaccgtcag ctccggcggc ggcggtagcc aatcggcgct gacacagccg 480

gcttccgcct cgggatcgcc tggacagtcg gtgaccatct cgtgcactgg aacctcctcc 540

gacgtgggcg gctacaatta tgtgtcatgg taccagcagc acccgggaaa ggcccctaag 600

ctgatgatct acgacgtgtc caatagacct agcggggtgt caaacagatt ctccggatcc 660

aaatccggaa acactgcctc cctgaccatt tccggactgc aggccgagga cgaagccgat 720

tactactgct cctcttacac ctcctcatcc accctctacg tgtttgggac tgggacccag 780

ctgaccgtcc tcactaccac cccggccccg cggcccccta caccggcacc gactattgcc 840

agccagcctc tctcgctgcg gccggaggcc tgccgcccag ccgccggcgg agccgtgcac 900

acccgcggtc tggacttcgc gtgcgatatc tacatctggg ctccgctggc cgggacttgt 960

ggcgtgctgc tgctgtctct ggtcatcaca ctgtactgca agcgcggaag aaagaagctg 1020

ctctacatct tcaagcaacc cttcatgcgg cctgtgcaga ccacccagga agaggatggc 1080

tgctcctgcc ggttcccgga ggaagaagag ggcggatgcg aactgcgcgt gaagttcagc 1140

cgaagcgccg acgccccggc ctaccagcag ggccagaacc aactgtacaa cgaactcaac 1200

ctgggtcgga gagaagagta cgacgtgctg gacaaaagac gcggcaggga ccccgagatg 1260

ggcggaaagc ctcgccgcaa gaacccgcag gagggcctct acaacgagct gcagaaggac 1320

aagatggccg aagcctactc agagatcggc atgaaggggg agcggaggcg cgggaagggc 1380

cacgacggtt tgtaccaagg actttccact gcgaccaagg acacctacga tgccctccat 1440

atgcaagccc tgccgccccg gggttccgga gctaccaact tctcgctgtt gaagcaggcc 1500

ggagatgtcg aggaaaaccc gggacctatg gccctgccag tgaccgcgct cctgctgccc 1560

ctggctctgc tgcttcacgc ggcccggcct gagattgtga tgactcagag cccggcgacc 1620

ctgtccctgt cccccgggga gagagcaacc ctgtcgtgcc gggcctccca agacatctca 1680

aagtacctca attggtatca gcagaagcca ggacaggctc cacggttgct gatctaccac 1740

acttcgagac tgcactcagg aatccccgcg cggttttccg gttccggctc cgggaccgac 1800

tacaccctga ccatcagctc gctccagcct gaggatttcg cagtgtactt ctgtcagcaa 1860

ggaaacaccc ttccatacac cttcggacag ggtaccaagc tggaaatcaa gggaggagga 1920

ggatctgggg gcggtggttc cggaggcggt ggaagccaag tgcagctcca ggaaagcgga 1980

cccgggctgg tcaagccgag cgaaaccctc tcactgactt gtactgtgtc cggagtgtcc 2040

ctgcctgact atggagtgtc ctggatccga cagccccccg gaaagggtct ggagtggatt 2100

ggggtcatct ggggctccga aactacctac taccagagca gcctcaagag ccgggtcacc 2160

atttcaaagg ataactccaa gaatcaagtg tccctgaagc tgtcctcagt gacagccgca 2220

gacaccgccg tgtactactg cgccaagcac tactactacg gaggctccta cgcaatggac 2280

tactggggac aaggcacttt ggtcactgtg tcaagcacca ccacccctgc gcctcggcct 2340

cctaccccgg ctcccactat cgcgagccag ccgctgagcc tgcggcctga ggcttgccga 2400

ccggccgctg gcggcgccgt gcatactcgg ggcctcgact ttgcctgtga catctacatc 2460

tgggcccccc tggccggaac gtgcggagtg ctgctgctgt cgctggtcat taccctgtat 2520

tgcaaacgcg gaaggaagaa gctgttgtac attttcaagc agcccttcat gcgcccggtg 2580

caaactactc aggaggaaga tggctgttcc tgtcggttcc ccgaagagga agaaggcggc 2640

tgcgagttga gggtcaagtt ctcccggtcc gccgatgctc ccgcctacca acaggggcag 2700

aaccagcttt ataacgaact gaacctgggc aggagggagg aatatgatgt gttggataag 2760

cgccggggcc gggacccaga aatgggggga aagcccagaa gaaagaaccc tcaagaggga 2820

ctttacaacg aattgcagaa agacaaaatg gccgaggcct actccgagat tgggatgaag 2880

ggcgaaagac ggagaggaaa ggggcacgac gggctctacc agggactcag caccgccacc 2940

aaagatacct acgacgccct gcatatgcag gcgctgccgc cgcgc 2985

<210> 832
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 832
Gly Asp Ser Met Leu Ser Asn Ser Asp
1 5

<210> 833
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 833
Tyr His Arg Ser Thr Trp Tyr
1 5

<210> 834
<211> 10

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 834
Gly Asp Ser Met Leu Ser Asn Ser Asp Thr
1 5 10

<210> 835
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 835
Thr Tyr His Arg Ser Thr Trp Tyr Asp
1 5

<210> 836
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 836
Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp
1 5 10 15

Val

<210> 837
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 837
Gly Val Ser Leu Pro Asp Tyr Gly Val Ser
1 5 10

<210> 838
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 838
Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys Ser
1 5 10 15

<210> 839
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 839
Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys Ser
1 5 10 15

<210> 840
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 840
gaaattgtga tgacccagtc acccgccact cttagccttt cacccggtga gcgcgcaacc 60

ctgtcttgca gagcctccca agacatctca aaatacctta attggtatca acagaagccc 120

ggacaggctc ctcgccttct gatctaccac accagccggc tccattctgg aatccctgcc 180

aggttcagcg gtagcggatc tgggaccgac tacaccctca ctatcagctc actgcagcca 240

gaggacttcg ctgtctattt ctgtcagcaa gggaacaccc tgccctacac ctttggacag 300

ggcaccaagc tcgagattaa aggtggaggt ggcagcggag gaggtgggtc cggcggtgga 360

ggaagccagg tccaactcca agaaagcgga ccgggtcttg tgaagccatc agaaactctt 420

tcactgactt gtactgtgag cggagtgtct ctccccgatt acggggtgtc ttggatcaga 480

cagccaccgg ggaagggtct ggaatggatt ggagtgattt ggggctctga gactacttac 540

taccaatcat ccctcaagtc acgcgtcacc atctcaaagg acaactctaa gaatcaggtg 600

tcactgaaac tgtcatctgt gaccgcagcc gacaccgccg tgtactattg cgctaagcat 660

tactattatg gcgggagcta cgcaatggat tactggggac agggtactct ggtcaccgtg 720

tccagc 726

<210> 841
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 841
gagattgtca tgactcagtc cccggccaca ctctccctgt cacccggaga aagagcaacc 60

ctgagctgca gggcgtccca ggacatctcg aagtacctga actggtacca gcagaagcct 120

ggacaagcac cccgcctcct gatctaccac acctcgcggc tgcattcggg aatccccgcc 180

agattctcag ggagcggatc aggaaccgac tacaccctga ctatctcgag cctgcaacca 240

gaggatttcg ccgtgtactt ctgccagcaa ggaaacaccc tgccctacac ctttggacag 300

ggaaccaagc tcgagattaa gggggggtggt ggatcgggag ggggtggatc aggaggaggc 360

ggctcacaag tccagctgca agaatccggt ccgggacttg tgaagccgtc cgaaaccctg 420

tcactgactt gcactgtgtc cggggtgtca ttgcccgact acggcgtgag ctggattcgg 480

cagccccctg gaaagggatt ggaatggatc ggcgtgatct ggggttcgga aactacctac 540

tatcagtcct cactgaagtc ccgcgtgacc atcagcaagg ataattccaa aaaccaagtg 600

tctctgaagc tctccagcgt cactgccgcc gatactgccg tgtactactg cgccaagcac 660

tactattacg gcggttcgta cgccatggac tactggggcc aagggacact cgtgaccgtg 720

tcatcc 726

<210> 842
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 842
caagtccagc tgcaagaatc cggtccggga cttgtgaagc cgtccgaaac cctgtcactg 60

acttgcactg tgtccggggt gtcattgccc gactacggcg tgagctggat tcggcagccc 120

cctggaaagg gattggaatg gatcggcgtg atctggggtt cggaaactac ctactatcag 180

tcctcactga agtcccgcgt gaccatcagc aaggataatt ccaaaaacca agtgtctctg 240

aagctctcca gcgtcactgc cgccgatact gccgtgtact actgcgccaa gcactactat 300

tacggcggtt cgtacgccat ggactactgg ggacaaggca ctcttgtgac tgtgtcaagc 360

ggcggtggag ggagcggtgg gggcggttca ggaggaggcg gatcagagat cgtgatgacc 420

caatccccag ccaccctgtc cctcagccct ggagaaagag ccaccctgag ctgccgggcc 480

tcccaggata tcagcaagta cttgaactgg taccaacaaa agccggggca ggcgccccgg 540

ctcctgatct accacacctc gcgcctccac tcaggtatcc ccgccagatt ctcagggagc 600

ggctccggta ctgactacac cctgactatt tcctcactgc agccagagga ctttgccgtg 660

tacttctgcc agcagggaaa cactctgccg tacaccttcg ggcagggaac gaagcttgaa 720

attaag 726

<210> 843
<211> 242
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 843
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1   5   10   15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
            20   25   30

Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
        35   40   45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys
    50   55   60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu
65   70   75   80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
                85   90   95

Lys His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln
            100   105   110

Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
        115   120   125

Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala
    130   135   140

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
145   150   155   160

Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly
                165   170   175

Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly
            180   185   190

Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu
        195   200   205

Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln

210 215 220

Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu
225 230 235 240

Ile Lys

<210> 844
<211> 726
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 844
gagattgtga tgactcagag cccggcgacc ctgtccctgt cccccgggga gagagcaacc 60

ctgtcgtgcc gggcctccca agacatctca aagtacctca attggtatca gcagaagcca 120

ggacaggctc cacggttgct gatctaccac acttcgagac tgcactcagg aatccccgcg 180

cggttttccg gttccggctc cgggaccgac tacaccctga ccatcagctc gctccagcct 240

gaggatttcg cagtgtactt ctgtcagcaa ggaaacaccc ttccatacac cttcggacag 300

ggtaccaagc tggaaatcaa gggaggagga ggatctgggg gcggtggttc cggaggcggt 360

ggaagccaag tgcagctcca ggaaagcgga cccgggctgg tcaagccgag cgaaaccctc 420

tcactgactt gtactgtgtc cggagtgtcc ctgcctgact atggagtgtc ctggatccga 480

cagccccccg gaaagggtct ggagtggatt ggggtcatct ggggctccga aactacctac 540

taccagagca gcctcaagag ccgggtcacc atttcaaagg ataactccaa gaatcaagtg 600

tccctgaagc tgtcctcagt gacagccgca gacaccgccg tgtactactg cgccaagcac 660

tactactacg gaggctccta cgcaatggac tactggggac aaggcacttt ggtcactgtg 720

tcaagc 726

<210> 845
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 845
gaagtgcagc tgcagcagtc agggcctggc ctggtcaagc cgtcgcagac cctctccctg 60

acatgcgcca ttagcgggga ctccatgctg agcaactcgg acacctggaa ctggattcgg 120

cagtcccctt cccggggact cgagtggctc ggacgcacct accatcggag cacttggtac 180

gacgactacg cctcctccgt gagaggtcgc gtgtcgatca acgtggatac ctcgaagaac 240

cagtatagct tgcaactgaa cgccgtgacc cctgaggata ccggagtgta ctattgtgcg 300

agagtcaggc tgcaagacgg aaactcctgg tccgacgcat ttgatgtctg gggacagggt 360

actatggtca cggtgtcatc tggaggcgga ggatcgcaaa gcgccctgac tcagccggct 420

tcggctagcg gttcaccggg gcagtccgtg actatctcct gcaccgggac ttcctccgac 480

gtgggaggct acaattacgt gtcctggtac cagcaacacc ccggcaaagc cccaaagctg 540

atgatctacg acgtcagcaa cagacccagc ggagtgtcca accggttcag cggctccaag 600

tccggcaaca ccgcctccct gaccatcagc gggcttcagg ccgaagatga ggcggattac 660

tactgctcct cgtacacctc aagctcaact ctgtacgtgt tcggcaccgg tactcagctc 720

accgtgctg 729

<210> 846
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 846
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Met Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

```
Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
    50                  55                  60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65                  70                  75                  80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
                85                  90                  95

Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
            100                 105                 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gln Ser Ala Leu Thr Gln Pro Ala Ser Ala Ser Gly
    130                 135                 140

Ser Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp
145                 150                 155                 160

Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys
                165                 170                 175

Ala Pro Lys Leu Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val
            180                 185                 190

Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr
        195                 200                 205

Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser
    210                 215                 220

Tyr Thr Ser Ser Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Gln Leu
225                 230                 235                 240

Thr Val Leu
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<210> 847
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 847
gaagtgcagc tgcagcagtc aggaccgggc ctggtcaaac cttcgcagac tctgtccctg 60

acttgcgcta taagcgggga ctccatgctg agcaattcgg acacttggaa ctggattcgc 120

caaagcccca gccggggtct ggaatggctg ggaaggacct accatcgctc tacttggtac 180

gacgactacg ccagctccgt gcgaggacgc gtgtccatca acgtggacac ctccaagaac 240

cagtactcgc ttcaactcaa cgcagtgacc cctgaagata ccggagtcta ctattgcgcc 300

cgcgtgcggc tccaggacgg gaactcctgg tcggacgctt tcgatgtctg gggacagggc 360

actatggtca ccgtcagctc cggcggcggc ggtagccaat cggcgctgac acagccggct 420

tccgcctcgg gatcgcctgg acagtcggtg accatctcgt gcactggaac ctcctccgac 480

gtgggcggct acaattatgt gtcatggtac cagcagcacc cgggaaaggc ccctaagctg 540

atgatctacg acgtgtccaa tagacctagc ggggtgtcaa acagattctc cggatccaaa 600

tccggaaaca ctgcctccct gaccatttcc ggactgcagg ccgaggacga agccgattac 660

tactgctcct cttacacctc ctcatccacc ctctacgtgt ttgggactgg gacccagctg 720

accgtcctc 729

<210> 848
<211> 759
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 848
gaagtgcagc ttcaacaatc aggaccagga ctcgtcaaac catcacagac cctctccctc 60

acatgtgcca tctccgggga ctccatgttg agcaattccg acacttggaa ttggattaga 120

caaagcccgt cccggggtct ggaatggttg ggacgcacct accaccggtc tacttggtac 180

gacgactacg cgtcatccgt gcggggaaga gtgtccatca acgtggacac ctccaagaac 240

cagtacagcc tgcagcttaa tgccgtgact cctgaggata cgggcgtcta ctactgcgcc 300

cgcgtccgcc tgcaagacgg gaacagctgg agcgatgcat tcgatgtctg gggccaggga 360

actatggtca ccgtgtcgtc tgggggcggt ggatcgggtg gcgggggttc gggggcggc 420

ggctctcagt ccgctcttac ccaaccggcc tcagcctcgg ggagccccgg ccagagcgtg 480

accatttcct gcaccggcac ttcatccgac gtgggcggct acaactacgt gtcctggtac 540

caacagcacc cgggaaaggc ccccaagctc atgatctacg acgtgtccaa caggccctcg 600

ggagtgtcca accggttctc gggttcgaaa tcgggaaaca cagccagcct gaccatcagc 660

ggactgcagg ctgaagatga agccgactac tactgctcct cctacacctc gtcatccacg 720

ctctacgtgt tcggcactgg aactcagctg actgtgctg 759

<210> 849
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 849
cagtccgctc ttacccaacc ggcctcagcc tcggggagcc ccggccagag cgtgaccatt 60

tcctgcaccg gcacttcatc cgacgtgggc ggctacaact acgtgtcctg gtaccaacag 120

cacccgggaa aggcccccaa gctcatgatc tacgacgtgt ccaacaggcc ctcgggagtg 180

tccaaccggt tctcgggttc gaaatcggga aacacagcca gcctgaccat cagcggactg 240

caggctgaag atgaagccga ctactactgc tcctcctaca cctcgtcatc cacgctctac 300

gtgttcggca ctggaactca gctgactgtg ctgggcggag gaggctccga agtgcagctt 360

caacaatcag gaccaggact cgtcaaacca tcacagaccc tctccctcac atgtgccatc 420

tccggggact ccatgttgag caattccgac acttggaatt ggattagaca aagcccgtcc 480

cggggtctgg aatggttggg acgcacctac caccggtcta cttggtacga cgactacgcg 540

tcatccgtgc ggggaagagt gtccatcaac gtggacacct ccaagaacca gtacagcctg 600

cagcttaatg ccgtgactcc tgaggatacg ggcgtctact actgcgcccg cgtccgcctg 660

caagacggga acagctggag cgatgcattc gatgtctggg gccagggaac tatggtcacc 720

gtgtcgtct 729

<210> 850
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 850
Gln Ser Ala Leu Thr Gln Pro Ala Ser Ala Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Gln Leu Thr Val Leu Gly
100 105 110

Gly Gly Gly Ser Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val
115 120 125

Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser
130 135 140

Met Leu Ser Asn Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser

145 150 155 160

Arg Gly Leu Glu Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr
165 170 175

Asp Asp Tyr Ala Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp
180 185 190

Thr Ser Lys Asn Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu
195 200 205

Asp Thr Gly Val Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly Asn
210 215 220

Ser Trp Ser Asp Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr
225 230 235 240

Val Ser Ser

<210> 851
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 851
cagtccgctc tgactcagcc ggcctcagct tcggggtccc ctggtcaaag cgtcactatt 60

tcctgtaccg gaacctcatc agacgtgggc ggctacaatt acgtgtcctg gtaccaacag 120

caccccggaa aggctcctaa gcttatgatc tacgacgtgt ccaaccggcc gtcaggagtg 180

tccaacagat tctccggctc caagagcgga aacactgcca gcttgaccat tagcggcttg 240

caggccgagg acgaagccga ctactactgc tctagctaca catcctcgtc taccctctac 300

gtgtttggaa cggggaccca gctgactgtg ctcgggggtg gaggatcaga ggtgcaactc 360

cagcagtccg gtcctggcct cgtgaaaccg tcccaaaccc tgtccctgac ttgcgccatc 420

tcgggcgact ccatgctgtc caattccgac acctggaact ggattagaca atcgcctagc 480

cggggactcg aatggctggg ccggacctac caccggtcca cgtggtatga cgactacgca 540

agctccgtcc ggggaagggt gtccattaac gtcgatacct ccaagaacca gtacagcctt 600

cagctgaacg ctgtgacccc cgaggatacc ggcgtctact actgtgcaag agtgcgattg 660

caggatggaa actcgtggtc ggacgcattc gatgtctggg gacagggaac tatggtgacc 720

gtgtcctcg 729

<210> 852
<211> 729
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 852
cagtccgctc tgactcagcc ggcctcagct tcggggtccc ctggtcaaag cgtcactatt 60

tcctgtaccg gaacctcatc agacgtgggc ggctacaatt acgtgtcctg gtaccaacag 120

caccccggaa aggctcctaa gcttatgatc tacgacgtgt ccaaccggcc gtcaggagtg 180

tccaacagat tctccggctc caagagcgga aacactgcca gcttgaccat tagcggcttg 240

caggccgagg acgaagccga ctactactgc tctagctaca catcctcgtc taccctctac 300

gtgtttggaa cggggaccca gctgactgtg ctcgggggtg gaggatcaga ggtgcaactc 360

cagcagtccg gtcctggcct cgtgaaaccg tcccaaaccc tgtccctgac ttgcgccatc 420

tcgggcgact ccatgctgtc caattccgac acctggaact ggattagaca atcgcctagc 480

cggggactcg aatggctggg ccggacctac caccggtcca cgtggtatga cgactacgca 540

agctccgtcc ggggaagggt gtccattaac gtcgatacct ccaagaacca gtacagcctt 600

cagctgaacg ctgtgacccc cgaggatacc ggcgtctact actgtgcaag agtgcgattg 660

caggatggaa actcgtggtc ggacgcattc gatgtctggg gacagggaac tatggtcact 720

gtgtcctcc 729

<210> 853
<211> 63
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 853
atggccctcc ctgtcaccgc cctgctgctt ccgctggctc ttctgctcca cgccgctcgg 60

ccc 63

<210> 854
<211> 63
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 854
atggccctgc ccgtgactgc gctcctgctt ccgttggccc tgctcctgca tgccgccaga 60

cct 63

<210> 855
<211> 63
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 855
atggccttac cagtgaccgc cttgctcctg ccgctggcct tgctgctcca cgccgccagg 60

ccg 63

<210> 856
<211> 63
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 856

atggcacttc ccgtcaccgc cctgctgctc ccactcgccc tccttctgca cgccgcccgc 60

ccc 63

<210> 857
<211> 63
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 857
atggccctgc cagtgaccgc gctcctgctg cccctggctc tgctgcttca cgcggcccgg 60

cct 63

<210> 858
<211> 207
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 858
accactaccc cagcaccgag gccacccacc ccggctccta ccatcgcctc ccagcctctg 60

tccctgcgtc cggaggcatg tagacccgca gctggtgggg ccgtgcatac ccggggtctt 120

gacttcgcct gcgatatcta catttgggcc cctctggctg gtacttgcgg ggtcctgctg 180

ctttcactcg tgatcactct ttactgt 207

<210> 859
<211> 207
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 859
actaccaccc cggccccgcg gccccctaca ccggcaccga ctattgccag ccagcctctc 60

tcgctgcggc cggaggcctg ccgcccagcc gccggcggag ccgtgcacac ccgcggtctg 120

gacttcgcgt gcgatatcta catctgggct ccgctggccg ggacttgtgg cgtgctgctg 180

ctgtctctgg tcatcacact gtactgc 207

<210> 860
<211> 207
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 860
accacgacgc cagcgccgcg accaccaaca ccggcgccca ccatcgcgtc gcagcccctg 60

tccctgcgcc cagaggcgtg ccggccagcg gcgggggggcg cagtgcacac gagggggctg 120

gacttcgcct gtgatatcta catctgggcg cccttggccg ggacttgtgg ggtccttctc 180

ctgtcactgg ttatcaccct ttactgc 207

<210> 861
<211> 207
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polynucleotide"

<400> 861
accaccaccc ctgcgcctcg gcctcctacc ccggctccca ctatcgcgag ccagccgctg 60

agcctgcggc ctgaggcttg ccgaccggcc gctggcggcg ccgtgcatac tcggggcctc 120

gactttgcct gtgacatcta catctgggcc cccctggccg gaacgtgcgg agtgctgctg 180

ctgtcgctgg tcattaccct gtattgc 207

<210> 862
<211> 126
<212> DNA
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 862
aagcgcggtc ggaagaagct gctgtacatc tttaagcaac ccttcatgag gcctgtgcag 60

actactcaag aggaggacgg ctgttcatgc cggttcccag aggaggagga aggcggctgc 120

gaactg 126

<210> 863
<211> 126
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 863
aagcgcggaa gaaagaagct gctctacatc ttcaagcaac ccttcatgcg gcctgtgcag 60

accacccagg aagaggatgg ctgctcctgc cggttcccgg aggaagaaga gggcggatgc 120

gaactg 126

<210> 864
<211> 126
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 864
aaacgcggaa ggaagaagct gttgtacatt ttcaagcagc ccttcatgcg cccggtgcaa 60

actactcagg aggaagatgg ctgttcctgt cggttccccg aagaggaaga aggcggctgc 120

gagttg 126

<210> 865
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 865
cgcgtgaaat tcagccgcag cgcagatgct ccagcctacc agcaggggca gaaccagctc 60

tacaacgaac tcaatcttgg tcggagagag gagtacgacg tgctggacaa gcggagagga 120

cgggacccag aaatgggcgg gaagccgcgc agaaagaatc cccaagaggg cctgtacaac 180

gagctccaaa aggataagat ggcagaagcc tatagcgaga ttggtatgaa aggggaacgc 240

agaagaggca aaggccacga cggactgtac cagggactca gcaccgccac caaggacacc 300

tatgacgctc ttcacatgca ggccctgccg cctcgg 336

<210> 866
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 866
cgcgtgaagt tcagccgaag cgccgacgcc ccggcctacc agcagggcca gaaccaactg 60

tacaacgaac tcaacctggg tcggagagaa gagtacgacg tgctggacaa aagacgcggc 120

agggaccccg agatgggcgg aaagcctcgc cgcaagaacc cgcaggaggg cctctacaac 180

gagctgcaga aggacaagat ggccgaagcc tactcagaga tcggcatgaa gggggagcgg 240

aggcgcggga agggccacga cggtttgtac caaggacttt ccactgcgac caaggacacc 300

tacgatgccc tccatatgca agccctgccg ccccgg 336

<210> 867
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polynucleotide"

<400> 867
agggtcaagt tctcccggtc cgccgatgct cccgcctacc aacaggggca gaaccagctt 60

tataacgaac tgaacctggg caggagggag gaatatgatg tgttggataa gcgccggggc 120

cgggacccag aaatgggggg aaagcccaga agaaagaacc ctcaagaggg actttacaac 180

gaattgcaga aagacaaaat ggccgaggcc tactccgaga ttgggatgaa gggcgaaaga 240

cggagaggaa aggggcacga cgggctctac cagggactca gcaccgccac caaagatacc 300

tacgacgccc tgcatatgca ggcgctgccg ccgcgc 336

<210> 868
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 868
ttggcagaag ccgccgcgaa a 21

<210> 869
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 869
Leu Ala Glu Ala Ala Ala Lys
1 5

<210> 870
<211> 45
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 870
ggtggaggtg gcagcggagg aggtgggtcc ggcggtggag gaagc 45

<210> 871
<211> 45
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 871
ggcggaggcg ggagcggagg aggaggctct ggcggaggag gaagc 45

<210> 872
<211> 45
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 872
ggcggtggag gctcgggggg gggcggctca ggaggaggcg gctca 45

<210> 873
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
oligonucleotide"

<400> 873
ggaagcggag ctactaactt cagcctgctg aagcaggctg gagacgtgga ggagaaccct 60

ggacct 66

<210> 874
<211> 22
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 874
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> 875
<211> 66
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      oligonucleotide"

<400> 875
ggttccggag ctaccaactt ctcgctgttg aagcaggccg gagatgtcga ggaaaacccg   60

ggacct   66

<210> 876
<211> 15
<212> DNA
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      oligonucleotide"

<400> 876
ggtggaggtg gcagc   15

<210> 877
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 877
Gly Gly Gly Gly Ser
1   5

<210> 878
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 878
Gly Ser Ser Ser Ser Gly Ser Ser Ser Ser Gly Ser Ser Ser Ser
1 5 10 15

<210> 879
<211> 217
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 879
Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
1 5 10 15

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
20 25 30

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
35 40 45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
50 55 60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65 70 75 80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
85 90 95

Ala Leu Ala Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
100 105 110

```
Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
        115                 120                 125


Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    130                 135                 140


Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
145                 150                 155                 160


Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
                165                 170                 175


Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
            180                 185                 190


Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
        195                 200                 205


Lys Ser Leu Ser Leu Ser Pro Gly Lys
    210                 215


<210> 880
<211> 217
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 880
Ala Pro Glu Ala Ala Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys
1               5                   10                  15


Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            20                  25                  30


Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
        35                  40                  45


Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    50                  55                  60
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Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65                  70                  75                  80


Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                85                  90                  95


Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
            100                 105                 110


Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
        115                 120                 125


Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    130                 135                 140


Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
145                 150                 155                 160


Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
                165                 170                 175


Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
            180                 185                 190


Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
        195                 200                 205


Lys Ser Leu Ser Leu Ser Pro Gly Lys
    210                 215


<210> 881
<211> 217
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 881
Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
1               5                   10                  15
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Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            20                  25                  30

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
        35                  40                  45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    50                  55                  60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65                  70                  75                  80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                85                  90                  95

Ala Leu Gly Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
            100                 105                 110

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
        115                 120                 125

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    130                 135                 140

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
145                 150                 155                 160

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
                165                 170                 175

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
            180                 185                 190

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
        195                 200                 205

Lys Ser Leu Ser Leu Ser Pro Gly Lys
    210                 215
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<210> 882
<211> 227
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 882
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

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 Gly 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 Arg Glu Glu Met 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> 883
<211> 217
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 883
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
1   5   10   15

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            20   25   30

Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
        35   40   45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    50   55   60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65   70   75   80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                85   90   95

Ala Leu Ala Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
            100   105   110

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
        115   120   125

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    130   135   140

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
145   150   155   160

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
                165   170   175

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
            180   185   190

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
        195   200   205

Lys Ser Leu Ser Leu Ser Pro Gly Lys
    210   215

<210> 884
<211> 227
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 884
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 Ala 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 Ala 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> 885
<211> 217
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 885
Ala Pro Glu Ala Ala Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
1 5 10 15

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
20 25 30

Val Val Asp Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
35 40 45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
50 55 60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65 70 75 80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
85 90 95

Ala Leu Ala Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
100 105 110

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
115 120 125

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
130 135 140

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
145 150 155 160

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
165 170 175

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
180 185 190

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
195 200 205

Lys Ser Leu Ser Leu Ser Pro Gly Lys
210 215

<210> 886
<211> 227
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 886
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 Lys 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 Ala 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> 887
<211> 217
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 887
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
1 5 10 15

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
20 25 30

Val Val Ala Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
35 40 45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
50 55 60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65 70 75 80

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Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                85                  90                  95


Ala Leu Ala Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
            100                 105                 110


Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
        115                 120                 125


Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    130                 135                 140


Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
145                 150                 155                 160


Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
                165                 170                 175


Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
            180                 185                 190


Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
        195                 200                 205


Lys Ser Leu Ser Leu Ser Pro Gly Lys
    210                 215


<210> 888
<211> 217
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 888
Ala Pro Glu Leu Leu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys
1               5                   10                  15


Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            20                  25                  30
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Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
        35                  40                  45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    50                  55                  60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65                  70                  75                  80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                85                  90                  95

Ala Leu Ala Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
            100                 105                 110

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
        115                 120                 125

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    130                 135                 140

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
145                 150                 155                 160

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
                165                 170                 175

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
            180                 185                 190

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
        195                 200                 205

Lys Ser Leu Ser Leu Ser Pro Gly Lys
    210                 215
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<210> 889
<211> 217
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 889
Ala Pro Glu Leu Leu Gly Ala Pro Ser Val Phe Leu Phe Pro Pro Lys
1 5 10 15

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
20 25 30

Val Val Ala Val Lys His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
35 40 45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
50 55 60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65 70 75 80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
85 90 95

Ala Leu Ala Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
100 105 110

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
115 120 125

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
130 135 140

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
145 150 155 160

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
165 170 175

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
180 185 190

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
195 200 205

Lys Ser Leu Ser Leu Ser Pro Gly Lys
210 215

<210> 890
<211> 227
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 890
Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
1 5 10 15

Ala 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 Ala Val Lys 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 Ala 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 Arg Glu Glu Met 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> 891
<211> 217
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 891
Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
1               5                   10                  15


Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
            20                  25                  30


Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
        35                  40                  45


Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
    50                  55                  60


Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65                  70                  75                  80
```

```
Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
                85                  90                  95


Ala Leu Ala Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
            100                 105                 110


Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
        115                 120                 125


Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
    130                 135                 140


Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
145                 150                 155                 160


Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
                165                 170                 175


Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
            180                 185                 190


Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
        195                 200                 205


Lys Ser Leu Ser Leu Ser Pro Gly Lys
    210                 215


<210> 892
<211> 226
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 892
Asp Ile Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1               5                   10                  15


Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Val Ser Asn
```

```
            20                  25                  30

Tyr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
        35                  40                  45

Ile Tyr Asp Asn Asn Lys Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
    50                  55                  60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln
65                  70                  75                  80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Ala Ile Gly Ser
                85                  90                  95

Tyr Ser Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gln
            100                 105                 110

Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe
        115                 120                 125

Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val
    130                 135                 140

Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
145                 150                 155                 160

Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr
                165                 170                 175

Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr
            180                 185                 190

Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val
        195                 200                 205

Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe Asn Arg Gly
    210                 215                 220

Glu Cys
225
```

<210> 893
<211> 723
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 893
Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Phe Tyr Thr Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ile Gly Tyr Ala Gly Asp Ser Lys Tyr Ala Ile Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

```
Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380
```

```
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    450                 455                 460

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
465                 470                 475                 480

Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe
                485                 490                 495

Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys
            500                 505                 510

Cys Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala
        515                 520                 525

Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp
    530                 535                 540

Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu
545                 550                 555                 560

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser
                565                 570                 575

Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
            580                 585                 590

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        595                 600                 605
```

Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu
610 615 620

Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr
625 630 635 640

Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro
645 650 655

Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro
660 665 670

Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala
675 680 685

Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys
690 695 700

Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Cys Gly Thr Lys Leu
705 710 715 720

Thr Val Leu

<210> 894
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 894
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys His Ala Ser Gln Asn Ile Tyr Val Trp
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile

```
        35                  40                  45

Tyr Lys Ala Ser Asn Leu His Thr Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Gly Gln Thr Tyr Pro Tyr
                85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala
            100                 105                 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
        115                 120                 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala
    130                 135                 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln
145                 150                 155                 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser
                165                 170                 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr
            180                 185                 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
        195                 200                 205

Phe Asn Arg Gly Glu Cys
    210
```

<210> 895
<211> 702
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 895

```
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45


Gly Cys Ile Tyr Pro Gly Asn Val Asn Thr Asn Tyr Asn Glu Lys Phe
    50                  55                  60


Lys Asp Arg Ala Thr Leu Thr Val Asp Thr Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Phe Cys
                85                  90                  95


Thr Arg Ser His Tyr Gly Leu Asp Trp Asn Phe Asp Val Trp Gly Gln
            100                 105                 110


Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125


Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
    130                 135                 140


Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160


Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175


Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190


Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205
```

```
Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415
```

```
Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Gly Gly Ser Glu Val Lys Leu Val Glu Ser Gly Gly Asp Leu Val
    450                 455                 460

Gln Pro Gly Asp Ser Leu Thr Leu Ser Cys Val Ala Ser Gly Phe Thr
465                 470                 475                 480

Phe Ser Lys Gln Gly Met His Trp Ile Arg Gln Ala Pro Lys Lys Gly
                485                 490                 495

Leu Glu Trp Ile Ala Met Ile Tyr Tyr Asp Ser Ser Lys Met Tyr Tyr
            500                 505                 510

Ala Asp Thr Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
        515                 520                 525

Asn Thr Leu Tyr Leu Glu Met Asn Ser Leu Arg Ser Glu Asp Thr Ala
    530                 535                 540

Met Tyr Tyr Cys Ala Ser Phe Trp Trp Asp Leu Asp Phe Asp His Trp
545                 550                 555                 560

Gly Gln Gly Val Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
                565                 570                 575

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
            580                 585                 590

Leu Val Thr Gln Thr Pro Val Ser Leu Pro Val Ser Leu Gly Gly His
        595                 600                 605

Val Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Arg Ser Glu Gly
    610                 615                 620

Thr Thr Tyr Phe Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln
625                 630                 635                 640
```

Leu Leu Ile Tyr Arg Val Ser Asn Arg Phe Ser Gly Val Pro Asp Arg
645 650 655

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg
660 665 670

Val Glu Pro Glu Asp Leu Gly Val Tyr Tyr Cys Leu Gln Ser Ser His
675 680 685

Phe Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys
690 695 700

<210> 896
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 896
Asn Tyr Asn Leu His
1 5

<210> 897
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 897
Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 898
<211> 13

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 898
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10

<210> 899
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 899
Gly Tyr Thr Phe Thr Asn Tyr
1 5

<210> 900
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 900
Tyr Pro Gly Asn Tyr Asp
1 5

<210> 901
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 901

Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1   5   10

<210> 902

<400> 902
000

<210> 903
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 903
Gly Tyr Thr Phe Thr Asn Tyr Asn
1   5

<210> 904
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 904
Ile Tyr Pro Gly Asn Tyr Asp Thr
1   5

<210> 905
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 905
Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1   5   10   15

<210> 906
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 906
Gly Tyr Thr Phe Thr Asn Tyr Asn Leu His
1 5 10

<210> 907
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 907
Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 908
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 908
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10

<210> 909
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 909
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 910
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 910
Arg Ala Thr Ser Ser Val Ser Ser Met Asn
1 5 10

<210> 911
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 911
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 912
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 912
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 913
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 913
Thr Ser Ser Val Ser Ser
1 5

<210> 914
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 914
Ala Thr Ser
1

<210> 915
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 915
Trp Thr Phe Asn Pro Pro
1 5

<210> 916
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 916
Ser Ser Val Ser Ser
1 5

<210> 917
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 917
Ala Thr Ser
1

<210> 918
<211> 9
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 918
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 919
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 919
Arg Ala Thr Ser Ser Val Ser Ser Met Asn
1 5 10

<210> 920
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 920
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 921
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 921
Gln Gln Trp Thr Phe Asn Pro Pro Thr

1 5

<210> 922
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 922
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Thr Ser Ser Val Ser Ser Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro Leu Ile His
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
65 70 75 80

Asp Ala Ala Val Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr
85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 923
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 923
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala

```
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20                  25                  30

Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
    130                 135                 140

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
145                 150                 155                 160

Ala Thr Leu Ser Cys Arg Ala Thr Ser Ser Val Ser Ser Met Asn Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro Leu Ile His Ala Thr
            180                 185                 190

Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Ala
    210                 215                 220
```

Ala Val Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr Phe Gly
225 230 235 240

Gln Gly Thr Lys Leu Glu Ile Lys
245

<210> 924
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 924
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Asn Tyr Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser
65 70 75 80

Tyr Asn Gln Lys Phe Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser
85 90 95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp
115 120 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
130 135 140

```
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu
                165                 170                 175

Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Thr Ser Ser Val
            180                 185                 190

Ser Ser Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro
        195                 200                 205

Leu Ile His Ala Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240

Glu Pro Glu Asp Ala Ala Val Tyr Tyr Cys Gln Gln Trp Thr Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350
```

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Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365


Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380


Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385                 390                 395                 400


Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415


Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430


Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445


Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460


Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465                 470                 475                 480


Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 925
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 925
Asn Tyr Asn Leu His
1               5


<210> 926
<211> 17
<212> PRT
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<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 926
Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 927
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 927
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10

<210> 928
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 928
Gly Tyr Thr Phe Thr Asn Tyr
1 5

<210> 929
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 929
Tyr Pro Gly Asn Tyr Asp
1 5

<210> 930
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 930
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10

<210> 931
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 931
Gly Tyr Thr Phe Thr Asn Tyr Asn
1 5

<210> 932
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 932
Ile Tyr Pro Gly Asn Tyr Asp Thr
1 5

<210> 933
<211> 15

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 933
Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10 15

<210> 934
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 934
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 935
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 935
Arg Ala Thr Ser Ser Val Ser Ser Met Asn
1 5 10

<210> 936
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 936
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 937
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 937
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 938
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 938
Thr Ser Ser Val Ser Ser
1 5

<210> 939
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 939
Ala Thr Ser
1

<210> 940
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 940
Trp Thr Phe Asn Pro Pro
1 5

<210> 941
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 941
Ser Ser Val Ser Ser
1 5

<210> 942

<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 942
Ala Thr Ser
1

<210> 943
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 943
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 944
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 944
Arg Ala Thr Ser Ser Val Ser Ser Met Asn
1 5 10

<210> 945
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 945
Ala Thr Ser Asn Leu Ala Ser
1   5

<210> 946
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 946
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1   5

<210> 947
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 947
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1   5   10   15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Thr Ser Ser Val Ser Ser Met
            20   25   30

Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro Leu Ile His
        35   40   45

Ala Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser
    50   55   60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
65   70   75   80

Asp Ala Ala Val Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr
                85   90   95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 948
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 948
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
130 135 140

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
145 150 155 160

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Ala Thr Leu Ser Cys Arg Ala Thr Ser Ser Val Ser Ser Met Asn Trp
                165                 170                 175


Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro Leu Ile His Ala Thr
            180                 185                 190


Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205


Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Ala
    210                 215                 220


Ala Val Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr Phe Gly
225                 230                 235                 240


Gln Gly Thr Lys Leu Glu Ile Lys
                245


<210> 949
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 949
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30


Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45


Thr Phe Thr Asn Tyr Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60


Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser
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65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser
                85                  90                  95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp
        115                 120                 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu
                165                 170                 175

Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Thr Ser Ser Val
            180                 185                 190

Ser Ser Met Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro
        195                 200                 205

Leu Ile His Ala Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240

Glu Pro Glu Asp Ala Ala Val Tyr Tyr Cys Gln Gln Trp Thr Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285
```

```
Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465                 470                 475                 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490
```

<210> 950

<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 950
Asn Tyr Asn Leu His
1 5

<210> 951
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 951
Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1 5 10 15

Gly

<210> 952
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 952
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10

<210> 953
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 953
Gly Tyr Thr Phe Thr Asn Tyr
1 5

<210> 954
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 954
Tyr Pro Gly Asn Tyr Asp
1 5

<210> 955
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 955
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10

<210> 956
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 956
Gly Tyr Thr Phe Thr Asn Tyr Asn
1 5

<210> 957
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 957
Ile Tyr Pro Gly Asn Tyr Asp Thr
1 5

<210> 958
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 958
Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1 5 10 15

<210> 959
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 959
Gly Tyr Thr Phe Thr Asn Tyr Asn Leu His
1 5 10

<210> 960
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 960
Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe Lys
1   5   10   15

Gly

<210> 961
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 961
Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val
1   5   10

<210> 962
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 962
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1   5   10   15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20   25   30

Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35   40   45

Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe
    50   55   60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65   70   75   80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 963
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 963
Arg Ala Thr Ser Ser Val Ser Ser Met Asn
1 5 10

<210> 964
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 964
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 965
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 965
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1   5

<210> 966
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 966
Thr Ser Ser Val Ser Ser
1   5

<210> 967
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 967
Ala Thr Ser
1

<210> 968
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 968
Trp Thr Phe Asn Pro Pro
1   5

<210> 969
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 969
Ser Ser Val Ser Ser
1 5

<210> 970
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 970
Ala Thr Ser
1

<210> 971
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 971
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 972
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 972
Arg Ala Thr Ser Ser Val Ser Ser Met Asn
1 5 10

<210> 973
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 973
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 974
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 974
Gln Gln Trp Thr Phe Asn Pro Pro Thr
1 5

<210> 975
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 975
Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Thr Ser Ser Val Ser Ser Met
20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile His
35 40 45

```
Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    50                  55                  60


Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65                  70                  75                  80


Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr
                85                  90                  95


Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
            100                 105


<210> 976
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 976
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20                  25                  30


Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe
    50                  55                  60


Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val Trp
            100                 105                 110
```

```
Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125


Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140


Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160


Val Thr Ile Thr Cys Arg Ala Thr Ser Ser Val Ser Ser Met Asn Trp
                165                 170                 175


Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile His Ala Thr
            180                 185                 190


Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205


Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220


Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr Phe Gly
225                 230                 235                 240


Gln Gly Thr Lys Leu Glu Ile Lys
                245


<210> 977
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 977
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
```

```
            20                  25                  30

Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45

Thr Phe Thr Asn Tyr Asn Leu His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser
                85                  90                  95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp
        115                 120                 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala
                165                 170                 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Thr Ser Ser Val
            180                 185                 190

Ser Ser Met Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro
        195                 200                 205

Leu Ile His Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240
```

```
Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
```

450 455 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465 470 475 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 978
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 978
Asn Tyr Trp Met His
1 5

<210> 979
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 979
Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 980
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 980
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1   5   10

<210> 981
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 981
Gly Tyr Thr Phe Thr Asn Tyr
1   5

<210> 982
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 982
Thr Pro Thr Thr Gly Tyr
1   5

<210> 983
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 983
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1   5   10

<210> 984
<211> 8
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 984
Gly Tyr Thr Phe Thr Asn Tyr Trp
1 5

<210> 985
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 985
Ile Thr Pro Thr Thr Gly Tyr Pro
1 5

<210> 986
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 986
Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10 15

<210> 987
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 987
Gly Tyr Thr Phe Thr Asn Tyr Trp Met His

1 5 10

<210> 988
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 988
Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 989
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 989
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 990
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 990
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

```
Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
    50                  55                  60


Lys Asp Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
            100                 105                 110


Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210> 991
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 991
Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
1               5                   10


<210> 992
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 992
Asn Thr Lys Thr Leu Ala Asp
1               5
```

<210> 993
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 993
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 994
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 994
Ser Gly Asn Ile His Asn Tyr
1 5

<210> 995
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 995
Asn Thr Lys
1

<210> 996
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 996
Phe Trp Ser Ser Pro Trp
1 5

<210> 997
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 997
Gly Asn Ile His Asn Tyr
1 5

<210> 998
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 998
Asn Thr Lys
1

<210> 999
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 999
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1000

<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1000
Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
1 5 10

<210> 1001
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1001
Asn Thr Lys Thr Leu Ala Asp
1 5

<210> 1002
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1002
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1003
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1003
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45

Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Val Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1004
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1004
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
50 55 60

```
Lys Asp Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile Tyr Asn
            180                 185                 190

Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
        195                 200                 205

Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Val Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp Thr Phe
225                 230                 235                 240

Gly Gly Gly Thr Lys Val Glu Ile Lys
                245
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<210> 1005
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1005
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Asn Tyr Trp Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Ala Asp Lys Ser
85 90 95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr
115 120 125

Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145 150 155 160

Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
165 170 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile
180 185 190

```
His Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys
        195                 200                 205

Leu Leu Ile Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser
225                 230                 235                 240

Leu Gln Pro Glu Asp Val Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser
                245                 250                 255

Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
            340                 345                 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
        355                 360                 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
    370                 375                 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
385                 390                 395                 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
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405 410 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
420 425 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
435 440 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
450 455 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465 470 475 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1006
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1006
Asn Tyr Trp Met His
1 5

<210> 1007
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1007
Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 1008
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1008
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1009
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1009
Gly Tyr Thr Phe Thr Asn Tyr
1 5

<210> 1010
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1010
Thr Pro Thr Thr Gly Tyr
1 5

<210> 1011
<211> 13
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1011
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1012
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1012
Gly Tyr Thr Phe Thr Asn Tyr Trp
1 5

<210> 1013
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1013
Ile Thr Pro Thr Thr Gly Tyr Pro
1 5

<210> 1014
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1014
Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10 15

<210> 1015
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1015
Gly Tyr Thr Phe Thr Asn Tyr Trp Met His
1 5 10

<210> 1016
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1016
Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 1017
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1017
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1018
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1018
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1019
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1019
Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
1 5 10

<210> 1020

<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1020
Asn Thr Lys Thr Leu Ala Asp
1 5

<210> 1021
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1021
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1022
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1022
Ser Gly Asn Ile His Asn Tyr
1 5

<210> 1023
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1023
Asn Thr Lys
1

<210> 1024
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1024
Phe Trp Ser Ser Pro Trp
1 5

<210> 1025
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1025
Gly Asn Ile His Asn Tyr
1 5

<210> 1026
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1026
Asn Thr Lys
1

<210> 1027
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1027
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1028
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1028
Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
1 5 10

<210> 1029
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1029
Asn Thr Lys Thr Leu Ala Asp
1 5

<210> 1030
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1030
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1031
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1031
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45

Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Val Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1032
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1032
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

```
Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20                  25                  30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
    50                  55                  60

Lys Asp Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile Tyr Asn
            180                 185                 190

Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
        195                 200                 205

Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220
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Val Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp Thr Phe
225 230 235 240

Gly Gly Gly Thr Lys Val Glu Ile Lys
245

<210> 1033
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1033
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Asn Tyr Trp Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu
65 70 75 80

Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr Ala Asp Lys Ser
85 90 95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr
115 120 125

Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
130 135 140

```
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160


Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
                165                 170                 175


Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile
            180                 185                 190


His Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys
        195                 200                 205


Leu Leu Ile Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg
    210                 215                 220


Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser
225                 230                 235                 240


Leu Gln Pro Glu Asp Val Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser
                245                 250                 255


Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr
            260                 265                 270


Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285


Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300


Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320


Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335


Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
            340                 345                 350


Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
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        355                 360                 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
    370                 375                 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
385                 390                 395                 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
                405                 410                 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
            420                 425                 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
        435                 440                 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
    450                 455                 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465                 470                 475                 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 1034
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1034
Asn Tyr Trp Met His
1               5


<210> 1035
<211> 17
<212> PRT
<213> Artificial Sequence
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<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1035
Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 1036
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1036
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1037
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1037
Gly Tyr Thr Phe Thr Asn Tyr
1 5

<210> 1038
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1038
Thr Pro Thr Thr Gly Tyr
1 5

<210> 1039
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1039
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1040
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1040
Gly Tyr Thr Phe Thr Asn Tyr Trp
1 5

<210> 1041
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1041
Ile Thr Pro Thr Thr Gly Tyr Pro
1 5

<210> 1042
<211> 15
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1042
Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10 15

<210> 1043
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1043
Gly Tyr Thr Phe Thr Asn Tyr Trp Met His
1 5 10

<210> 1044
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1044
Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 1045
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 1045
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1046
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1046
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1047
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1047
Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
1 5 10

<210> 1048
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1048
Asn Thr Lys Thr Leu Ala Asp
1 5

<210> 1049
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1049
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1050
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1050
Ser Gly Asn Ile His Asn Tyr
1 5

<210> 1051
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1051
Asn Thr Lys
1

<210> 1052
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1052
Phe Trp Ser Ser Pro Trp
1 5

<210> 1053
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1053
Gly Asn Ile His Asn Tyr
1 5

<210> 1054
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1054
Asn Thr Lys
1

<210> 1055
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1055
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1056
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1056
Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
1 5 10

<210> 1057
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1057
Asn Thr Lys Thr Leu Ala Asp
1 5

<210> 1058

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1058
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1059
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1059
Ala Ile Arg Met Thr Gln Ser Pro Phe Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Ala Lys Ala Pro Lys Leu Phe Ile
35 40 45

Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1060

<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1060
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Met Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ile
130 135 140

Arg Met Thr Gln Ser Pro Phe Ser Leu Ser Ala Ser Val Gly Asp Arg
145 150 155 160

Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
165 170 175

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Trp Tyr Gln Gln Lys Pro Ala Lys Ala Pro Lys Leu Phe Ile Tyr Asn
            180                 185                 190


Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
        195                 200                 205


Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220


Phe Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp Thr Phe
225                 230                 235                 240


Gly Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 1061
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1061

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


His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30


Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45


Thr Phe Thr Asn Tyr Trp Met His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60


Gly Leu Glu Trp Met Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu
65                  70                  75                  80


Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Met Thr Ala Asp Lys Ser
                85                  90                  95
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Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr
        115                 120                 125

Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Ala Ile Arg Met Thr Gln Ser Pro Phe Ser Leu Ser Ala
                165                 170                 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile
            180                 185                 190

His Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Ala Lys Ala Pro Lys
        195                 200                 205

Leu Phe Ile Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser
225                 230                 235                 240

Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser
                245                 250                 255

Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
```

305 310 315 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
325 330 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
340 345 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
355 360 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
370 375 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
385 390 395 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
405 410 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
420 425 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
435 440 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
450 455 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465 470 475 480

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1062
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1062
Asn Tyr Trp Met His
1 5

<210> 1063
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1063
Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 1064
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1064
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1065
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1065
Gly Tyr Thr Phe Thr Asn Tyr

1 5

<210> 1066
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1066
Thr Pro Thr Thr Gly Tyr
1 5

<210> 1067
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1067
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1068
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1068
Gly Tyr Thr Phe Thr Asn Tyr Trp
1 5

<210> 1069
<211> 8
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1069
Ile Thr Pro Thr Thr Gly Tyr Pro
1 5

<210> 1070
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1070
Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10 15

<210> 1071
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1071
Gly Tyr Thr Phe Thr Asn Tyr Trp Met His
1 5 10

<210> 1072
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1072
Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe Lys
1 5 10 15

Asp

<210> 1073
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1073
Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr
1 5 10

<210> 1074
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1074
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1075
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1075
Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
1 5 10

<210> 1076
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1076
Asn Thr Lys Thr Leu Ala Asp
1 5

<210> 1077
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1077
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1078

<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1078
Ser Gly Asn Ile His Asn Tyr
1 5

<210> 1079
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1079
Asn Thr Lys
1

<210> 1080
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1080
Phe Trp Ser Ser Pro Trp
1 5

<210> 1081
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1081
Gly Asn Ile His Asn Tyr
1   5

<210> 1082
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1082
Asn Thr Lys
1

<210> 1083
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1083
Gln His Phe Trp Ser Ser Pro Trp Thr
1   5

<210> 1084
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1084
Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
1   5   10

<210> 1085
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1085
Asn Thr Lys Thr Leu Ala Asp
1 5

<210> 1086
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1086
Gln His Phe Trp Ser Ser Pro Trp Thr
1 5

<210> 1087
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1087
Ala Ile Arg Met Thr Gln Ser Pro Phe Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Ala Lys Ala Pro Lys Leu Phe Ile
35 40 45

Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro

65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1088
<211> 249
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1088
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
20 25 30

Trp Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
115 120 125

```
Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Ile
    130                 135                 140

Arg Met Thr Gln Ser Pro Phe Ser Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
                165                 170                 175

Trp Tyr Gln Gln Lys Pro Ala Lys Ala Pro Lys Leu Phe Ile Tyr Asn
            180                 185                 190

Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
        195                 200                 205

Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
    210                 215                 220

Phe Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp Thr Phe
225                 230                 235                 240

Gly Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 1089
<211> 493
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1089

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

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30

Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45
```

```
Thr Phe Thr Asn Tyr Trp Met His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60

Gly Leu Glu Trp Met Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu
65                  70                  75                  80

Tyr Asn Gln Lys Phe Lys Asp Arg Val Thr Ile Thr Ala Asp Lys Ser
                85                  90                  95

Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110

Ala Val Tyr Tyr Cys Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr
        115                 120                 125

Ala Leu Asp Tyr Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Ala Ile Arg Met Thr Gln Ser Pro Phe Ser Leu Ser Ala
                165                 170                 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile
            180                 185                 190

His Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Ala Lys Ala Pro Lys
        195                 200                 205

Leu Phe Ile Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg
    210                 215                 220

Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser
225                 230                 235                 240

Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln His Phe Trp Ser
                245                 250                 255

Ser Pro Trp Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr
```

```
            260                 265                 270

Thr Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln
        275                 280                 285

Pro Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala
    290                 295                 300

Val His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala
305                 310                 315                 320

Pro Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr
                325                 330                 335

Leu Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln
            340                 345                 350

Pro Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser
        355                 360                 365

Cys Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys
    370                 375                 380

Phe Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln
385                 390                 395                 400

Leu Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu
                405                 410                 415

Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg
            420                 425                 430

Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met
        435                 440                 445

Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly
    450                 455                 460

Lys Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp
465                 470                 475                 480
```

Thr Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1090
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1090
Ser Tyr Asn Met His
1 5

<210> 1091
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1091
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe Lys
1 5 10 15

Gly

<210> 1092
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1092
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1093
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1093
Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> 1094
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1094
Tyr Pro Gly Asn Gly Asp
1 5

<210> 1095
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1095
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1096
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1096
Gly Tyr Thr Phe Thr Ser Tyr Asn
1 5

<210> 1097
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1097
Ile Tyr Pro Gly Asn Gly Asp Thr
1 5

<210> 1098
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1098
Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10 15

<210> 1099
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1099
Gly Tyr Thr Phe Thr Ser Tyr Asn Met His
1 5 10

<210> 1100
<211> 17
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1100
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe Lys
1 5 10 15

Gly

<210> 1101
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1101
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1102
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1102
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

```
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
    50                  55                  60


Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
            100                 105                 110


Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210> 1103
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1103
Arg Ala Ser Ser Ser Val Ser Ser Met His
1               5                   10


<210> 1104
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1104
Ala Thr Ser Asn Leu Ala Ser
1               5


<210> 1105
<211> 9
<212> PRT
<213> Artificial Sequence
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<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1105
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1106
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1106
Ser Ser Ser Val Ser Ser
1 5

<210> 1107
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1107
Ala Thr Ser
1

<210> 1108
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1108
Trp Ile Phe Asn Pro Pro
1 5

<210> 1109
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1109
Ser Ser Val Ser Ser
1 5

<210> 1110
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1110
Ala Thr Ser
1

<210> 1111
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1111
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1112
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1112
Arg Ala Ser Ser Ser Val Ser Ser Met His
1 5 10

<210> 1113
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1113
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1114
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1114
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1115
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1115
Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Ser Met

```
            20                  25                  30

His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile Phe
        35                  40                  45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
    50                  55                  60

Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65                  70                  75                  80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr
                85                  90                  95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
            100                 105


<210> 1116
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1116
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr
65                  70                  75                  80
```

```
Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Ser Met His Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile Phe Ala Thr
            180                 185                 190

Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220

Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr Phe Gly
225                 230                 235                 240

Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 1117
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1117
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1   5   10   15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20   25   30

Lys Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35   40   45

Thr Phe Thr Ser Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln
    50   55   60

Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser
65   70   75   80

Tyr Asn Pro Lys Phe Lys Gly Arg Val Thr Met Thr Ala Asp Lys Ser
                85   90   95

Thr Arg Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100   105   110

Ala Val Tyr Tyr Cys Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp
        115   120   125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130   135   140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145   150   155   160

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala
                165   170   175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val
            180   185   190

Ser Ser Met His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro
        195   200   205

Leu Ile Phe Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe

```
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430
```

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
435 440 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
450 455 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465 470 475 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1118
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1118
Ser Tyr Asn Met His
1 5

<210> 1119
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1119
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe Lys
1 5 10 15

Gly

<210> 1120
<211> 13
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1120
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1121
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1121
Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> 1122
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1122
Tyr Pro Gly Asn Gly Asp
1 5

<210> 1123
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1123
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val

1 5 10

<210> 1124
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1124
Gly Tyr Thr Phe Thr Ser Tyr Asn
1 5

<210> 1125
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1125
Ile Tyr Pro Gly Asn Gly Asp Thr
1 5

<210> 1126
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1126
Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10 15

<210> 1127
<211> 10
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1127
Gly Tyr Thr Phe Thr Ser Tyr Asn Met His
1 5 10

<210> 1128
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1128
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe Lys
1 5 10 15

Gly

<210> 1129
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1129
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1130
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1130

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                   10                  15


Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30


Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45


Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
    50                  55                  60


Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr
65                  70                  75                  80


Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
            100                 105                 110


Gly Gln Gly Thr Thr Val Thr Val Ser Ser
        115                 120


<210> 1131
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1131
Arg Ala Ser Ser Ser Val Ser Ser Met His
1               5                   10


<210> 1132
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
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<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1132
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1133
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1133
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1134
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1134
Ser Ser Ser Val Ser Ser
1 5

<210> 1135
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1135
Ala Thr Ser
1

<210> 1136

<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1136
Trp Ile Phe Asn Pro Pro
1 5

<210> 1137
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1137
Ser Ser Val Ser Ser
1 5

<210> 1138
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1138
Ala Thr Ser
1

<210> 1139
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1139
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1   5

<210> 1140
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1140
Arg Ala Ser Ser Ser Val Ser Ser Met His
1   5   10

<210> 1141
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1141
Ala Thr Ser Asn Leu Ala Ser
1   5

<210> 1142
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1142
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1   5

<210> 1143
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1143
Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Ser Ser Val Ser Ser Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro Leu Ile Phe
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
65 70 75 80

Asp Ala Ala Val Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1144
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1144
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

```
Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile
    130                 135                 140

Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg
145                 150                 155                 160

Ala Thr Leu Ser Cys Arg Ala Ser Ser Ser Val Ser Ser Met His Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro Leu Ile Phe Ala Thr
            180                 185                 190

Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205

Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Ala
    210                 215                 220

Ala Val Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr Phe Gly
225                 230                 235                 240

Gly Gly Thr Lys Val Glu Ile Lys
                245
```

<210> 1145
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1145
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1 5 10 15

His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
20 25 30

Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
35 40 45

Thr Phe Thr Ser Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln
50 55 60

Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser
65 70 75 80

Tyr Asn Pro Lys Phe Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser
85 90 95

Thr Arg Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
100 105 110

Ala Val Tyr Tyr Cys Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp
115 120 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145 150 155 160

Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu

```
                165                 170                 175

Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Ser Ser Val
            180                 185                 190

Ser Ser Met His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Pro
        195                 200                 205

Leu Ile Phe Ala Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240

Glu Pro Glu Asp Ala Ala Val Tyr Tyr Cys Gln Gln Trp Ile Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335

Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380
```

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385 390 395 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
405 410 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
420 425 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
435 440 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
450 455 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465 470 475 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
485 490

<210> 1146
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1146
Ser Tyr Asn Met His
1 5

<210> 1147
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1147
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe Lys
1   5   10   15

Gly

<210> 1148
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1148
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1   5   10

<210> 1149
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1149
Gly Tyr Thr Phe Thr Ser Tyr
1   5

<210> 1150
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1150
Tyr Pro Gly Asn Gly Asp
1   5

<210> 1151
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1151
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1 5 10

<210> 1152
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1152
Gly Tyr Thr Phe Thr Ser Tyr Asn
1 5

<210> 1153
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1153
Ile Tyr Pro Gly Asn Gly Asp Thr
1 5

<210> 1154
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1154
Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1   5   10   15

<210> 1155
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1155
Gly Tyr Thr Phe Thr Ser Tyr Asn Met His
1   5   10

<210> 1156
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1156
Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe Lys
1   5   10   15

Gly

<210> 1157
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1157
Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val
1   5   10

<210> 1158
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1158
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
50 55 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1159
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1159
Arg Ala Ser Ser Ser Val Ser Ser Met His
1   5   10

<210> 1160
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1160
Ala Thr Ser Asn Leu Ala Ser
1   5

<210> 1161
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1161
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1   5

<210> 1162
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1162
Ser Ser Ser Val Ser Ser
1   5

<210> 1163
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1163
Ala Thr Ser
1

<210> 1164
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1164
Trp Ile Phe Asn Pro Pro
1 5

<210> 1165
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1165
Ser Ser Val Ser Ser
1 5

<210> 1166
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1166
Ala Thr Ser
1

<210> 1167
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1167
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1168
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1168
Arg Ala Ser Ser Ser Val Ser Ser Met His
1 5 10

<210> 1169
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1169
Ala Thr Ser Asn Leu Ala Ser
1 5

<210> 1170
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1170
Gln Gln Trp Ile Phe Asn Pro Pro Thr
1 5

<210> 1171
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1171
Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Ser Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile Phe
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 1172
<211> 248
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1172

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Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                  10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Asn Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
        35                  40                  45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
    50                  55                  60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Arg Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
            100                 105                 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile
    130                 135                 140

Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala Ser Val Gly Asp Arg
145                 150                 155                 160

Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val Ser Ser Met His Trp
                165                 170                 175

Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro Leu Ile Phe Ala Thr
            180                 185                 190

Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser
        195                 200                 205
```

```
Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
    210                 215                 220


Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr Phe Gly
225                 230                 235                 240


Gly Gly Thr Lys Val Glu Ile Lys
                245


<210> 1173
<211> 492
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1173
Met Ala Leu Pro Val Thr Ala Leu Leu Leu Pro Leu Ala Leu Leu Leu
1               5                   10                  15


His Ala Ala Arg Pro Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val
            20                  25                  30


Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr
        35                  40                  45


Thr Phe Thr Ser Tyr Asn Met His Trp Val Arg Gln Ala Pro Gly Gln
    50                  55                  60


Gly Leu Glu Trp Met Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser
65                  70                  75                  80


Tyr Asn Pro Lys Phe Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser
                85                  90                  95


Thr Arg Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
            100                 105                 110


Ala Val Tyr Tyr Cys Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp
```

```
        115                 120                 125

Tyr Phe Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly
    130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Phe Leu Ser Ala
                165                 170                 175

Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Val
            180                 185                 190

Ser Ser Met His Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Pro
        195                 200                 205

Leu Ile Phe Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe
    210                 215                 220

Ser Gly Ser Gly Ser Gly Thr Glu Tyr Thr Leu Thr Ile Ser Ser Leu
225                 230                 235                 240

Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn
                245                 250                 255

Pro Pro Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Thr Thr Thr
            260                 265                 270

Pro Ala Pro Arg Pro Pro Thr Pro Ala Pro Thr Ile Ala Ser Gln Pro
        275                 280                 285

Leu Ser Leu Arg Pro Glu Ala Cys Arg Pro Ala Ala Gly Gly Ala Val
    290                 295                 300

His Thr Arg Gly Leu Asp Phe Ala Cys Asp Ile Tyr Ile Trp Ala Pro
305                 310                 315                 320

Leu Ala Gly Thr Cys Gly Val Leu Leu Leu Ser Leu Val Ile Thr Leu
                325                 330                 335
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```
Tyr Cys Lys Arg Gly Arg Lys Lys Leu Leu Tyr Ile Phe Lys Gln Pro
            340                 345                 350

Phe Met Arg Pro Val Gln Thr Thr Gln Glu Glu Asp Gly Cys Ser Cys
        355                 360                 365

Arg Phe Pro Glu Glu Glu Glu Gly Gly Cys Glu Leu Arg Val Lys Phe
    370                 375                 380

Ser Arg Ser Ala Asp Ala Pro Ala Tyr Gln Gln Gly Gln Asn Gln Leu
385                 390                 395                 400

Tyr Asn Glu Leu Asn Leu Gly Arg Arg Glu Glu Tyr Asp Val Leu Asp
                405                 410                 415

Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys Pro Arg Arg Lys
            420                 425                 430

Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys Asp Lys Met Ala
        435                 440                 445

Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg Arg Arg Gly Lys
    450                 455                 460

Gly His Asp Gly Leu Tyr Gln Gly Leu Ser Thr Ala Thr Lys Asp Thr
465                 470                 475                 480

Tyr Asp Ala Leu His Met Gln Ala Leu Pro Pro Arg
                485                 490


<210> 1174
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1174
Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala
1               5                   10                  15
```

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20   25   30

Asn Leu His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile
        35   40   45

Gly Ala Ile Tyr Pro Gly Asn Tyr Asp Thr Ser Tyr Asn Gln Lys Phe
    50   55   60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65   70   75   80

Met Leu Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
                85   90   95

Ala Arg Val Asp Phe Gly His Ser Arg Tyr Trp Tyr Phe Asp Val Trp
            100   105   110

Gly Ala Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 1175
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1175
Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1   5   10   15

Glu Lys Val Thr Met Thr Cys Arg Ala Thr Ser Ser Val Ser Ser Met
            20   25   30

Asn Trp Tyr Gln Gln Lys Pro Gly Ser Phe Pro Arg Pro Trp Ile His
        35   40   45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser

```
    50                  55                  60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65                  70                  75                  80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Thr Phe Asn Pro Pro Thr
                85                  90                  95

Phe Gly Ala Gly Ala Lys Leu Glu Leu Lys
            100                 105

<210> 1176
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1176
Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala
1               5                   10                  15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
            20                  25                  30

Asn Met His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Pro Lys Phe
    50                  55                  60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Arg Thr Ala Tyr
65                  70                  75                  80

Ile His Leu Ser Ser Leu Thr Ser Glu Asp Ser Val Val Tyr Tyr Cys
                85                  90                  95

Ala Arg Ser Tyr Phe Tyr Gly Ser Ser Ser Trp Tyr Phe Asp Val Trp
            100                 105                 110
```

Gly Ala Gly Thr Thr Val Thr Val Ser Ser
        115   120

<210> 1177
<211> 106
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1177
Gln Ile Ile Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1   5   10   15

Glu Lys Val Thr Leu Thr Cys Arg Ala Ser Ser Ser Val Ser Ser Met
            20   25   30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Phe
        35   40   45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Thr Gly Ser
    50   55   60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu
65   70   75   80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ile Phe Asn Pro Pro Thr
                85   90   95

Phe Gly Gly Gly Thr Ser Leu Glu Ile Lys
            100   105

<210> 1178
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1178

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Gln Val His Leu Gln Gln Ser Gly Ala Glu Leu Ala Lys Pro Gly Ala
1               5                   10                  15


Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr
            20                  25                  30


Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
        35                  40                  45


Gly Phe Ile Thr Pro Thr Thr Gly Tyr Pro Glu Tyr Asn Gln Lys Phe
    50                  55                  60


Lys Asp Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65                  70                  75                  80


Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
                85                  90                  95


Ala Arg Arg Lys Val Gly Lys Gly Val Tyr Tyr Ala Leu Asp Tyr Trp
            100                 105                 110


Gly Gln Gly Thr Ser Val Thr Val Ser Ser
        115                 120


<210> 1179
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1179
Asp Ile Leu Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Val Gly
1               5                   10                  15


Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr
            20                  25                  30


Leu Ala Trp Tyr Gln Gln Lys Gln Gly Asn Ser Pro Gln Leu Leu Val
        35                  40                  45
```

Tyr Asn Thr Lys Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
    50   55   60

Ser Gly Ser Gly Thr Gln Tyr Ser Leu Lys Ile Asn Ser Leu Gln Thr
65   70   75   80

Glu Asp Phe Gly Thr Tyr Tyr Cys Gln His Phe Trp Ser Ser Pro Trp
                85   90   95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
            100   105

<210> 1180
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1180
Gly Asp Ser Met Leu Ser Asn Ser Asp
1   5

<210> 1181
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1181
Tyr His Arg Ser Thr Trp Tyr
1   5

<210> 1182
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1182
Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 1183
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1183
Gly Asp Ser Met Leu Ser Asn Ser Asp Thr
1 5 10

<210> 1184
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1184
Thr Tyr His Arg Ser Thr Trp Tyr Asp
1 5

<210> 1185
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1185
Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp
1 5 10 15

Val

<210> 1186
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1186
Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
1 5 10

<210> 1187
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1187
Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr
1 5 10

<210> 1188
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1188
Ser Ser Asp Val Gly Gly Tyr Asn Tyr
1 5

<210> 1189
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1189
Asp Val Ser Asn Arg Pro Ser
1 5

<210> 1190
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1190
Asp Val Ser
1

<210> 1191
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1191
Asp Val Ser
1

<210> 1192
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1192
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1 5 10

<210> 1193
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1193
Tyr Thr Ser Ser Ser Thr Leu Tyr
1 5

<210> 1194
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1194
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1 5 10

<210> 1195
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1195
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Met Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala

```
    50                  55                  60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65                  70                  75                  80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
                85                  90                  95

Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
            100                 105                 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gln Ser Ala Leu Thr Gln Pro Ala Ser Ala Ser Gly
    130                 135                 140

Ser Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp
145                 150                 155                 160

Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys
                165                 170                 175

Ala Pro Lys Leu Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val
            180                 185                 190

Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr
        195                 200                 205

Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser
    210                 215                 220

Tyr Thr Ser Ser Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Gln Leu
225                 230                 235                 240

Thr Val Leu
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<210> 1196
<211> 238
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1196
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Met Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
50 55 60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65 70 75 80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
85 90 95

Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
100 105 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gln
115 120 125

Ser Ala Leu Thr Gln Pro Ala Ser Ala Ser Gly Ser Pro Gly Gln Ser
130 135 140

Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn
145 150 155 160

Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met
165 170 175

Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe Ser
180 185 190

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Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln
        195                 200                 205


Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser
    210                 215                 220


Thr Leu Tyr Val Phe Gly Thr Gly Thr Gln Leu Thr Val Leu
225                 230                 235


<210> 1197
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1197
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Met Leu Ser Asn
            20                  25                  30


Ser Asp Thr Trp Asn Trp Ile Arg Lys Ser Pro Ser Arg Gly Leu Glu
        35                  40                  45


Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
    50                  55                  60


Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65                  70                  75                  80


Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
                85                  90                  95


Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
            100                 105                 110


Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
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115 120 125

<210> 1198
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1198
Gln Ser Ala Leu Thr Gln Pro Ala Ser Ala Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Asp His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Gln Leu Thr Val Leu
100 105 110

<210> 1199
<211> 243
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1199
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln

```
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Met Leu Ser Asn
            20                  25                  30

Ser Asp Thr Trp Asn Trp Ile Arg Lys Ser Pro Ser Arg Gly Leu Glu
        35                  40                  45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
    50                  55                  60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65                  70                  75                  80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
                85                  90                  95

Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
            100                 105                 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gln Ser Ala Leu Thr Gln Pro Ala Ser Ala Ser Gly
    130                 135                 140

Ser Pro Gly Gln Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp
145                 150                 155                 160

Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln Asp His Pro Gly Lys
                165                 170                 175

Ala Pro Lys Leu Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val
            180                 185                 190

Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr
        195                 200                 205

Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser
    210                 215                 220
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Tyr Thr Ser Ser Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Gln Leu
225 230 235 240

Thr Val Leu

<210> 1200
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1200
Ser Asn Ser Asp Thr Trp Asn
1 5

<210> 1201
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1201
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val
1 5 10 15

Arg Gly

<210> 1202
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1202

Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1   5   10   15

<210> 1203
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1203
Gly Asp Ser Val Leu Ser Asn Ser Asp
1   5

<210> 1204
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1204
Tyr His Arg Ser Thr Trp Tyr
1   5

<210> 1205
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1205
Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1   5   10   15

<210> 1206
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1206
Gly Asp Ser Val Leu Ser Asn Ser Asp Thr
1 5 10

<210> 1207
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1207
Thr Tyr His Arg Ser Thr Trp Tyr Asp
1 5

<210> 1208
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1208
Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp
1 5 10 15

Val

<210> 1209
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1209
Gly Asp Ser Val Leu Ser Asn Ser Asp Thr Trp Asn
1 5 10

<210> 1210
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1210
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val
1 5 10 15

Arg Gly

<210> 1211
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1211
Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 1212
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1212
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Pro Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Leu Ser Asn
            20   25   30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
        35   40   45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
    50   55   60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65   70   75   80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
                85   90   95

Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
            100   105   110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
        115   120   125

<210> 1213
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1213
Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
1   5   10

<210> 1214
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1214

Asp Val Ser Asn Arg Pro Ser
1 5

<210> 1215
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1215
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1 5 10

<210> 1216
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1216
Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr
1 5 10

<210> 1217
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1217
Asp Val Ser
1

<210> 1218
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1218
Tyr Thr Ser Ser Ser Thr Leu Tyr
1 5

<210> 1219
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1219
Ser Ser Asp Val Gly Gly Tyr Asn Tyr
1 5

<210> 1220
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1220
Asp Val Ser
1

<210> 1221
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1221
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1 5 10

<210> 1222
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1222
Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
1 5 10

<210> 1223
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1223
Asp Val Ser Asn Arg Pro Ser
1 5

<210> 1224
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1224
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1 5 10

<210> 1225
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

polypeptide"

<400> 1225
Gln Ser Ala Leu Thr Gln Pro Ala Ser Ala Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Gln Leu Thr Val Leu
100 105 110

<210> 1226
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1226
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Pro Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

```
Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
    50                  55                  60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65                  70                  75                  80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
                85                  90                  95

Tyr Tyr Cys Ala Arg Val Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
            100                 105                 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Pro Gln Ser
    130                 135                 140

Ala Leu Thr Gln Pro Ala Ser Ala Ser Gly Ser Pro Gly Gln Ser Val
145                 150                 155                 160

Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr
                165                 170                 175

Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile
            180                 185                 190

Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly
        195                 200                 205

Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala
    210                 215                 220

Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr
225                 230                 235                 240

Leu Tyr Val Phe Gly Thr Gly Thr Gln Leu Thr Val Leu
                245                 250
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<210> 1227
<211> 7

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1227
Asn Asn Asn Ala Ala Trp Asn
1 5

<210> 1228
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1228
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asn Asp Tyr Val Gly Ser Val
1 5 10 15

Lys Ser

<210> 1229
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1229
Glu Thr Asp Tyr Gly Asp Tyr Gly Ala Phe Asp Ile
1 5 10

<210> 1230
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1230
Gly Asp Ser Val Ser Asn Asn Asn Ala
1 5

<210> 1231
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1231
Tyr His Arg Ser Thr Trp Tyr
1 5

<210> 1232
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1232
Glu Thr Asp Tyr Gly Asp Tyr Gly Ala Phe Asp Ile
1 5 10

<210> 1233
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1233
Gly Asp Ser Val Ser Asn Asn Asn Ala Ala
1 5 10

<210> 1234

<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1234
Thr Tyr His Arg Ser Thr Trp Tyr Asn
1 5

<210> 1235
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1235
Ala Arg Glu Thr Asp Tyr Gly Asp Tyr Gly Ala Phe Asp Ile
1 5 10

<210> 1236
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1236
Gly Asp Ser Val Ser Asn Asn Asn Ala Ala Trp Asn
1 5 10

<210> 1237
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1237
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asn Asp Tyr Val Gly Ser Val
1   5   10   15

Lys Ser

<210> 1238
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1238
Glu Thr Asp Tyr Gly Asp Tyr Gly Ala Phe Asp Ile
1   5   10

<210> 1239
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1239
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1   5   10   15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Asn Asn
            20   25   30

Asn Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
        35   40   45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asn Asp Tyr Val
    50   55   60

Gly Ser Val Lys Ser Arg Ile Thr Ile Asn Pro Asp Thr Ser Lys Asn
65   70   75   80

Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val
85 90 95

Tyr Tyr Cys Ala Arg Glu Thr Asp Tyr Gly Asp Tyr Gly Ala Phe Asp
100 105 110

Ile Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1240
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1240
Thr Gly Ser Arg Asn Asp Ile Gly Ala Tyr Glu Ser Val Ser
1 5 10

<210> 1241
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1241
Gly Val Asn Asn Arg Pro Ser
1 5

<210> 1242
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1242

Ser Ser His Thr Thr Thr Ser Thr Leu Tyr Val
1 5 10

<210> 1243
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1243
Ser Arg Asn Asp Ile Gly Ala Tyr Glu Ser
1 5 10

<210> 1244
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1244
Gly Val Asn
1

<210> 1245
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1245
His Thr Thr Thr Ser Thr Leu Tyr
1 5

<210> 1246
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1246
Arg Asn Asp Ile Gly Ala Tyr Glu Ser
1 5

<210> 1247
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1247
Gly Val Asn
1

<210> 1248
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1248
Ser Ser His Thr Thr Thr Ser Thr Leu Tyr Val
1 5 10

<210> 1249
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1249
Thr Gly Ser Arg Asn Asp Ile Gly Ala Tyr Glu Ser Val Ser
1 5 10

<210> 1250
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1250
Gly Val Asn Asn Arg Pro Ser
1 5

<210> 1251
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1251
Ser Ser His Thr Thr Thr Ser Thr Leu Tyr Val
1 5 10

<210> 1252
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1252
Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Ser Arg Asn Asp Ile Gly Ala Tyr
20 25 30

Glu Ser Val Ser Trp Tyr Gln Gln His Pro Gly Asn Ala Pro Lys Leu
35 40 45

```
Ile Ile His Gly Val Asn Asn Arg Pro Ser Gly Val Phe Asp Arg Phe
    50                  55                  60


Ser Val Ser Gln Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65                  70                  75                  80


Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser His Thr Thr Thr
                85                  90                  95


Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
            100                 105                 110


<210> 1253
<211> 250
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1253
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15


Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Asn Asn
            20                  25                  30


Asn Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
        35                  40                  45


Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asn Asp Tyr Val
    50                  55                  60


Gly Ser Val Lys Ser Arg Ile Thr Ile Asn Pro Asp Thr Ser Lys Asn
65                  70                  75                  80


Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val
                85                  90                  95


Tyr Tyr Cys Ala Arg Glu Thr Asp Tyr Gly Asp Tyr Gly Ala Phe Asp
            100                 105                 110
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Ile Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly
        115                 120                 125


Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ser Ala Leu Thr
    130                 135                 140


Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser Ile Thr Ile Ser
145                 150                 155                 160


Cys Thr Gly Ser Arg Asn Asp Ile Gly Ala Tyr Glu Ser Val Ser Trp
                165                 170                 175


Tyr Gln Gln His Pro Gly Asn Ala Pro Lys Leu Ile Ile His Gly Val
            180                 185                 190


Asn Asn Arg Pro Ser Gly Val Phe Asp Arg Phe Ser Val Ser Gln Ser
        195                 200                 205


Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu
    210                 215                 220


Ala Asp Tyr Tyr Cys Ser Ser His Thr Thr Thr Ser Thr Leu Tyr Val
225                 230                 235                 240


Phe Gly Thr Gly Thr Lys Val Thr Val Leu
                245                 250


<210> 1254
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1254
Ser Asn Ser Ala Ala Trp Asn
1               5


<210> 1255
<211> 18
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<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1255
Arg Thr Phe Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala Val Ser Val
1 5 10 15

Lys Gly

<210> 1256
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1256
Gly Asp Tyr Tyr Tyr Gly Leu Asp Val
1 5

<210> 1257
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1257
Gly Asp Ser Val Ser Ser Asn Ser Ala
1 5

<210> 1258
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1258
Phe Tyr Arg Ser Lys Trp Tyr
1 5

<210> 1259
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1259
Gly Asp Tyr Tyr Tyr Gly Leu Asp Val
1 5

<210> 1260
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1260
Gly Asp Ser Val Ser Ser Asn Ser Ala Ala
1 5 10

<210> 1261
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1261
Thr Phe Tyr Arg Ser Lys Trp Tyr Asn
1 5

<210> 1262

<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1262
Ala Gly Gly Asp Tyr Tyr Tyr Gly Leu Asp Val
1 5 10

<210> 1263
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1263
Gly Asp Ser Val Ser Ser Asn Ser Ala Ala Trp Asn
1 5 10

<210> 1264
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1264
Arg Thr Phe Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala Val Ser Val
1 5 10 15

Lys Gly

<210> 1265
<211> 9
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1265
Gly Asp Tyr Tyr Tyr Gly Leu Asp Val
1 5

<210> 1266
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1266
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Asn Pro Ser Gln
1 5 10 15

Thr Leu Ser Ile Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Ser Asn
20 25 30

Ser Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Phe Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala
50 55 60

Val Ser Val Lys Gly Arg Ile Thr Ile Ser Pro Asp Thr Ser Lys Asn
65 70 75 80

Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val
85 90 95

Tyr Tyr Cys Ala Gly Gly Asp Tyr Tyr Tyr Gly Leu Asp Val Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 1267
<211> 14

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1267
Thr Gly Ser Ser Ser Asp Val Gly Gly Tyr Asn Ser Val Ser
1 5 10

<210> 1268
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1268
Glu Val Ile Asn Arg Pro Ser
1 5

<210> 1269
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1269
Ser Ser Tyr Thr Ser Ser Ser Thr Tyr Val
1 5 10

<210> 1270
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1270

Ser Ser Ser Asp Val Gly Gly Tyr Asn Ser
1   5   10

<210> 1271
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1271
Glu Val Ile
1

<210> 1272
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1272
Tyr Thr Ser Ser Ser Thr Tyr
1   5

<210> 1273
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1273
Ser Ser Asp Val Gly Gly Tyr Asn Ser
1   5

<210> 1274
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1274
Glu Val Ile
1

<210> 1275
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1275
Ser Ser Tyr Thr Ser Ser Ser Thr Tyr Val
1 5 10

<210> 1276
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1276
Thr Gly Ser Ser Ser Asp Val Gly Gly Tyr Asn Ser Val Ser
1 5 10

<210> 1277
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1277
Glu Val Ile Asn Arg Pro Ser
1 5

<210> 1278
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1278
Ser Ser Tyr Thr Ser Ser Ser Thr Tyr Val
1 5 10

<210> 1279
<211> 110
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1279
Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Ser Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Ser Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Val Ile Asn Arg Pro Ser Gly Val Ser His Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
100 105 110

<210> 1280
<211> 246
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1280
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Asn Pro Ser Gln
1 5 10 15

Thr Leu Ser Ile Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Ser Asn
20 25 30

Ser Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Phe Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala
50 55 60

Val Ser Val Lys Gly Arg Ile Thr Ile Ser Pro Asp Thr Ser Lys Asn
65 70 75 80

Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val
85 90 95

Tyr Tyr Cys Ala Gly Gly Asp Tyr Tyr Tyr Gly Leu Asp Val Trp Gly
100 105 110

Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Gln Ser Ala Leu Thr Gln Pro Ala
130 135 140

Ser Val Ser Gly Ser Pro Gly Gln Ser Ile Thr Ile Ser Cys Thr Gly
145 150 155 160

Ser Ser Ser Asp Val Gly Gly Tyr Asn Ser Val Ser Trp Tyr Gln Gln
165 170 175

```
His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Glu Val Ile Asn Arg
            180                 185                 190


Pro Ser Gly Val Ser His Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr
        195                 200                 205


Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr
    210                 215                 220


Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr Tyr Val Phe Gly Thr Gly
225                 230                 235                 240


Thr Lys Val Thr Val Leu
                245


<210> 1281
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1281
Ser Asn Ser Asp Thr Trp Asn
1               5


<210> 1282
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1282
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val
1               5                   10                  15


Arg Gly
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<210> 1283
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1283
Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 1284
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1284
Gly Asp Ser Val Leu Ser Asn Ser Asp
1 5

<210> 1285
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1285
Tyr His Arg Ser Thr Trp Tyr
1 5

<210> 1286
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1286
Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 1287
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1287
Gly Asp Ser Val Leu Ser Asn Ser Asp Thr
1 5 10

<210> 1288
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1288
Thr Tyr His Arg Ser Thr Trp Tyr Asp
1 5

<210> 1289
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1289
Ala Arg Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp
1 5 10 15

Val

<210> 1290
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1290
Gly Asp Ser Val Leu Ser Asn Ser Asp Thr Trp Asn
1 5 10

<210> 1291
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1291
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val
1 5 10 15

Arg Gly

<210> 1292
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1292
Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 1293
<211> 127

<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1293
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
50 55 60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65 70 75 80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
85 90 95

Tyr Tyr Cys Ala Arg Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
100 105 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120 125

<210> 1294
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1294
Thr Gly Ser Ser Ser Asp Ile Gly Gly Phe Asn Tyr Val Ser
1 5 10

<210> 1295
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1295
Glu Val Thr Asn Arg Pro Ser
1 5

<210> 1296
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1296
Ser Ser Tyr Ala Ser Gly Ser Pro Leu Tyr Val
1 5 10

<210> 1297
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1297
Ser Ser Ser Asp Ile Gly Gly Phe Asn Tyr
1 5 10

<210> 1298
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1298
Glu Val Thr
1

<210> 1299
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1299
Tyr Ala Ser Gly Ser Pro Leu Tyr
1 5

<210> 1300
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1300
Ser Ser Asp Ile Gly Gly Phe Asn Tyr
1 5

<210> 1301
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1301
Glu Val Thr
1

<210> 1302

<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1302
Ser Ser Tyr Ala Ser Gly Ser Pro Leu Tyr Val
1 5 10

<210> 1303
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1303
Thr Gly Ser Ser Ser Asp Ile Gly Gly Phe Asn Tyr Val Ser
1 5 10

<210> 1304
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1304
Glu Val Thr Asn Arg Pro Ser
1 5

<210> 1305
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1305
Ser Ser Tyr Ala Ser Gly Ser Pro Leu Tyr Val
1 5 10

<210> 1306
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1306
Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Ser Ser Ser Asp Ile Gly Gly Phe
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Ala Gly Glu Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Val Thr Asn Arg Pro Ser Gly Val Ser Asp Arg Phe
50 55 60

Ser Gly Ser Lys Ser Asp Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Ser Gly
85 90 95

Ser Pro Leu Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
100 105 110

<210> 1307
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1307
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1   5   10   15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Leu Ser Asn
            20   25   30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
        35   40   45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
    50   55   60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65   70   75   80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
                85   90   95

Tyr Tyr Cys Ala Arg Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
            100   105   110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly
        115   120   125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ser
    130   135   140

Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser Ile
145   150   155   160

Thr Ile Ser Cys Thr Gly Ser Ser Ser Asp Ile Gly Gly Phe Asn Tyr
                165   170   175

Val Ser Trp Tyr Gln Gln His Ala Gly Glu Ala Pro Lys Leu Met Ile
            180   185   190

Tyr Glu Val Thr Asn Arg Pro Ser Gly Val Ser Asp Arg Phe Ser Gly
        195   200   205

Ser Lys Ser Asp Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala

210 215 220

Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Ser Gly Ser Pro
225 230 235 240

Leu Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
245 250

<210> 1308
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1308
Ser Asn Ser Asp Thr Trp Asn
1 5

<210> 1309
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1309
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val
1 5 10 15

Arg Gly

<210> 1310
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1310
Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1   5   10   15

<210> 1311
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1311
Gly Asp Ser Val Leu Ser Asn Ser Asp
1   5

<210> 1312
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1312
Tyr His Arg Ser Thr Trp Tyr
1   5

<210> 1313
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1313
Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1   5   10   15

<210> 1314
<211> 10
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1314
Gly Asp Ser Val Leu Ser Asn Ser Asp Thr
1 5 10

<210> 1315
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1315
Thr Tyr His Arg Ser Thr Trp Tyr Asp
1 5

<210> 1316
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1316
Ala Arg Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp
1 5 10 15

Val

<210> 1317
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 1317
Gly Asp Ser Val Leu Ser Asn Ser Asp Thr Trp Asn
1 5 10

<210> 1318
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1318
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val
1 5 10 15

Arg Gly

<210> 1319
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1319
Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 1320
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1320
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

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Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Leu Ser Asn
            20                  25                  30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
        35                  40                  45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
    50                  55                  60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65                  70                  75                  80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
                85                  90                  95

Tyr Tyr Cys Ala Arg Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
            100                 105                 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
        115                 120                 125
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<210> 1321
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1321
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Thr Gly Thr Ser Ser Asp Ile Gly Gly Tyr Asn Tyr Val Ser
1               5                   10
```

<210> 1322
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1322
Glu Val Ser Asn Arg Pro Ser
1 5

<210> 1323
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1323
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1 5 10

<210> 1324
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1324
Thr Ser Ser Asp Ile Gly Gly Tyr Asn Tyr
1 5 10

<210> 1325
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1325
Glu Val Ser
1

<210> 1326
<211> 8
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1326
Tyr Thr Ser Ser Ser Thr Leu Tyr
1 5

<210> 1327
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1327
Ser Ser Asp Ile Gly Gly Tyr Asn Tyr
1 5

<210> 1328
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1328
Glu Val Ser
1

<210> 1329
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1329
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val

1 5 10

<210> 1330
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1330
Thr Gly Thr Ser Ser Asp Ile Gly Gly Tyr Asn Tyr Val Ser
1 5 10

<210> 1331
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1331
Glu Val Ser Asn Arg Pro Ser
1 5

<210> 1332
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1332
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1 5 10

<210> 1333
<211> 111
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1333
Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Phe Ser Cys Thr Gly Thr Ser Ser Asp Ile Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Thr Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> 1334
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1334
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

```
Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
    50                  55                  60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65                  70                  75                  80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
                85                  90                  95

Tyr Tyr Cys Ala Arg Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
            100                 105                 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Ser Gly Gly Ser Gln Ser
    130                 135                 140

Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser Ile
145                 150                 155                 160

Thr Phe Ser Cys Thr Gly Thr Ser Ser Asp Ile Gly Gly Tyr Asn Tyr
                165                 170                 175

Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile
            180                 185                 190

Tyr Glu Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly
        195                 200                 205

Thr Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala
    210                 215                 220

Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr
225                 230                 235                 240

Leu Tyr Val Phe Gly Thr Gly Thr Lys Leu Thr Val Leu
                245                 250
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<210> 1335
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1335
Ser Asn Ser Asp Thr Trp Asn
1 5

<210> 1336
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1336
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val
1 5 10 15

Arg Gly

<210> 1337
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1337
Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 1338
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1338
Gly Asp Ser Val Leu Ser Asn Ser Asp
1 5

<210> 1339
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1339
Tyr His Arg Ser Thr Trp Tyr
1 5

<210> 1340
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1340
Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 1341
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1341
Gly Asp Ser Val Leu Ser Asn Ser Asp Thr
1 5 10

<210> 1342
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1342
Thr Tyr His Arg Ser Thr Trp Tyr Asp
1 5

<210> 1343
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1343
Ala Arg Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp
1 5 10 15

Val

<210> 1344
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1344
Gly Asp Ser Val Leu Ser Asn Ser Asp Thr Trp Asn
1 5 10

<210> 1345
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1345
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val
1 5 10 15

Arg Gly

<210> 1346
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1346
Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 1347
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1347
Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala

```
    50                  55                  60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65                  70                  75                  80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
                85                  90                  95

Tyr Tyr Cys Ala Arg Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
            100                 105                 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
        115                 120                 125


<210> 1348
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1348
Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
1               5                   10


<210> 1349
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1349
Glu Val Ser Asn Arg Pro Ser
1               5


<210> 1350
<211> 11
<212> PRT
<213> Artificial Sequence
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<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1350
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1 5 10

<210> 1351
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1351
Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr
1 5 10

<210> 1352
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1352
Glu Val Ser
1

<210> 1353
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1353
Tyr Thr Ser Ser Ser Thr Leu Tyr
1 5

<210> 1354
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1354
Ser Ser Asp Val Gly Gly Tyr Asn Tyr
1 5

<210> 1355
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1355
Glu Val Ser
1

<210> 1356
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1356
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1 5 10

<210> 1357
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic

peptide"

<400> 1357
Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
1 5 10

<210> 1358
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1358
Glu Val Ser Asn Arg Pro Ser
1 5

<210> 1359
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1359
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1 5 10

<210> 1360
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1360
Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

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Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
        35                  40                  45

Met Ile Tyr Glu Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
    50                  55                  60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65                  70                  75                  80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
                85                  90                  95

Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
            100                 105                 110
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<210> 1361
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1361

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Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Leu Ser Asn
            20                  25                  30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
        35                  40                  45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
    50                  55                  60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65                  70                  75                  80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
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```
                85                  90                  95

Tyr Tyr Cys Ala Arg Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
            100                 105                 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly
        115                 120                 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Ser Gly Gly Ser Gln Ser
    130                 135                 140

Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser Ile
145                 150                 155                 160

Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr
                165                 170                 175

Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile
            180                 185                 190

Tyr Glu Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly
        195                 200                 205

Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala
    210                 215                 220

Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr
225                 230                 235                 240

Leu Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
                245                 250


<210> 1362
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1362
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Ser Asn Ser Asp Thr Trp Asn
1 5

<210> 1363
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1363
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val
1 5 10 15

Arg Gly

<210> 1364
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1364
Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 1365
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1365
Gly Asp Ser Val Leu Ser Asn Ser Asp
1 5

<210> 1366

<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1366
Tyr His Arg Ser Thr Trp Tyr
1 5

<210> 1367
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1367
Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 1368
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1368
Gly Asp Ser Val Leu Ser Asn Ser Asp Thr
1 5 10

<210> 1369
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1369
Thr Tyr His Arg Ser Thr Trp Tyr Asp
1 5

<210> 1370
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1370
Ala Arg Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp
1 5 10 15

Val

<210> 1371
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1371
Gly Asp Ser Val Leu Ser Asn Ser Asp Thr Trp Asn
1 5 10

<210> 1372
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1372
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val
1 5 10 15

Arg Gly

<210> 1373
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1373
Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 1374
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1374
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
50 55 60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65 70 75 80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
85 90 95

Tyr Tyr Cys Ala Arg Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
100 105 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120 125

<210> 1375
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1375
Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
1 5 10

<210> 1376
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1376
Asp Val Ser Asn Arg Pro Ser
1 5

<210> 1377
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1377
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1 5 10

<210> 1378

<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1378
Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr
1 5 10

<210> 1379
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1379
Asp Val Ser
1

<210> 1380
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1380
Tyr Thr Ser Ser Ser Thr Leu Tyr
1 5

<210> 1381
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1381
Ser Ser Asp Val Gly Gly Tyr Asn Tyr
1   5

<210> 1382
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1382
Asp Val Ser
1

<210> 1383
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1383
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1   5   10

<210> 1384
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      peptide"

<400> 1384
Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
1   5   10

<210> 1385
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1385
Asp Val Ser Asn Arg Pro Ser
1 5

<210> 1386
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1386
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Val
1 5 10

<210> 1387
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1387
Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu

65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Leu Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
100 105 110

<210> 1388
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1388
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
50 55 60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65 70 75 80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
85 90 95

Tyr Tyr Cys Ala Arg Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
100 105 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ser
130 135 140

Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser Ile
145 150 155 160

Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr
165 170 175

Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile
180 185 190

Tyr Asp Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly
195 200 205

Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala
210 215 220

Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr
225 230 235 240

Leu Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
245 250

<210> 1389
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1389
Ser Asn Ser Asp Thr Trp Asn
1 5

<210> 1390
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1390
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val
1 5 10 15

Arg Gly

<210> 1391
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1391
Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 1392
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1392
Gly Asp Ser Val Leu Ser Asn Ser Asp
1 5

<210> 1393
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1393
Tyr His Arg Ser Thr Trp Tyr

1 5

<210> 1394
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1394
Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 1395
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1395
Gly Asp Ser Val Leu Ser Asn Ser Asp Thr
1 5 10

<210> 1396
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1396
Thr Tyr His Arg Ser Thr Trp Tyr Asp
1 5

<210> 1397
<211> 17
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1397
Ala Arg Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp
1 5 10 15

Val

<210> 1398
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1398
Gly Asp Ser Val Leu Ser Asn Ser Asp Thr Trp Asn
1 5 10

<210> 1399
<211> 18
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1399
Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala Ser Ser Val
1 5 10 15

Arg Gly

<210> 1400
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<221> source

<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1400
Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp Ala Phe Asp Val
1 5 10 15

<210> 1401
<211> 127
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1401
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
50 55 60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65 70 75 80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
85 90 95

Tyr Tyr Cys Ala Arg Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
100 105 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120 125

<210> 1402
<211> 14
<212> PRT

<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1402
Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
1 5 10

<210> 1403
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1403
Glu Val Ser Asn Arg Pro Ser
1 5

<210> 1404
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1404
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Ile
1 5 10

<210> 1405
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1405
Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr

1 5 10

<210> 1406
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1406
Glu Val Ser
1

<210> 1407
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1407
Tyr Thr Ser Ser Ser Thr Leu Tyr
1 5

<210> 1408
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1408
Ser Ser Asp Val Gly Gly Tyr Asn Tyr
1 5

<210> 1409
<211> 3
<212> PRT
<213> Artificial Sequence

<220>

<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1409
Glu Val Ser
1

<210> 1410
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1410
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Ile
1 5 10

<210> 1411
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1411
Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
1 5 10

<210> 1412
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
peptide"

<400> 1412
Glu Val Ser Asn Arg Pro Ser
1 5

<210> 1413
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic peptide"

<400> 1413
Ser Ser Tyr Thr Ser Ser Ser Thr Leu Tyr Ile
1 5 10

<210> 1414
<211> 111
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic polypeptide"

<400> 1414
Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser
85 90 95

Ser Thr Leu Tyr Ile Phe Gly Thr Gly Thr Lys Val Thr Val Leu
100 105 110

<210> 1415
<211> 253
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1415
Glu Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Leu Ser Asn
20 25 30

Ser Asp Thr Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr His Arg Ser Thr Trp Tyr Asp Asp Tyr Ala
50 55 60

Ser Ser Val Arg Gly Arg Val Ser Ile Asn Val Asp Thr Ser Lys Asn
65 70 75 80

Gln Tyr Ser Leu Gln Leu Asn Ala Val Thr Pro Glu Asp Thr Gly Val
85 90 95

Tyr Tyr Cys Ala Arg Asp Arg Leu Gln Asp Gly Asn Ser Trp Ser Asp
100 105 110

Ala Phe Asp Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ser
130 135 140

Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser Ile
145 150 155 160

Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr
165 170 175

```
Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile
            180                 185                 190


Tyr Glu Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly
        195                 200                 205


Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala
    210                 215                 220


Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Ser Ser Ser Thr
225                 230                 235                 240


Leu Tyr Ile Phe Gly Thr Gly Thr Lys Val Thr Val Leu
                245                 250


<210> 1416
<211> 719
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
      polypeptide"

<400> 1416
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15


Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
            20                  25                  30


Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45


Ser Ser Ile Phe Tyr Thr Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val
    50                  55                  60


Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80


Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
                85                  90                  95
```

```
Ala Arg Ile Gly Tyr Ala Gly Asp Ser Lys Tyr Ala Ile Trp Gly Gln
            100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
        115                 120                 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
    130                 135                 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145                 150                 155                 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
                165                 170                 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
            180                 185                 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
    290                 295                 300
```

```
Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
                405                 410                 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    450                 455                 460

Gly Gly Gly Gly Ser Glu Val Lys Leu Val Glu Ser Gly Gly Asp Leu
465                 470                 475                 480

Val Gln Pro Gly Asp Ser Leu Thr Leu Ser Cys Val Ala Ser Gly Phe
                485                 490                 495

Thr Phe Ser Lys Gln Gly Met His Trp Ile Arg Gln Ala Pro Lys Lys
            500                 505                 510

Gly Leu Glu Trp Ile Ala Met Ile Tyr Tyr Asp Ser Ser Lys Met Tyr
        515                 520                 525
```

```
Tyr Ala Asp Thr Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser
    530                 535                 540

Lys Asn Thr Leu Tyr Leu Glu Met Asn Ser Leu Arg Ser Glu Asp Thr
545                 550                 555                 560

Ala Met Tyr Tyr Cys Ala Ser Phe Trp Trp Asp Leu Asp Phe Asp His
                565                 570                 575

Trp Gly Gln Gly Val Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser
            580                 585                 590

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
        595                 600                 605

Ile Leu Val Thr Gln Thr Pro Val Ser Leu Pro Val Ser Leu Gly Gly
    610                 615                 620

His Val Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Arg Ser Glu
625                 630                 635                 640

Gly Thr Thr Tyr Phe Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro
                645                 650                 655

Gln Leu Leu Ile Tyr Arg Val Ser Asn Arg Phe Ser Gly Val Pro Asp
            660                 665                 670

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser
        675                 680                 685

Arg Val Glu Pro Glu Asp Leu Gly Val Tyr Tyr Cys Leu Gln Ser Ser
    690                 695                 700

His Phe Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Leu Lys
705                 710                 715
```

<210> 1417
<211> 723
<212> PRT
<213> Artificial Sequence

<220>
<221> source
<223> /note="Description of Artificial Sequence: Synthetic
polypeptide"

<400> 1417
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Gly Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Phe Tyr Thr Gly Ser Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ile Gly Tyr Ala Gly Asp Ser Lys Tyr Ala Ile Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val
115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala
130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser
145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro
180 185 190

```
Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys
        195                 200                 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp
    210                 215                 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Ala Ala Gly Gly
225                 230                 235                 240

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
                245                 250                 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Lys His Glu
            260                 265                 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
        275                 280                 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
    290                 295                 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
305                 310                 315                 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu
                325                 330                 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
            340                 345                 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
        355                 360                 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
    370                 375                 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
385                 390                 395                 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
```

```
                405                 410                 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
            420                 425                 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
        435                 440                 445

Gly Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
    450                 455                 460

Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu
465                 470                 475                 480

Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe
                485                 490                 495

Thr Phe Asn Lys Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys
            500                 505                 510

Cys Leu Glu Trp Val Ala Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala
        515                 520                 525

Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp
    530                 535                 540

Asp Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu
545                 550                 555                 560

Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser
                565                 570                 575

Tyr Ile Ser Tyr Trp Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
            580                 585                 590

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
        595                 600                 605

Ser Gly Gly Gly Gly Ser Gln Thr Val Val Thr Gln Glu Pro Ser Leu
    610                 615                 620
```

```
Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr
625                 630                 635                 640


Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn Trp Val Gln Gln Lys Pro
                645                 650                 655


Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Lys Phe Leu Ala Pro
            660                 665                 670


Gly Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala
        675                 680                 685


Leu Thr Leu Ser Gly Val Gln Pro Glu Asp Glu Ala Glu Tyr Tyr Cys
    690                 695                 700


Val Leu Trp Tyr Ser Asn Arg Trp Val Phe Gly Cys Gly Thr Lys Leu
705                 710                 715                 720


Thr Val Leu
```