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(54) Title: TRISPECIFIC BINDING MOLECULES AGAINST TUMOR-ASSOCIATED ANTIGENS AND USES THEREOF

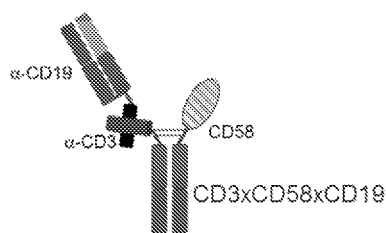
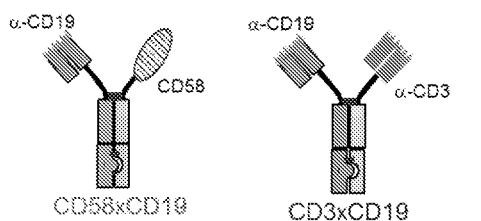


FIG. 2

(57) Abstract: The present disclosure provides trispecific binding molecules that specifically bind to CD2, CD3 and a tumor-associated antigen, conjugates comprising the trispecific binding molecules, and pharmaceutical compositions comprising the trispecific binding molecules and the conjugates. The disclosure further provides methods of using the trispecific binding molecules to treat cancers that express the tumor-associated antigens. The disclosure yet further provides recombinant host cells engineered to express the trispecific binding molecules and methods of producing the trispecific binding molecules by culturing the host cells under conditions in which the trispecific binding molecules are expressed.



TRISPECIFIC BINDING MOLECULES AGAINST TUMOR-ASSOCIATED ANTIGENS AND USES THEREOF

1. CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the priority benefit of U.S. provisional application no. 62/589,331, filed November 21, 2017, the contents of which are incorporated herein in their entireties by reference thereto.

2. SEQUENCE LISTING

[0002] 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 November 19, 2018, is named NOV-001WO_SL.txt and is 592,187 bytes in size.

3. BACKGROUND

[0003] Redirected targeted T-cell lysis (RTCC) is an exciting mechanism for first line treatment and refractory settings. Antibodies and antibody fragments with their exquisite selectivity have been successfully engineered in a variety of formats to allow for the dual specificities required to cross-link T-cells to a single receptor on the target cell.

[0004] First line treatments for some indications or the indications themselves may promote immune suppressive environments to promote T-cell anergy, reducing the efficacy of existing RTCC therapies. Acute myeloid lymphoma, for example, has been shown to be a particularly evasive disease in the context of avoid immune surveillance (Teague and Klein, 2013, Journal for ImmunoTherapy of Cancer 1:13). The solid tumor micro-environment can also provide mechanisms of escape and promote survival of tumor cells through a variety of pathways (Vaney *et al.*, 2015, Seminars in Cancer Biology 35:S151-S184).

[0005] Therefore, there is a need for improved RTCC approaches.

4. SUMMARY

[0006] The present disclosure extends the principles of RTCC by providing multispecific binding molecules that engage a tumor-associated antigen ("TAA") and CD2 in addition to CD3 or other component of a TCR complex on T-cells.

[0007] The present invention is based, at least in part, on the finding that engaging CD2 in addition to a component of a TCR complex will improve the clinical outcomes of RTCC therapy by activating T cell subpopulations that would be refractory to stimulation using bispecific engagers that target only a TAA and a TCR complex. As shown in the Examples, the outcome of treating tumors with trispecific binding molecules that engage a TAA, CD2 and CD3 results in

improved anti-tumor activity as compared to engaging the TAA and CD3 only, particularly in the presence of anergic T-cells. Without being bound by theory, the inventors believe that combining CD2- and TCR complex-engagement in a single multispecific molecule can stimulate both a primary signaling pathway that promotes T-cell mediated lysis of tumor cells (by clustering TCRs, for example) and a second co-stimulatory pathway to induce T-cell proliferation and potentially overcome anergy.

[0008] Accordingly, the present disclosure provides trispecific binding molecules (“TBMs”) that bind to (1) a tumor-associated antigen (“TAA”), (2) CD2, and (3) CD3 or other component of a TCR complex. The TBMs comprise at least three antigen-binding modules (“ABMs”) that can bind TAA, CD2 and a component of a TCR complex. In some embodiments, each antigen-binding module is capable of binding its respective target at the same time as each of the other antigen-binding modules is bound to its respective target. Each ABM may be immunoglobulin- or non-immunoglobulin-based, and therefore the TBMs of the disclosure can include immunoglobulin-based ABMs, non-immunoglobulin-based ABMs, or a combination thereof. Immunoglobulin-based ABMs that can be used in the TBMs of the disclosure are described in Section 6.2.1 and specific embodiments 31 to 406, 575 to 583, 591 to 660, 662 to 667, 671, 673 to 762 and 830 to 898, *infra*. Non-immunoglobulin-based ABMs that can be used in the TBMs of the disclosure are described in Section 6.2.2 and specific embodiments 2 to 30, 403 to 406 and 584 to 589, *infra*. Further features of exemplary ABMs that bind to a component of a TCR complex are described in Section 6.5 and specific embodiments 38 to 106, 590 to 667, and 1045, *infra*. Further features of exemplary ABMs that bind to CD2 are described in Section 6.6 and specific embodiments 2 to 37, 403 to 406, 575 to 589, and 1044, *infra*. Further features of exemplary ABMs that bind to TAAs are described in Section 6.7 and specific embodiments 107 to 276, 346 to 406, 668 to 762, and 1046 *infra*.

[0009] The ABMs of a TBM of the disclosure (or portions thereof) can be connected to each other, for example, by short peptide linkers or by an Fc domain. Methods and components for connecting ABMs to form a TBM are described in Section 6.3 and specific embodiments 401 to 453, 763 to 829 and 899 to 957, *infra*.

[0010] TBMs of the disclosure have at least three ABMs (*i.e.*, a TBM is at least trivalent), but can also have more than three ABMs. For example, a TBM can have four ABMs (*i.e.*, is tetravalent), five ABMs (*i.e.*, is pentavalent), or six ABMs (*i.e.*, is hexavalent), provided that the TBM has at least one ABM that can bind a TAA, at least one ABM that can bind CD2, and at least one ABM that can bind a component of a TCR complex. Exemplary trivalent, tetravalent, pentavalent, and hexavalent TBM configurations are shown in FIG. 1 and described in Section 6.4 and specific embodiments 958 to 1042, *infra*.

[0011] The disclosure further provides nucleic acids encoding the TBMs of the disclosure (either in a single nucleic acid or a plurality of nucleic acids) and recombinant host cells and cell lines engineered to express the nucleic acids and TBMs of the disclosure. Exemplary nucleic acids, host cells, and cell lines are described in Section 6.8 and specific embodiments 570 to 573 and 1169 to 1176, *infra*.

[0012] The present disclosure further provides drug conjugates comprising the TBMs of the disclosure. Such conjugates are referred to herein as “antibody-drug conjugates” or “ADCs” for convenience, notwithstanding that some or all of the ABMs can be non-immunoglobulin domains. Examples of ADCs are described in Section 6.9 and specific embodiments 469 to 507 and 1054 to 1093, *infra*.

[0013] The present disclosure further provides preparations comprising a TBM or conjugate of the disclosure. Examples of preparations are described in Section 6.10 and specific embodiments 508 to 565 and 1094 to 1151, *infra*.

[0014] Pharmaceutical compositions comprising the TBMs and ADCs of the disclosure are also provided. Examples of pharmaceutical compositions are described in Section 6.11 and specific embodiments 566 and 1152, *infra*.

[0015] Further provided herein are methods of using the TBMs, the ADCs, and the pharmaceutical compositions of the disclosure, for example for treating proliferative conditions (e.g., cancers), on which the TAAs are expressed. Exemplary methods are described in Section 6.12 and specific embodiments 567 to 568 and 1153 to 1155, *infra*.

[0016] The disclosure further provides methods of using the TBMs, the ADCs, and the pharmaceutical compositions of the disclosure in combination with other agents and therapies. Exemplary agents, therapies, and methods of combination therapy are described in Section 6.13 and specific embodiments 569 and 1156 to 1168, *infra*.

5. BRIEF DESCRIPTION OF THE FIGURES

[0017] FIGS. 1A-1U: Exemplary TBM configurations. FIG. 1A illustrates components of the exemplary TBM configurations illustrated in FIGS. 1B-1Z. Not all regions connecting the different domains of each chain are illustrated (e.g., the linker connecting the VH and VL domains of an scFv, the hinge connecting the CH2 and CH3 domains of an Fc, *etc.*, are omitted). FIG. 1B-1O and 1V-Z illustrate trivalent TBMs; FIGS. 1P-1R illustrate tetravalent TBMs; FIG. 1S illustrates a pentavalent TBM, and FIGS. 1T-1U illustrate hexavalent TBMs.

[0018] FIG. 2: Schematics of the bispecific and trispecific constructs of Example 1.

[0019] FIGS. 3A-3D: Results of a re-directed T cell cytotoxicity assay using human CD-19-expressing Nalm6 target cells and a bispecific construct targeting human CD3 and human growth hormone, a bispecific construct targeting human CD3 and human CD19, and a TBM

targeting human CD3, human CD2 and human CD19. FIG 3A-3B: results obtained using pan T effector cells from a first donor after 24 hour (FIG. 3A) and 48 hour (FIG. 3B) incubations. FIG 3C-3D: results obtained using pan T effector cells from a second donor after 24 hour (FIG. 3C) and 48 hour (FIG. 3D) incubations.

[0020] FIGS. 4A-4B: Results of a re-directed T cell cytotoxicity assay using human CD-19-expressing Daudi target cells and a bispecific construct targeting human CD3 and human growth hormone, a bispecific construct targeting human CD3 and human CD19, and a TBM targeting human CD3, human CD2 and human CD19. FIG 4A: results obtained using pan T effector cells from a first donor after a 48-hour incubation. FIG 4B: results obtained using pan T effector cells from a second donor after a 48 hour incubation.

[0021] FIG. 5: Results of a re-directed T cell cytotoxicity assay using negative control human K562 target cells and a bispecific construct targeting human CD3 and human growth hormone, a bispecific construct targeting human CD3 and human CD19, and a TBM targeting human CD3, human CD2 and human CD19.

[0022] FIG. 6A-6E: Results of a re-directed T cell cytotoxicity assay using human CD-19-expressing Nalm6 target cells and a bispecific construct targeting human CD3 and human growth hormone, a bispecific construct targeting human CD3 and human CD19, and a TBM targeting human CD3, human CD2 and human CD19. FIG. 6A-6E show results obtained using pan T effector cells from five different donors.

[0023] FIG. 7: Results of a re-directed T cell cytotoxicity assay using human CD-19-expressing Nalm6 target cells and a bispecific construct targeting human CD3 and human growth hormone, a bispecific construct targeting human CD3 and human CD19, and a TBM targeting human CD3, human CD2 and human CD19. FIG. 7 shows results obtained using human cryopreserved PBMCs from a patient diagnosed with acute myeloid leukemia.

[0024] FIGS. 8A-8D: Results of a re-directed T cell cytotoxicity assay using human CD-19-expressing Nalm6 target cells and a bispecific construct targeting human CD3 and human growth hormone, a bispecific construct targeting human CD3 and human CD19, and a TBM targeting human CD3, human CD2 and human CD19. FIG. 8A-8D show results obtained from target cell rechallenges at 48 hours, 72 hours, 96 hours, and 120 hours, respectively.

[0025] FIG. 9A-9B: Cell proliferation assay results. CD4⁺ sorted cells are shown in FIG 9A and CD8⁺ sorted cells are shown in FIG. 9B.

[0026] FIGS. 10A-10F: Results of a cytokine release assay using human CD-19-expressing Nalm6 target cells and a bispecific construct targeting human CD3 and human growth hormone, a bispecific construct targeting human CD3 and human CD19, and a TBM targeting

human CD3, human CD2 and human CD19. FIG. 10A: IFN γ ; FIG. 10B: TNF α ; FIG. 10C: IL2; FIG. 10D: IL10; FIG. 10E: IL6; FIG. 10F: figure legend.

[0027] FIG. 11: Results of a granzyme B ELISpot assay using human CD-19-expressing Nalm6 target cells and a bispecific construct targeting human CD3 and human growth hormone, a bispecific construct targeting human CD3 and human CD19, and a TBM targeting human CD3, human CD2 and human CD19.

[0028] FIGS. 12A-C: Schematics of the trispecific constructs of Example 2. FIG. 12A: AB2-1; FIG. 12B: AB2-2; FIG. 12C: AB2-3.

[0029] FIG. 13: Results of a re-directed T cell cytotoxicity assay using human CD-19-expressing Nalm6 target cells and TBMs targeting human CD3, human CD2 and human CD19 (Example 2).

[0030] FIG. 14: Results of a re-directed T cell cytotoxicity assay using human CD-19-expressing Nalm6 target cells and a bispecific construct targeting human CD3 and human growth hormone, a bispecific construct targeting human CD3 and human CD19, and a TBM targeting human CD3, human CD2 and human CD19 (Example 2). Fig. 14 shows results obtained using cynomolgus monkey pan T effector cells.

[0031] FIG. 15: Results of a NFAT activation assay using TBMs targeting human CD3, human CD2 and human CD19 (Example 2).

[0032] FIGS. 16A-E: Schematics of the trispecific constructs of Example 3. FIG. 16A: AB3-1; FIG. 16B: AB3-2; FIG. 16C: AB3-3; FIG. 16D: AB3-4; FIG. 16E: AB3-5.

[0033] FIG. 17: Results of a re-directed T cell cytotoxicity assay using human CD-19-expressing Nalm6 target cells and TBMs targeting human CD3, human CD2 and human CD19 (Example 3).

[0034] FIG. 18: Results of a NFAT activation assay using TBMs targeting human CD3, human CD2 and human CD19 (Example 3).

[0035] FIGS. 19A-C: Schematics of the trispecific constructs of Example 4. FIG. 19A: AB4-1; FIG. 19B: AB4-2; FIG. 19C: AB4-3.

[0036] FIG. 20: Results of a re-directed T cell cytotoxicity assay using human CD-19-expressing Nalm6 target cells and TBMs targeting human CD3, human CD2 and human CD19 (Example 4).

[0037] FIG. 21: Results of a NFAT activation assay using TBMs targeting human CD3, human CD2 and human CD19 (Example 4).

[0038] FIGS. 22A-22D: Results of a cytokine release assay using TBMs targeting human CD3, human CD2 and human CD19 (Example 4). FIG. 22A: IL-2; FIG. 22B: TNF α ; FIG. 22C: IFN γ ; FIG. 22D: figure legend

[0039] FIGS. 23A-23B: Schematics of the bispecific and trispecific constructs of Example 5. FIG. 23A: bispecific construct; FIG. 23B: trispecific construct.

[0040] FIG. 24: Results of a re-directed T cell cytotoxicity assay using human CD-19-expressing Nalm6 target cells and either bispecific constructs targeting human CD3 and human CD19 or TBMs targeting human CD3, human CD2 and human CD19 (Example 5).

[0041] FIGS. 25A-25B: Results of a cytokine release assay using human CD-19-expressing Nalm6 target cells and bispecific constructs targeting human CD3 and human CD19, and TBMs targeting human CD3, human CD2 and human CD19 (Example 5). FIG. 25A shows results for constructs having CD3 binding arms corresponding to BMA031 and FIG. 25B shows results for constructs having CD3 binding arms corresponding to OKT3. Results for trispecific constructs are shown in black; results for bispecific constructs are shown in gray.

[0042] FIGS. 26A-26B: Schematics of the bispecific and trispecific constructs of Example 6. FIG. 26A: bispecific construct; FIG. 26B: trispecific construct.

[0043] FIG. 27: Results of a re-directed T cell cytotoxicity assay using human Her2-expressing HCC1954 target cells and a bispecific construct targeting human CD3 and human Her2 or a TBM targeting human CD3, human CD2 and human Her2 (Example 6).

[0044] FIG. 28: Results of a cytokine release assay using human Her2-expressing HCC1954 target cells and a bispecific construct targeting human CD3 and human Her2, and TBMs targeting human CD3, human CD2 and either human Her2 or GH (Example 6).

[0045] FIGS. 29A-B: Schematics of the bispecific and trispecific constructs of Example 7. FIG. 29A: bispecific construct; FIG. 29B: trispecific construct.

[0046] FIG. 30: Results of a re-directed T cell cytotoxicity assay using human mesothelin-expressing OVCAR8 target cells and a bispecific construct targeting human CD3 and human mesothelin or a TBM targeting human CD3, human CD2 and human mesothelin (Example 7).

[0047] FIG. 31: Results of a cytokine release assay using human Mesothelin-expressing OvcAR8 target cells and a bispecific construct targeting human CD3 and human mesothelin (MSLN), and TBMs targeting human CD3, human CD2 and either human mesothelin or GH (Example 6).

[0048] FIG. 32: Schematics of the trispecific construct of Example 8.

6. DETAILED DESCRIPTION

6.1. Definitions

[0049] As used herein, the following terms are intended to have the following meanings:

[0050] **Antigen-binding module**: The term “antigen-binding module” or “ABM” as used herein refers to a portion of a TBM of the disclosure that has the ability to bind to an antigen non-covalently, reversibly and specifically. An ABM may be immunoglobulin- or non-immunoglobulin-based. As used herein, the terms “ABM1” and “CD2 ABM” (and the like) refers to an ABM that binds specifically to CD2, the terms “ABM2” and “TCR ABM” (and the like) refers to an ABM that binds specifically to a component of a TCR complex, and the term “ABM3” and “TAA ABM” (and the like) refer to an ABM that binds specifically to a tumor-associated antigen. The terms ABM1, ABM2, and ABM3 are used merely for convenience and are not intended to convey any particular configuration of a TBM. In some embodiments, a TCR ABM binds to CD3 (referred to herein a “CD3 ABM” or the like). Accordingly, disclosures relating to ABM2 and TCR ABMs are also applicable to CD3 ABMs.

[0051] **Antibody**: The term “antibody” as used herein refers to a polypeptide (or set of polypeptides) of the immunoglobulin family that is capable of binding an antigen non-covalently, reversibly and specifically. For example, a naturally occurring “antibody” of the IgG type is a tetramer comprising at least two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds. Each heavy chain is comprised of a heavy chain variable region (abbreviated herein as VH) and a heavy chain constant region. The heavy chain constant region is comprised of three domains, CH1, CH2 and CH3. Each light chain is comprised of a light chain variable region (abbreviated herein as VL) and a light chain constant region. The light chain constant region is comprised of one domain (abbreviated herein as CL). The VH and VL regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDR), interspersed with regions that are more conserved, termed framework regions (FR). Each VH and VL is composed of three CDRs and four FRs arranged from amino-terminus to carboxy-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. The variable regions of the heavy and light chains contain a binding domain that interacts with an antigen. The constant regions of the antibodies may mediate the binding of the immunoglobulin to host tissues or factors, including various cells of the immune system (e.g., effector cells) and the first component (C1q) of the classical complement system. The term “antibody” includes, but is not limited to, monoclonal antibodies, human antibodies, humanized antibodies, camelised antibodies, chimeric antibodies, bispecific or multispecific antibodies and anti-idiotypic (anti-Id) antibodies (including, e.g., anti-Id antibodies to antibodies of the disclosure). The antibodies can be of any isotype/class (e.g., IgG, IgE, IgM, IgD, IgA and IgY) or subclass (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2).

[0052] Both the light and heavy chains are divided into regions of structural and functional homology. The terms “constant” and “variable” are used functionally. In this regard, it will be appreciated that the variable domains of both the light (VL) and heavy (VH) chain portions determine antigen recognition and specificity. Conversely, the constant domains of the light chain (CL) and the heavy chain (CH1, CH2 or CH3) confer important biological properties such as secretion, transplacental mobility, Fc receptor binding, complement binding, and the like. By convention the numbering of the constant region domains increases as they become more distal from the antigen-binding site or amino-terminus of the antibody. The N-terminus is a variable region and at the C-terminus is a constant region; the CH3 and CL domains actually comprise the carboxy-terminus of the heavy and light chain, respectively.

[0053] Antibody fragment: The term “antibody fragment” of an antibody as used herein refers to one or more portions of an antibody. In some embodiments, these portions are part of the contact domain(s) of an antibody. In some other embodiments, these portion(s) are antigen-binding fragments that retain the ability of binding an antigen non-covalently, reversibly and specifically, sometimes referred to herein as the “antigen-binding fragment”, “antigen-binding fragment thereof,” “antigen-binding portion”, and the like. Examples of binding fragments include, but are not limited to, single-chain Fvs (scFv), a Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CH1 domains; a F(ab)2 fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; a Fd fragment consisting of the VH and CH1 domains; a Fv fragment consisting of the VL and VH domains of a single arm of an antibody; a dAb fragment (Ward *et al.*, (1989) Nature 341:544-546), which consists of a VH domain; and an isolated complementarity determining region (CDR). Thus, the term “antibody fragment” encompasses both proteolytic fragments of antibodies (*e.g.*, Fab and F(ab)2 fragments) and engineered proteins comprising one or more portions of an antibody (*e.g.*, an scFv).

[0054] Antibody fragments can also be incorporated into single domain antibodies, maxibodies, minibodies, intrabodies, diabodies, triabodies, tetrabodies, v-NAR and bis-scFv (see, *e.g.*, Hollinger and Hudson, 2005, Nature Biotechnology 23: 1126-1136). Antibody fragments can be grafted into scaffolds based on polypeptides such as Fibronectin type III (Fn3) (see U.S. Pat. No. 6,703,199, which describes fibronectin polypeptide monobodies).

[0055] Antibody fragments can be incorporated into single chain molecules comprising a pair of tandem Fv segments (for example, VH-CH1-VH-CH1) which, together with complementary light chain polypeptides (for example, VL-VC-VL-VC), form a pair of antigen-binding regions (Zapata *et al.*, 1995, Protein Eng. 8:1057-1062; and U.S. Pat. No. 5,641,870).

[0056] Antigen-binding domain: The term “antigen-binding domain” refers a portion of a molecule that has the ability to bind to an antigen non-covalently, reversibly and specifically.

Exemplary antigen-binding domains include antigen-binding fragments and portions of both immunoglobulin and non-immunoglobulin based scaffolds that retain the ability of binding an antigen non-covalently, reversibly and specifically. As used herein, the term “antigen-binding domain” encompasses antibody fragments that retain the ability of binding an antigen non-covalently, reversibly and specifically.

[0057] Half Antibody: The term “half antibody” refers to a molecule that comprises at least one ABM or ABM chain and can associate with another molecule comprising an ABM or ABM chain through, *e.g.*, a disulfide bridge or molecular interactions (*e.g.*, knob-in-hole interactions between Fc heterodimers). A half antibody can be composed of one polypeptide chain or more than one polypeptide chains (*e.g.*, the two polypeptide chains of a Fab). In a preferred embodiment, a half-antibody comprises an Fc region.

[0058] An example of a half antibody is a molecule comprising a heavy and light chain of an antibody (*e.g.*, an IgG antibody). Another example of a half antibody is a molecule comprising a first polypeptide comprising a VL domain and a CL domain, and a second polypeptide comprising a VH domain, a CH1 domain, a hinge domain, a CH2 domain, and a CH3 domain, wherein said VL and VH domains form an ABM. Yet another example of a half antibody is a polypeptide comprising an scFv domain, a CH2 domain and a CH3 domain.

[0059] A half antibody might include more than one ABM, for example a half-antibody comprising (in N- to C-terminal order) an scFv domain, a CH2 domain, a CH3 domain, and another scFv domain.

[0060] Half antibodies might also include an ABM chain that when associated with another ABM chain in another half antibody forms a complete ABM.

[0061] Thus, a TBM can comprise one, more typically two, or even more than two half antibodies, and a half antibody can comprise one or more ABMs or ABM chains.

[0062] In some TBMs, a first half antibody will associate, *e.g.*, heterodimerize, with a second half antibody. In other TBMs, a first half antibody will be covalently linked to a second half antibody, for example through disulfide bridges or chemical crosslinking. In yet other TBMs, a first half antibody will associate with a second half antibody through both covalent attachments and non-covalent interactions, for example disulfide bridges and knob-in-hole interactions.

[0063] The term “half antibody” is intended for descriptive purposes only and does not connote a particular configuration or method of production. Descriptions of a half antibody as a “first” half antibody, a “second” half antibody, a “left” half antibody, a “right” half antibody or the like are merely for convenience and descriptive purposes.

[0064] Complementarity Determining Region: The terms “complementarity determining region” or “CDR,” as used herein, refer to the sequences of amino acids within antibody

variable regions which confer antigen specificity and binding affinity. For example, in general, there are three CDRs in each heavy chain variable region (e.g., CDR-H1, CDR-H2, and CDR-H3) and three CDRs in each light chain variable region (CDR-L1, CDR-L2, and CDR-L3). 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) and ImMunoGenTics (IMGT) numbering (Lefranc, 1999, The Immunologist 7:132-136 (1999); Lefranc *et al.*, 2003, Dev. Comp. Immunol. 27:55-77 ("IMGT" numbering scheme). For example, for classic formats, under Kabat, the CDR amino acid residues in the heavy chain variable domain (VH) are numbered 31-35 (CDR-H1), 50-65 (CDR-H2), and 95-102 (CDR-H3); and the CDR amino acid residues in the light chain variable domain (VL) are numbered 24-34 (CDR-L1), 50-56 (CDR-L2), and 89-97 (CDR-L3). Under Chothia, the CDR amino acids in the VH are numbered 26-32 (CDR-H1), 52-56 (CDR-H2), and 95-102 (CDR-H3); and the amino acid residues in VL are numbered 26-32 (CDR-L1), 50-52 (CDR-L2), and 91-96 (CDR-L3). By combining the CDR definitions of both Kabat and Chothia, the CDRs consist of amino acid residues 26-35 (CDR-H1), 50-65 (CDR-H2), and 95-102 (CDR-H3) in human VH and amino acid residues 24-34 (CDR-L1), 50-56 (CDR-L2), and 89-97 (CDR-L3) in human VL. Under IMGT the CDR amino acid residues in the VH are numbered approximately 26-35 (CDR-H1), 51-57 (CDR-H2) and 93-102 (CDR-H3), and the CDR amino acid residues in the VL are numbered approximately 27-32 (CDR-L1), 50-52 (CDR-L2), and 89-97 (CDR-L3) (numbering according to "Kabat"). Under IMGT, the CDR regions of an antibody can be determined using the program IMGT/DomainGap Align.

[0065] Single Chain Fv or scFv: The term "single-chain Fv" or "scFv" as used herein refers to antibody fragments comprise the VH and VL domains of an antibody, wherein these domains are present in a single polypeptide chain. Preferably, the Fv polypeptide further comprises a polypeptide linker between the VH and VL domains which enables the scFv to form the desired structure for antigen-binding. For a review of scFv see Plückthun in The Pharmacology of Monoclonal Antibodies, vol. 113, Rosenberg and Moore eds., (1994) Springer-Verlag, New York, pp. 269-315.

[0066] Diabody: The term "diabody" as used herein refers to small antibody fragments with two antigen-binding sites, typically formed by pairing of scFv chains. Each scFv comprises a heavy chain variable domain (VH) connected to a light chain variable domain (VL) in the same polypeptide chain (VH-VL, where the VH is either N-terminal or C-terminal to the VL). Unlike a typical scFv in which the VH and VL are separated by a linker that allows the VH and VL on the same polypeptide chain to pair and form an antigen-binding domain, diabodies typically comprise a linker that is too short to allow pairing between the VH and VL domains on the same

chain, forcing the VH and VL domains to pair with the complementary domains of another chain and create two antigen-binding sites. Diabodies are described more fully in, for example, EP 404,097; WO 93/11161; and Hollinger *et al.*, 1993, Proc. Natl. Acad. Sci. USA 90:6444-6448.

[0067] Fv: The term “Fv” refers to the minimum antibody fragment derivable from an immunoglobulin that contains a complete target recognition and binding site. This region consists of a dimer of one heavy and one light chain variable domain in a tight, noncovalent association (VH-VL dimer). It is in this configuration that the three CDRs of each variable domain interact to define a target binding site on the surface of the VH-VL dimer. Often, the six CDRs confer target binding specificity to the antibody. However, in some instances even a single variable domain (or half of an Fv comprising only three CDRs specific for a target) can have the ability to recognize and bind target. The reference to a VH-VL dimer herein is not intended to convey any particular configuration. By way of example and not limitation, the VH and VL can come together in any configuration described herein to form a half antibody, or can each be present on a separate half antibody and come together to form an antigen binding domain when the separate half antibodies associate, for example to form a TBM of the disclosure. When present on a single polypeptide chain (*e.g.*, a scFv), the VH and be N-terminal or C-terminal to the VL.

[0068] Multispecific binding molecules: The term “multispecific binding molecules” refers to molecules that specifically bind 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).

[0069] Trispecific binding molecules: The term “trispecific binding molecules” or “TBMs” refers to molecules that specifically bind to three antigens and comprise three or more antigen-binding domains. The TBMs of the disclosure comprise at least one antigen-binding domain which is specific for a component of a TCR complex, at least one antigen-binding domain which is specific for CD2, and at least one antigen-binding domain which is specific for a TAA. 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). Representative TBMs are illustrated in FIG. 1. TBMs can comprise one, two, three, four or even more polypeptide chains. For example, the TBM illustrated in FIG. 1M comprises a single polypeptide chain comprising three scFvs connected by ABM linkers one a single polypeptide chain. The TBM illustrated in FIG. 1K comprises two polypeptide chains comprising three scFvs connected by, *inter alia*, an Fc domain. The TBM illustrated in FIG. 1J comprises three polypeptide chains forming an scFv, a ligand, and a Fab connected by, *inter alia*, an Fc domain. The TBM illustrated in FIG. 1C comprises four polypeptide chains forming three Fabs

connected by, *inter alia*, an Fc domain. The TBM illustrated in FIG. 1T comprises 6 polypeptide chains forming four Fabs and two scFvs connected by, *inter alia*, an Fc domain.

[0070] VH: The term “VH” refers to the variable region of an immunoglobulin heavy chain of an antibody, including the heavy chain of an Fv, scFv, dsFv or Fab.

[0071] VL: The term “VL” refers to the variable region of an immunoglobulin light chain, including the light chain of an Fv, scFv, dsFv or Fab.

[0072] Operably linked: The term “operably linked” refers to a functional relationship between two or more peptide or polypeptide domains or nucleic acid (e.g., DNA) segments. In the context of a fusion protein or other polypeptide, the term “operably linked” means that two or more amino acid segments are linked so as to produce a functional polypeptide. For example, in the context of a TBM of the disclosure, separate ABMs (or chains of an ABM) can be through peptide linker sequences. In the context of a nucleic acid encoding a fusion protein, such as a polypeptide chain of a TBM of the disclosure, “operably linked” means that the two nucleic acids are joined such that the amino acid sequences encoded by the two nucleic acids remain in-frame. In the context of transcriptional regulation, the term refers to the functional relationship of a transcriptional regulatory sequence to a transcribed sequence. For example, a promoter or enhancer sequence is operably linked to a coding sequence if it stimulates or modulates the transcription of the coding sequence in an appropriate host cell or other expression system.

[0073] Associated: The term “associated” in the context of a TBM refers to a functional relationship between two or more polypeptide chains. In particular, the term “associated” means that two or more polypeptides are associated with one another, e.g., non-covalently through molecular interactions or covalently through one or more disulfide bridges or chemical cross-linkages, so as to produce a functional TBM in which ABM1, ABM2 and ABM3 can bind their respective targets. Examples of associations that might be present in a TBM of the disclosure include (but are not limited to) associations between Fc regions in an Fc domain (homodimeric or, more preferably, heterodimeric as described in Section 6.3.1.5), associations between VH and VL regions in a Fab or Fv, and associations between CH1 and CL in a Fab.

[0074] ABM chain: Individual ABMs can exist as one (e.g., in the case of an scFv) polypeptide chain or form through the association of more than one polypeptide chains (e.g., in the case of a Fab). As used herein, the term “ABM chain” refers to all or a portion of an ABM that exists on a single polypeptide chain. The use of the term “ABM chain” is intended for convenience and descriptive purposes only and does not connote a particular configuration or method of production.

[0075] Host cell or recombinant host cell: The terms “host cell” or “recombinant host cell” refer to a cell that has been genetically-engineered, e.g., through introduction of a heterologous

nucleic acid. It should be understood that such terms are intended to refer not only to the particular subject cell but to the progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term "host cell" as used herein. A host cell may carry the heterologous nucleic acid transiently, *e.g.*, on an extrachromosomal heterologous expression vector, or stably, *e.g.*, through integration of the heterologous nucleic acid into the host cell genome. For purposes of expressing a TBM of the disclosure, a host cell is preferably a cell line of mammalian origin or mammalian-like characteristics, such as monkey kidney cells (COS, *e.g.*, COS-1, COS-7), HEK293, baby hamster kidney (BHK, *e.g.*, BHK21), Chinese hamster ovary (CHO), NSO, PerC6, BSC-1, human hepatocellular carcinoma cells (*e.g.*, Hep G2), SP2/0, HeLa, Madin-Darby bovine kidney (MDBK), myeloma and lymphoma cells, or derivatives and/or engineered variants thereof. The engineered variants include, *e.g.*, glycan profile modified and/or site-specific integration site derivatives.

[0076] Sequence identity: The term percent "identity," in the context of two or more nucleic acids or polypeptide sequences, refers to two or more sequences that are the same. Two sequences are "substantially identical" if two sequences have a specified percentage of amino acid residues or nucleotides that are the same (*e.g.*, 60% identity, optionally 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% identity over a specified region, or, when not specified, over the entire sequence), when compared and aligned for maximum correspondence over a comparison window, or designated region as measured using one of the following sequence comparison algorithms or by manual alignment and visual inspection. Optionally, the identity exists over a region that is at least about 50 nucleotides (or, in the case of a peptide or polypeptide, at least about 10 amino acids) in length, or more preferably over a region that is 100 to 500 or 1000 or more nucleotides (or 20, 50, 200 or more amino acids) in length.

[0077] For sequence comparison, typically one sequence acts as a reference sequence, to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are entered into a computer, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated. Default program parameters can be used, or alternative parameters can be designated. The sequence comparison algorithm then calculates the percent sequence identities for the test sequences relative to the reference sequence, based on the program parameters. Methods of alignment of sequences for comparison are well known in the art. Optimal alignment of sequences for comparison can be conducted, *e.g.*, by the local homology algorithm of Smith and Waterman, 1970, *Adv. Appl. Math.* 2:482c, by the homology alignment algorithm of Needleman and

Wunsch, 1970, J. Mol. Biol. 48:443, by the search for similarity method of Pearson and Lipman, 1988, Proc. Nat'l. Acad. Sci. USA 85:2444, by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, WI), or by manual alignment and visual inspection (see, e.g., Brent *et al.*, 2003, Current Protocols in Molecular Biology).

[0078] Two examples of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul *et al.*, 1977, Nuc. Acids Res. 25:3389-3402; and Altschul *et al.*, 1990, J. Mol. Biol. 215:403-410, respectively. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information.

[0079] The percent identity between two amino acid sequences can also be determined using the algorithm of Meyers and Miller, 1988, Comput. Appl. Biosci. 4:11-17, which has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4. In addition, the percent identity between two amino acid sequences can be determined using the Needleman and Wunsch, 1970, J. Mol. Biol. 48:444-453) algorithm which has been incorporated into the GAP program in the GCG software package (available at www.gcg.com), using either a Blossum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6.

[0080] Conservative Sequence Modifications: The term “conservative sequence modifications” refers to amino acid modifications that do not significantly affect or alter the binding characteristics of a TBM or a component thereof (e.g., an ABM or an Fc region). Such conservative modifications include amino acid substitutions, additions and deletions. Modifications can be introduced into a TBM of the disclosure by standard techniques known in the art, such as site-directed mutagenesis and PCR-mediated mutagenesis. Conservative amino acid substitutions are ones in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine, tryptophan), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine). Thus, one or more amino acid residues within a TBM of the disclosure can be replaced with other amino acid residues from the same side chain family and the altered TBM can be tested for, e.g., binding to target molecules and/or effective heterodimerization and/or effector function.

[0081] Mutation or modification: The terms “mutation” and “modification” in the context of a polypeptide as used herein can include substitution, addition or deletion of one or more amino acids.

[0082] Antibody Numbering Systems: In the present specification, the references to numbered amino acid residues in antibody domains are based on the EU numbering system unless otherwise specified (for example, in Tables 7B and 7C). This system was originally devised by Edelman *et al.*, 1969, Proc. Nat’l Acad. Sci. USA 63:78-85 and is described in detail in Kabat *et al.*, 1991, in Sequences of Proteins of Immunological Interest, US Department of Health and Human Services, NIH, USA.

[0083] dsFv: The term “dsFv” refers to disulfide-stabilized Fv fragments. In a dsFv, a VH and VL are connected by an interdomain disulfide bond. To generate such molecules, one amino acid each in the framework region of in VH and VL are mutated to a cysteine, which in turn form a stable interchain disulfide bond. Typically, position 44 in the VH and position 100 in the VL are mutated to cysteines. See Brinkmann, 2010, Antibody Engineering 181-189, DOI:10.1007/978-3-642-01147-4_14. The term dsFv encompasses both what is known in the art a dsFv (a molecule in which the VH and VL are connected by an interchain disulfide bond but not a linker peptide) or scdsFv (a molecule in which the VH and VL are connected by a linker as well as an interchain disulfide bond).

[0084] Tandem of VH Domains: The term “a tandem of VH domains (or VHs)” as used herein refers to a string of VH domains, consisting of multiple numbers of identical VH domains of an antibody. Each of the VH domains, except the last one at the end of the tandem, has its C-terminus connected to the N-terminus of another VH domain with or without a linker. A tandem has at least 2 VH domains, and in particular embodiments of the TBMs of the disclosure has 3, 4, 5, 6, 7, 8, 9, or 10 VH domains. The tandem of VH can be produced by joining the encoding nucleic acids of each VH domain in a desired order using recombinant methods with or without a linker (*e.g.*, as described in Section 6.3.3) that enables them to be made as a single polypeptide chain. The N-terminus of the first VH domain in the tandem is defined as the N-terminus of the tandem, while the C-terminus of the last VH domain in the tandem is defined as the C-terminus of the tandem.

[0085] Tandem of VL Domains: The term “a tandem of VL domains (or VLs)” as used herein refers to a string of VL domains, consisting of multiple numbers of identical VL domains of an antibody. Each of the VL domains, except the last one at the end of the tandem, has its C-terminus connected to the N-terminus of another VL with or without a linker. A tandem has at least 2 VL domains, and in particular embodiments of the TBMs of the disclosure has 3, 4, 5, 6, 7, 8, 9, or 10 VL domains. The tandem of VL can be produced by joining the encoding nucleic acids of each VL domain in a desired order using recombinant methods with or without a linker

(e.g., as described in Section 6.3.3) that enables them to be made as a single polypeptide chain. The N-terminus of the first VL domain in the tandem is defined as the N-terminus of the tandem, while the C-terminus of the last VL domain in the tandem is defined as the C-terminus of the tandem.

[0086] Monovalent: The term “monovalent” as used herein in the context of an antigen-binding molecule refers to an antigen-binding molecule that has a single antigen-binding domain.

[0087] Bivalent: The term “bivalent” as used herein in the context of an antigen-binding molecule refers to an antigen-binding molecule that has two antigen-binding domains. The domains can be the same or different. Accordingly, a bivalent antigen-binding molecule can be monospecific or bispecific.

[0088] Trivalent: The term “trivalent” as used herein in the context of an antigen-binding molecule (e.g., a TBM) refers to an antigen-binding molecule that has three antigen-binding domains. The TBMs of the disclosure are trispecific and specifically bind to CD2, a component of a TCR complex and a TAA. Accordingly, the trivalent TBMs of the disclosure have at least three antigen-binding domains that each bind to a different antigen. Examples of trivalent TBMs of the disclosure are shown schematically in FIGS. 1B-1U.

[0089] Tetravalent: The term “tetravalent” as used herein in the context of an antigen-binding molecule (e.g., a TBM) refers to an antigen-binding molecule that has four antigen-binding domains. The TBMs of the disclosure are trispecific and specifically bind to CD2, a component of a TCR complex and a TAA. Accordingly, the tetravalent TBMs of the disclosure generally have two antigen-binding domains that bind to the same antigen (preferably the TAA) and two antigen-binding domains that each bind to a separate antigen (preferably CD2 and a component of a TCR complex). Examples of tetravalent TBMs of the disclosure are shown schematically in FIGS. 1P-1R.

[0090] Pentavalent: The term “pentavalent” as used herein in the context of an antigen-binding molecule (e.g., a TBM) refers to an antigen-binding molecule that has five antigen-binding domains. The TBMs of the disclosure are trispecific and specifically bind to CD2, a component of a TCR complex and a TAA. Accordingly, the pentavalent TBMs of the disclosure generally have either (a) two pairs of antigen-binding domains that each bind to the same antigen and a single antigen-binding domain that binds to the third antigen or (b) three antigen-binding domains that bind to the same antigen and two antigen-binding domains that each bind to a separate antigen. An example of a pentavalent TBM of the disclosure is shown schematically in FIG. 1S.

[0091] Hexavalent: The term “hexavalent” as used herein in the context of an antigen-binding molecule (e.g., a TBM) refers to an antigen-binding molecule that has six antigen-binding domains. The TBMs of the disclosure are trispecific and specifically bind to CD2, a component of a TCR complex and a TAA. The hexavalent TBMs of the disclosure generally have three pairs of antigen-binding domains that each bind to the same antigen, although different configurations (e.g., three antigen-binding domains that bind to the TAA, two antigen-binding domains that bind to a component of a TCR complex, and one antigen-binding domain that binds to CD2, or three antigen-binding domains that bind to the TAA, two antigen-binding domains that bind to CD2, and one antigen-binding domain that binds to a component of a TCR complex) are within the scope of the disclosure. Examples of hexavalent TBMs of the disclosure are shown schematically in FIGS. 1T-1U.

[0092] Specifically (or selectively) binds: The term “specifically (or selectively) binds” to an antigen or an epitope refers to a binding reaction that is determinative of the presence of a cognate antigen or an epitope in a heterogeneous population of proteins and other biologics. The binding reaction can be but need not be mediated by an antibody or antibody fragment, but can also be mediated by, for example, any type of ABM described in Section 6.2, such as a ligand, a DARPin, *etc.* An ABM of the disclosure typically also has a dissociation rate constant (KD) (k_{off}/k_{on}) of less than $5 \times 10^{-2}M$, less than $10^{-2}M$, less than $5 \times 10^{-3}M$, less than $10^{-3}M$, less than $5 \times 10^{-4}M$, less than $10^{-4}M$, less than $5 \times 10^{-5}M$, less than $10^{-5}M$, less than $5 \times 10^{-6}M$, less than $10^{-6}M$, less than $5 \times 10^{-7}M$, less than $10^{-7}M$, less than $5 \times 10^{-8}M$, less than $10^{-8}M$, less than $5 \times 10^{-9}M$, or less than $10^{-9}M$, and binds to the target antigen with an affinity that is at least two-fold greater than its affinity for binding to a non-specific antigen (e.g., HSA). The term “specifically binds” does not exclude cross-species reactivity. For example, an antigen-binding module (e.g., an antigen-binding fragment of an antibody) that “specifically binds” to an antigen from one species may also “specifically bind” to that antigen in one or more other species. Thus, such cross-species reactivity does not itself alter the classification of an antigen-binding module as a “specific” binder. In certain embodiments, an antigen-binding module of the disclosure (e.g., ABM1, ABM2 and/or ABM3) that specifically binds to a human antigen has cross-species reactivity with one or more non-human mammalian species, e.g., a primate species (including but not limited to one or more of *Macaca fascicularis*, *Macaca mulatta*, and *Macaca nemestrina*) or a rodent species, e.g., *Mus musculus*. In other embodiments, the antigen-binding module of the disclosure (e.g., ABM1, ABM2 and/or ABM3) does not have cross-species reactivity.

[0093] Monoclonal Antibody: The term “monoclonal antibody” as used herein refers to polypeptides, including antibodies, antibody fragments, molecules (including TBMs), *etc.* that are derived from the same genetic source.

[0094] Humanized: The term “humanized” forms of non-human (e.g., murine) antibodies are chimeric antibodies that contain minimal sequence derived from non-human immunoglobulin. For the most part, humanized antibodies are human immunoglobulins (recipient antibody) in which residues from a hypervariable region of the recipient are replaced by residues from a hypervariable region of a non-human species (donor antibody) such as mouse, rat, rabbit or non-human primate having the desired specificity, affinity, and capacity. In some instances, framework region (FR) residues of the human immunoglobulin are replaced by corresponding non-human residues. Furthermore, humanized antibodies may comprise residues that are not found in the recipient antibody or in the donor antibody. These modifications are made to further refine antibody performance. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the hypervariable loops correspond to those of a non-human immunoglobulin and all or substantially all of the FRs are those of a human immunoglobulin sequence. The humanized antibody optionally will 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.*, 1986, Nature 321:522-525; Riechmann *et al.*, 1988, Nature 332:323-329; and Presta, 1992, Curr. Op. Struct. Biol. 2:593-596. See also the following review articles and references cited therein: Vaswani and Hamilton, 1998, Ann. Allergy, Asthma & Immunol. 1:105-115; Harris, 1995, Biochem. Soc. Transactions 23:1035-1038; Hurle and Gross, 1994, Curr. Op. Biotech. 5:428-433.

[0095] Human Antibody: The term “human antibody” as used herein includes antibodies having variable regions in which both the framework and CDR regions are derived from sequences of human origin. Furthermore, if the antibody contains a constant region, the constant region also is derived from such human sequences, e.g., human germline sequences, or mutated versions of human germline sequences or antibody containing consensus framework sequences derived from human framework sequences analysis, for example, as described in Knappik *et al.*, 2000, J Mol Biol 296, 57-86. The structures and locations of immunoglobulin variable domains, e.g., CDRs, may be defined using well known numbering schemes, e.g., the Kabat numbering scheme, the Chothia numbering scheme, or a combination of Kabat and Chothia (see, e.g., Lazikani *et al.*, 1997, J. Mol. Biol. 273:927-948; Kabat *et al.*, 1991, Sequences of Proteins of Immunological Interest, 5th edit., NIH Publication no. 91-3242 U.S. Department of Health and Human Services; Chothia *et al.*, 1987, J. Mol. Biol. 196:901-917; Chothia *et al.*, 1989, Nature 342:877-883).

[0096] Human antibodies may include amino acid residues not encoded by human sequences (e.g., mutations introduced by random or site-specific mutagenesis *in vitro* or by somatic mutation *in vivo*, or a conservative substitution to promote stability or manufacturing). However, the term “human antibody”, as used herein, is not intended to include antibodies in which CDR

sequences derived from the germline of another mammalian species, such as a mouse, have been grafted onto human framework sequences.

[0097] Chimeric Antibody: The term “chimeric antibody” (or antigen-binding fragment thereof) is an antibody molecule (or antigen-binding fragment thereof) in which (a) the constant region, or a portion thereof, is altered, replaced or exchanged so that the antigen-binding site (variable region) is linked to a constant region of a different or altered class, effector function and/or species, or an entirely different molecule which confers new properties to the chimeric antibody, e.g., an enzyme, toxin, hormone, growth factor, drug, etc.; or (b) the variable region, or a portion thereof, is altered, replaced or exchanged with a variable region having a different or altered antigen specificity. For example, a mouse antibody can be modified by replacing its constant region with the constant region from a human immunoglobulin. Due to the replacement with a human constant region, the chimeric antibody can retain its specificity in recognizing the antigen while having reduced antigenicity in human as compared to the original mouse antibody.

[0098] Effector Function: The term “effector function” refers to an activity of an antibody molecule that is mediated by binding through a domain of the antibody other than the antigen-binding domain, usually mediated by binding of effector molecules. Effector function includes complement-mediated effector function, which is mediated by, for example, binding of the C1 component of the complement to the antibody. Activation of complement is important in the opsonization and lysis of cell pathogens. The activation of complement also stimulates the inflammatory response and may also be involved in autoimmune hypersensitivity. Effector function also includes Fc receptor (FcR)-mediated effector function, which may be triggered upon binding of the constant domain of an antibody to an Fc receptor (FcR). Binding of antibody to Fc receptors on cell surfaces triggers a number of important and diverse biological responses including engulfment and destruction of antibody-coated particles, clearance of immune complexes, lysis of antibody-coated target cells by killer cells (called antibody-dependent cell-mediated cytotoxicity, or ADCC), release of inflammatory mediators, placental transfer and control of immunoglobulin production. An effector function of an antibody may be altered by altering, e.g., enhancing or reducing, the affinity of the antibody for an effector molecule such as an Fc receptor or a complement component. Binding affinity will generally be varied by modifying the effector molecule binding site, and in this case it is appropriate to locate the site of interest and modify at least part of the site in a suitable way. It is also envisaged that an alteration in the binding site on the antibody for the effector molecule need not alter significantly the overall binding affinity but may alter the geometry of the interaction rendering the effector mechanism ineffective as in non-productive binding. It is further envisaged that an effector function may also be altered by modifying a site not directly involved in effector molecule binding, but otherwise involved in performance of the effector function.

[0099] Recognize: The term “recognize” as used herein refers to an ABM that finds and interacts (*e.g.*, binds) with its epitope.

[0100] Epitope: An epitope, or antigenic determinant, is a portion of an antigen recognized by an antibody or other antigen-binding moiety as described herein. An epitope can be linear or conformational.

[0101] Nucleic Acid: The term “nucleic acid” is used herein interchangeably with the term “polynucleotide” and refers to deoxyribonucleotides or ribonucleotides and polymers thereof in either single- or double-stranded form. The term encompasses nucleic acids containing known nucleotide analogs or modified backbone residues or linkages, which are synthetic, naturally occurring, and non-naturally occurring, which have similar binding properties as the reference nucleic acid, and which are metabolized in a manner similar to the reference nucleotides. Examples of such analogs include, without limitation, phosphorothioates, phosphoramidates, methyl phosphonates, chiral-methyl phosphonates, 2-O-methyl ribonucleotides, peptide-nucleic acids (PNAs).

[0102] Unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conservatively modified variants thereof (*e.g.*, degenerate codon substitutions) and complementary sequences, as well as the sequence explicitly indicated. Specifically, as detailed below, 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.*, (1991) *Nucleic Acid Res.* 19:5081; Ohtsuka *et al.*, (1985) *J. Biol. Chem.* 260:2605-2608; and Rossolini *et al.*, (1994) *Mol. Cell. Probes* 8:91-98).

[0103] Vector: The term “vector” is intended to refer to a polynucleotide molecule capable of transporting another polynucleotide to which it has been linked. One type of vector is a “plasmid”, which refers to a circular double stranded DNA loop into which additional DNA segments may be ligated. Another type of vector is a viral vector, wherein additional DNA segments may be ligated into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (*e.g.*, bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (*e.g.*, non-episomal mammalian vectors) can be integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operably linked. Such vectors are referred to herein as “recombinant expression vectors” (or simply, “expression vectors”). In general, expression vectors of utility in recombinant DNA techniques are often in the form of plasmids. In the present specification, “plasmid” and “vector” may be used interchangeably as the plasmid is the most commonly used form of vector. However, the disclosure is intended to

include such other forms of expression vectors, such as viral vectors (e.g., replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

[0104] Binding Sequences: In reference to Tables 7, 8, 9, 11, 12 or 13 (including subparts thereof), the term “binding sequences” means an ABM having a full set of CDRs, a VH-VL pair, or an scFv set forth in that table.

[0105] VH-VL or VH-VL Pair: In reference to a VH-VL pair, whether on the same polypeptide chain or on different polypeptide chains, the terms “VH-VL” and “VH-VL pair” are used for convenience and are not intended to convey any particular orientation, unless the context dictates otherwise. Thus, a scFv comprising a “VH-VL” or “VH-VL pair” can have the VH and VL domains in any orientation, for example the VH N-terminal to the VL or the VL N-terminal to the VH.

[0106] Polypeptide and Protein: The terms “polypeptide” and “protein” are used interchangeably herein to refer to a polymer of amino acid residues. The phrases also apply to amino acid polymers in which one or more amino acid residue is an artificial chemical mimetic of a corresponding naturally occurring amino acid, as well as to naturally occurring amino acid polymers and non-naturally occurring amino acid polymer. Unless otherwise indicated, a particular polypeptide sequence also implicitly encompasses conservatively modified variants thereof.

[0107] Subject: The term “subject” includes human and non-human animals. Non-human animals include all vertebrates, e.g., mammals and non-mammals, such as non-human primates, sheep, dog, cow, chickens, amphibians, and reptiles. Except when noted, the terms “patient” or “subject” are used herein interchangeably.

[0108] Cancer: The term “cancer” refers to a disease characterized by the uncontrolled (and often rapid) 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, adrenal gland cancer, autonomic ganglial cancer, biliary tract cancer, bone cancer, endometrial cancer, eye cancer, fallopian tube cancer, genital tract cancers, large intestinal cancer, cancer of the meninges, oesophageal cancer, peritoneal cancer, pituitary cancer, penile cancer, placental cancer, pleura cancer, salivary gland cancer, small intestinal cancer, stomach cancer, testicular cancer, thymus cancer, thyroid cancer, upper aerodigestive cancers, urinary tract cancer, vaginal cancer, vulva cancer, lymphoma, leukemia, lung cancer and the like, e.g., any TAA-positive cancers of any of the foregoing types.

[0109] Tumor: The term “tumor” is used interchangeably with the term “cancer” 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.

[0110] Tumor-Associated Antigen: The term “tumor-associated antigen” or “TAA” refers to a molecule (typically a protein, carbohydrate, lipid or some combination thereof) 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 TAA 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 TAA 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 TAA 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 TAA 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. Accordingly, the term “TAA” encompasses antigens that are specific to cancer cells, sometimes known in the art as tumor-specific antigens (“TSAs”).

[0111] Treat, Treatment, Treating: 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 TBMs of the disclosure. 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.

6.2. Antigen Binding Modules

[0112] Typically, one or more ABMs of the TBMs of the disclosure comprise immunoglobulin-based antigen-binding domains, for example the sequences of antibody fragments or derivatives. These antibody fragments and derivatives typically include the CDRs of an antibody and can include larger fragments and derivatives thereof, *e.g.*, Fabs, scFabs, Fvs, and scFvs.

6.2.1. Immunoglobulin Based Modules

6.2.1.1. Fabs

[0113] In certain aspects, an ABM of the disclosure is a Fab domain. Fab domains can be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain, or through recombinant expression. Fab domains typically comprise a CH1 domain attached to a VH domain which pairs with a CL domain attached to a VL domain.

[0114] In a wild-type immunoglobulin, the VH domain is paired with the VL domain to constitute the Fv region, and the CH1 domain is paired with the CL domain to further stabilize the binding module. A disulfide bond between the two constant domains can further stabilize the Fab domain.

[0115] For the TBMs of the disclosure, it is advantageous to use Fab heterodimerization strategies to permit the correct association of Fab domains belonging to the same ABM and minimize aberrant pairing of Fab domains belonging to different ABMs. For example, the Fab heterodimerization strategies shown in Table 1 below can be used:

TABLE 1 Fab Heterodimerization Strategies						
Name	STRATEGY	VH	CH1	VL	CL	REFERENCE
F1	CrossMabCH1-CL	WT	CL domain	WT	CH1 domain	Schaefer <i>et al.</i> , 2011, Cancer Cell 2011; 20:472-86; PMID:22014573.
F2	orthogonal Fab VHVRD1CH1C RD2 - VLVRD1C λ CR D2	39K, 62E	H172A, F174G	1R, 38D, (36F)	L135Y, S176W	Lewis <i>et al.</i> , 2014, Nat Biotechnol 32:191-8
F3	orthogonal Fab VHVRD2CH1wt - VLVRD2C λ wt	39Y	WT	38R	WT	Lewis <i>et al.</i> , 2014, Nat Biotechnol 32:191-8
F4	TCR C α C β	39K	TCR C α	38D	TCR C β	Wu <i>et al.</i> , 2015, MAbs 7:364-76
F5	CR3	WT	T192E	WT	N137K, S114A	Golay <i>et al.</i> , 2016, J Immunol 196:3199-211.
F6	MUT4	WT	L143Q, S188V	WT	V133T, S176V	Golay <i>et al.</i> , 2016, J Immunol 196:3199-211.
F7	DuetMab	WT	F126C	WT	S121C	Mazor <i>et al.</i> , 2015, MAbs 7:377-89; Mazor <i>et al.</i> , 2015, MAbs 7:461-669.

[0116] Accordingly, in certain embodiments, correct association between the two polypeptides of a Fab is promoted by exchanging the VL and VH domains of the Fab for each other or exchanging the CH1 and CL domains for each other, e.g., as described in WO 2009/080251.

[0117] Correct Fab pairing can also be promoted by introducing one or more amino acid modifications in the CH1 domain and one or more amino acid modifications in the CL domain of the Fab and/or one or more amino acid modifications in the VH domain and one or more amino acid modifications in the VL domain. The amino acids that are modified are typically part of the VH:VL and CH1:CL interface such that the Fab components preferentially pair with each other rather than with components of other Fabs.

[0118] In one embodiment, the one or amino acid modifications are limited to the conserved framework residues of the variable (VH, VL) and constant (CH1, CL) domains as indicated by the Kabat numbering of residues. Almagro, 2008, *Frontiers In Bioscience* 13:1619-1633 provides a definition of the framework residues on the basis of Kabat, Chothia, and IMGT numbering schemes.

[0119] In one embodiment, the modifications introduced in the VH and CH1 and/or VL and CL domains are complementary to each other. Complementarity at the heavy and light chain interface can be achieved on the basis of steric and hydrophobic contacts, electrostatic/charge interactions or a combination of the variety of interactions. The complementarity between protein surfaces is broadly described in the literature in terms of lock and key fit, knob into hole, protrusion and cavity, donor and acceptor etc., all implying the nature of structural and chemical match between the two interacting surfaces.

[0120] In one embodiment, the one or more introduced modifications introduce a new hydrogen bond across the interface of the Fab components. In one embodiment, the one or more introduced modifications introduce a new salt bridge across the interface of the Fab components. Exemplary substitutions are described in WO 2014/150973 and WO 2014/082179, the contents of which are hereby incorporated by reference.

[0121] In some embodiments, the Fab domain comprises a 192E substitution in the CH1 domain and 114A and 137K substitutions in the CL domain, which introduces a salt-bridge between the CH1 and CL domains (see, Golay *et al.*, 2016, *J Immunol* 196:3199-211).

[0122] In some embodiments, the Fab domain comprises a 143Q and 188V substitutions in the CH1 domain and 113T and 176V substitutions in the CL domain, which serves to swap hydrophobic and polar regions of contact between the CH1 and CL domain (see, Golay *et al.*, 2016, *J Immunol* 196:3199-211).

[0123] In some embodiments, the Fab domain can comprise modifications in some or all of the VH, CH1, VL, CL domains to introduce orthogonal Fab interfaces which promote correct assembly of Fab domains (Lewis *et al.*, 2014 *Nature Biotechnology* 32:191–198). In an embodiment, 39K, 62E modifications are introduced in the VH domain, H172A, F174G modifications are introduced in the CH1 domain, 1R, 38D, (36F) modifications are introduced in

the VL domain, and L135Y, S176W modifications are introduced in the CL domain. In another embodiment, a 39Y modification is introduced in the VH domain and a 38R modification is introduced in the VL domain.

[0124] Fab domains can also be modified to replace the native CH1:CL disulfide bond with an engineered disulfide bond, thereby increasing the efficiency of Fab component pairing. For example, an engineered disulfide bond can be introduced by introducing a 126C in the CH1 domain and a 121C in the CL domain (see, Mazor *et al.*, 2015, MAbs 7:377-89).

[0125] Fab domains can also be modified by replacing the CH1 domain and CL domain with alternative domains that promote correct assembly. For example, Wu *et al.*, 2015, MAbs 7:364-76, describes substituting the CH1 domain with the constant domain of the α T cell receptor and substituting the CL domain with the β domain of the T cell receptor, and pairing these domain replacements with an additional charge-charge interaction between the VL and VH domains by introducing a 38D modification in the VL domain and a 39K modification in the VH domain.

[0126] ABMs of the disclosure can comprise a single chain Fab fragment, which is a polypeptide consisting of an antibody heavy chain variable domain (VH), an antibody constant domain 1 (CH1), an antibody light chain variable domain (VL), an antibody light chain constant domain (CL) and a linker. In some embodiments, the antibody domains and the linker have one of the following orders in N-terminal to C-terminal direction: a) VH-CH1-linker-VL-CL, b) VL-CL-linker-VH-CH1, c) VH-CL-linker-VL-CH1 or d) VL-CH1-linker-VH-CL. The linker can be a polypeptide of at least 30 amino acids, preferably between 32 and 50 amino acids. The single chain Fab domains are stabilized via the natural disulfide bond between the CL domain and the CH1 domain.

[0127] In an embodiment the antibody domains and the linker in the single chain Fab fragment have one of the following orders in N-terminal to C-terminal direction: a) VH-CH1-linker-VL-CL, or b) VL-CL-linker-VH-CH1, more preferably VL-CL-linker-VH-CH1.

[0128] In another embodiment the antibody domains and the linker in the single chain Fab fragment have one of the following orders in N-terminal to C-terminal direction: a) VH-CL-linker-VL-CH1 or b) VL-CH1-linker-VH-CL.

[0129] Optionally in the single chain Fab fragment, additionally to the natural disulfide bond between the CL-domain and the CH1 domain, also the antibody heavy chain variable domain (VH) and the antibody light chain variable domain (VL) are disulfide stabilized by introduction of a disulfide bond between the following positions: i) heavy chain variable domain position 44 to light chain variable domain position 100, ii) heavy chain variable domain position 105 to light chain variable domain position 43, or iii) heavy chain variable domain position 101 to light chain variable domain position 100 (numbering according to EU index of Kabat).

[0130] Such further disulfide stabilization of single chain Fab fragments is achieved by the introduction of a disulfide bond between the variable domains VH and VL of the single chain Fab fragments. Techniques to introduce unnatural disulfide bridges for stabilization for a single chain Fv are described e.g. in WO 94/029350, Rajagopal *et al.*, 1997, Prot. Engin. 10:1453-59; Kobayashi *et al.*, 1998, Nuclear Medicine & Biology, 25:387-393; and Schmidt, *et al.*, 1999, Oncogene 18:1711-1721. In one embodiment the optional disulfide bond between the variable domains of the single chain Fab fragments is between heavy chain variable domain position 44 and light chain variable domain position 100. In one embodiment the optional disulfide bond between the variable domains of the single chain Fab fragments is between heavy chain variable domain position 105 and light chain variable domain position 43 (numbering according to EU index of Kabat).

6.2.1.2. scFvs

[0131] Single chain Fv or “scFv” antibody fragments comprise the VH and VL domains of an antibody in a single polypeptide chain, are capable of being expressed as a single chain polypeptide, and retain the specificity of the intact antibody from which it is derived. Generally, the scFv polypeptide further comprises a polypeptide linker between the VH and VL domain that enables the scFv to form the desired structure for target binding. Examples of linkers suitable for connecting the VH and VL chains of an scFv are the ABM linkers identified in Section 6.3.3, for example any of the linkers designated L1 through L54.

[0132] Unless specified, as used herein an scFv may have the VL and VH variable regions in either order, e.g., with respect to the N-terminal and C-terminal ends of the polypeptide, the scFv may comprise VL-linker-VH or may comprise VH-linker-VL.

[0133] To create an scFv-encoding nucleic acid, the VH and VL-encoding DNA fragments are operably linked to another fragment encoding a linker, e.g., encoding any of the ABM linkers described in Section 6.3.3 (such as the amino acid sequence (Gly4~Ser)3) (SEQ ID NO: 1),, such that the VH and VL sequences can be expressed as a contiguous single-chain protein, with the VL and VH regions joined by the flexible linker (see e.g., Bird *et al.*, 1988, Science 242:423-426; Huston *et al.*, 1988, Proc. Natl. Acad. Sci. USA 85:5879-5883; McCafferty *et al.*, 1990, Nature 348:552-554).

6.2.1.3. Other immunoglobulin-based modules

[0134] TBMs of the disclosure can also comprise ABMs having an immunoglobulin format which is other than Fab or scFv, for example Fv, dsFv, (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain (also called a nanobody).

[0135] An ABM can be a single domain antibody composed of a single VH or VL domain which exhibits sufficient affinity to the target. In a specific embodiment, the single domain antibody is a

camelid VHH domain (see, e.g., Riechmann, 1999, *Journal of Immunological Methods* 231:25-38; WO 94/04678).

6.2.2. Non-Immunoglobulin Based Modules

[0136] In certain embodiments, one or more of the ABMs of the disclosure are derived from non-antibody scaffold proteins (including, but not limited to, designed ankyrin repeat proteins (DARPs), Avimers (short for avidity multimers), Anticalin/Lipocalins, Centyrins, Kunitz domains, Adnexins, Affilins, Affitins (also known as Nonfitins), Knottins, Pronectins, Versabodies, Duocalins, and Fynomers), ligands, receptors, cytokines or chemokines.

[0137] Non-immunoglobulin scaffolds that can be used in the TBMs of the disclosure include those listed in Tables 3 and 4 of Mintz and Crea, 2013, *Bioprocess International* 11(2):40-48; in Figure 1, Table 1 and Figure I of Vazquez-Lombardi *et al.*, 2015, *Drug Discovery Today* 20(10):1271-83; in Table 1 and Box 2 of Skrlec *et al.*, 2015, *Trends in Biotechnology* 33(7):408-18. The contents of Tables 3 and 4 of Mintz and Crea, 2013, *Bioprocess International* 11(2):40-48; in Figure 1, Table 1 and Figure I of Vazquez-Lombardi *et al.*, 2015, *Drug Discovery Today* 20(10):1271-83; in Table 1 and Box 2 of Skrlec *et al.*, 2015, *Trends in Biotechnology* 33(7):408-18 (collectively, "Scaffold Disclosures") are incorporated by reference herein. In a particular embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Adnexins. In another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Avimers. In another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Affibodies. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Anticalins. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to DARPs. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Kunitz domains. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Knottins. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Pronectins. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Nanofitins. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Affilins. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Adnectins. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to ABDs. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Adhirons. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Affimers. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Alphabodies. In yet another

embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Armadillo Repeat Proteins. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Atrimers/Tetranectins. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Obodies/OB-folds. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Centyrins. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Repebodies. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Anticalins. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Atrimers. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to bicyclic peptides. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to cys-knots. In yet another embodiment, the Scaffold Disclosures are incorporated by reference for what they disclose relating to Fn3 scaffolds (including Adnectins, Centyrins, Pronectins, and Tn3).

[0138] In an embodiment, an ABM of the disclosure can be a designed ankyrin repeat protein ("DARPin"). DARPins are antibody mimetic proteins that typically exhibit highly specific and high-affinity target protein binding. They are typically genetically engineered and derived from natural ankyrin proteins and consist of at least three, usually four or five repeat motifs of these proteins. Their molecular mass is about 14 or 18 kDa (kilodaltons) for four- or five-repeat DARPins, respectively. Examples of DARPins can be found, for example in U.S. Pat. No. 7,417,130. Multispecific binding molecules comprising DARPin binding modules and immunoglobulin-based binding modules are disclosed in, for example, U.S. Publication No. 2015/0030596 A1.

[0139] In another embodiment, an ABM of the disclosure can be an Affibody. An Affibody is well known in the art and refers to affinity proteins based on a 58 amino acid residue protein domain, derived from one of the IgG binding domain of staphylococcal protein A.

[0140] In another embodiment, an ABM of the disclosure can be an Anticalin. Anticalins are well known in the art and refer to another antibody mimetic technology, wherein the binding specificity is derived from Lipocalins. Anticalins may also be formatted as dual targeting protein, called Duocalins.

[0141] In another embodiment, an ABM of the disclosure can be a Versabody. Versabodies are well known in the art and refer to another antibody mimetic technology. They are small proteins of 3-5 kDa with >15% cysteines, which form a high disulfide density scaffold, replacing the hydrophobic core the typical proteins have.

[0142] Other non-immunoglobulin ABMs include “A” domain oligomers (also known as Avimers) (see for example, U.S. Patent Application Publication Nos. 2005/0164301, 2005/0048512, and 2004/017576), Fn3 based protein scaffolds (see for example, U.S. Patent Application Publication 2003/0170753), VASP polypeptides, Avian pancreatic polypeptide (aPP), Tetranectin (based on CTLD3), Affililin (based on γ B-crystallin/ubiquitin), Knottins, SH3 domains, PDZ domains, Tendamistat, Neocarzinostatin, Protein A domains, Lipocalins, Transferrin, and Kunitz domains. In one aspect, ABMs useful in the construction of the TBMs of the disclosure comprise fibronectin-based scaffolds as exemplified in WO 2011/130324.

[0143] Moreover, in certain aspects, an ABM comprises a ligand binding domain of a receptor or a receptor binding domain of a ligand. For example, if the TAA is the EGF receptor, ABM3 can comprise a portion of EGF that binds EGFR, and if the TAA is the PDGF receptor, ABM3 can comprise a portion of PDGF that binds PDGF, and so on and so forth. In a specific embodiment, ABM1 is a CD2 ligand, in particular a CD58 moiety as described in Section 6.6.2. The respective binding domains of numerous ligand/receptor pairs are well known in the art, and thus can be readily selected and adapted for use in the TBMs of the disclosure.

6.3. Connectors

[0144] It is contemplated that the TBMs of the disclosure can in some instances include pairs of ABMs or ABM chains (e.g., the VH-CH1 or VL-CL component of a Fab) connected directly to one another, e.g., as a fusion protein without a linker. More preferably, the TBMs of the disclosure comprise connector moieties linking individual ABMs or ABM chains. The use of connector moieties can improve target binding, for example by increasing flexibility of the ABMs within a TBM and thus reducing steric hindrance. The ABMs can be connected to one another through, for example, Fc domains (each Fc domain representing a pair of associated Fc regions) and/or ABM linkers. The use of Fc domains will typically require the use of hinge regions as connectors of the ABMs or ABM chains for optimal antigen binding. Thus, the term “connector” encompasses, but is not limited to, Fc regions, Fc domains, hinge regions, and

[0145] Examples of Fc domains (formed by the pairing of two Fc regions), hinge regions and ABM linkers are described in Sections 6.3.1, 6.3.2, and 6.3.3, respectively.

6.3.1. Fc domains

[0146] The TBMs of the disclosure can include an Fc domain derived from any suitable species. In one embodiment the Fc domain is derived from a human Fc domain.

[0147] The Fc domain may be derived from any suitable class of antibody, including IgA (including subclasses IgA1 and IgA2), IgD, IgE, IgG (including subclasses IgG1, IgG2, IgG3 and IgG4), and IgM. In one embodiment, the Fc domain is derived from IgG1, IgG2, IgG3 or

IgG4. In one embodiment the Fc domain is derived from IgG1. In one embodiment the Fc domain is derived from IgG4.

[0148] The Fc domain comprises two polypeptide chains, each referred to as a heavy chain Fc region. The two heavy chain Fc regions dimerize to create the Fc domain. The two Fc regions within the Fc domain may be the same or different from one another. In a native antibody the Fc regions are typically identical, but for the purpose of producing multispecific binding molecules, *e.g.*, the TBMs of the disclosure, the Fc regions might advantageously be different to allow for heterodimerization, as described in Section 6.3.1.5 below.

[0149] Typically each heavy chain Fc region comprises or consists of two or three heavy chain constant domains.

[0150] In native antibodies, the heavy chain Fc region of IgA, IgD and IgG is composed of two heavy chain constant domains (CH2 and CH3) and that of IgE and IgM is composed of three heavy chain constant domains (CH2, CH3 and CH4). These dimerize to create an Fc domain.

[0151] In the present disclosure, the heavy chain Fc region can comprise heavy chain constant domains from one or more different classes of antibody, for example one, two or three different classes.

[0152] In one embodiment the heavy chain Fc region comprises CH2 and CH3 domains derived from IgG1.

[0153] In one embodiment the heavy chain Fc region comprises CH2 and CH3 domains derived from IgG2.

[0154] In one embodiment the heavy chain Fc region comprises CH2 and CH3 domains derived from IgG3.

[0155] In one embodiment the heavy chain Fc region comprises CH2 and CH3 domains derived from IgG4.

[0156] In one embodiment the heavy chain Fc region comprises a CH4 domain from IgM. The IgM CH4 domain is typically located at the C-terminus of the CH3 domain.

[0157] In one embodiment the heavy chain Fc region comprises CH2 and CH3 domains derived from IgG and a CH4 domain derived from IgM.

[0158] It will be appreciated that the heavy chain constant domains for use in producing a heavy chain Fc region for the TBMs of the present disclosure may include variants of the naturally occurring constant domains described above. Such variants may comprise one or more amino acid variations compared to wild type constant domains. In one example the heavy chain Fc region of the present disclosure comprises at least one constant domain that varies in sequence from the wild type constant domain. It will be appreciated that the variant constant

domains may be longer or shorter than the wild type constant domain. Preferably the variant constant domains are at least 60% identical or similar to a wild type constant domain. In another example the variant constant domains are at least 70% identical or similar. In another example the variant constant domains are at least 80% identical or similar. In another example the variant constant domains are at least 90% identical or similar. In another example the variant constant domains are at least 95% identical or similar. Exemplary Fc variants are described in Sections 6.3.1.1 through 6.3.1.5, *infra*.

[0159] IgM and IgA occur naturally in humans as covalent multimers of the common H2L2 antibody unit. IgM occurs as a pentamer when it has incorporated a J-chain, or as a hexamer when it lacks a J-chain. IgA occurs as monomer and dimer forms. The heavy chains of IgM and IgA possess an 18 amino acid extension to the C-terminal constant domain, known as a tailpiece. The tailpiece includes a cysteine residue that forms a disulfide bond between heavy chains in the polymer, and is believed to have an important role in polymerization. The tailpiece also contains a glycosylation site. In certain embodiments, the TBMs of the present disclosure do not comprise a tailpiece.

[0160] The Fc domains that are incorporated into the TBMs of the present disclosure may comprise one or more modifications that alter the functional properties of the proteins, for example, binding to Fc-receptors such as FcRn or leukocyte receptors (for example, as described in Section 6.3.1.1), binding to complement (for example as described in Section 6.3.1.2), modified disulfide bond architecture (for example as described in Section 6.3.1.3), or altered glycosylation patterns (for example as described in Section 6.3.1.4). The Fc domains can also be altered to include modifications that improve manufacturability of asymmetric TBMs, for example by allowing heterodimerization, which is the preferential pairing of non-identical Fc regions over identical Fc regions. Heterodimerization permits the production of TBMs in which different ABMs are connected to one another by an Fc domain containing Fc regions that differ in sequence. Examples of heterodimerization strategies are exemplified in Section 6.3.1.5 (and subsections thereof).

[0161] It will be appreciated that any of the modifications described in Sections 6.3.1.1 through 6.3.1.5 can be combined in any suitable manner to achieve the desired functional properties and/or combined with other modifications to alter the properties of the TBMs.

6.3.1.1. Fc Domains with Altered FcR Binding

[0162] The Fc domains of the TBMs of the disclosure may show altered binding to one or more Fc-receptors (FcRs) in comparison with the corresponding native immunoglobulin. The binding to any particular Fc-receptor may be increased or decreased. In one embodiment, the Fc domain comprises one or more modifications which alter its Fc-receptor binding profile.

[0163] Human cells can express a number of membrane bound FcRs selected from FcαR, FcεR, FcγR, FcRn and glycan receptors. Some cells are also capable of expressing soluble (ectodomain) FcR (Fridman *et al.*, 1993, J Leukocyte Biology 54: 504-512 for review). FcγR can be further divided by affinity of IgG binding (high/low) and biological effect (activating/inhibiting). Human FcγRI is widely considered to be the sole ‘high affinity’ receptor whilst all of the others are considered as medium to low. FcγRIIb is the sole receptor with ‘inhibitory’ functionality by virtue of its intracellular ITIM motif whilst all of the others are considered as ‘activating’ by virtue of ITAM motifs or pairing with the common FcγR--γchain. FcγRIIIb is also unique in that although activatory it associates with the cell via a GPI anchor. In total, humans express six “standard” FcγRs: FcγRI, FcγRIIa, FcγRIIb, FcγRIIc, FcγRIIIa FcγRIIIb. In addition to these sequences there are a large number of sequence or allotypic variants spread across these families. Some of these have been found to have important functional consequence and so are sometimes considered to be receptor sub-types of their own. Examples include FcγRIIa^{H134R}, FcγRIIb^{I190T}, FcγRIIIa^{F158V} and FcγRIIb^{NA1}, FcγRIIIb^{NA2} FcγRIII^{SH}. Each receptor sequence has been shown to have different affinities for the 4 sub-classes of IgG: IgG1, IgG2, IgG3 and IgG4 (Bruhns, 1993, Blood 113:3716-3725). Other species have somewhat different numbers and functionality of FcγR, with the mouse system being the best studied to date and comprising of 4 FcγR, FcγRI FcγRIIb FcγRIII FcγRIV (Bruhns, 2012, Blood 119:5640-5649). Human FcγRI on cells is normally considered to be ‘occupied’ by monomeric IgG in normal serum conditions due to its affinity for IgG1/IgG3/IgG4 (about 10⁻⁸ M) and the concentration of these IgG in serum (about 10 mg/ml). Hence cells bearing FcγRI on their surface are considered to be capable for “screening” or “sampling” of their antigenic environment vicariously through the bound polyspecific IgG. The other receptors having lower affinities for IgG sub-classes (in the range of about 10⁻⁵ - 10⁻⁷ M) are normally considered to be “unoccupied.” The low affinity receptors are hence inherently sensitive to the detection of and activation by antibody involved immune complexes. The increased Fc density in an antibody immune complex results in increased functional affinity of binding avidity to low affinity FcγR. This has been demonstrated *in vitro* using a number of methods (Shields *et al.*, 2001, J Biol Chem 276(9):6591-6604; Lux *et al.*, 2013, J Immunol 190:4315-4323). It has also been implicated as being one of the primary modes of action in the use of anti-RhD to treat ITP in humans (Crow, 2008, Transfusion Medicine Reviews 22:103-116).

[0164] Many cell types express multiple types of FcγR and so binding of IgG or antibody immune complex to cells bearing FcγR can have multiple and complex outcomes depending upon the biological context. Most simply, cells can either receive an activatory, inhibitory or mixed signal. This can result in events such as phagocytosis (*e.g.*, macrophages and neutrophils), antigen processing (*e.g.*, dendritic cells), reduced IgG production (*e.g.*, B-cells) or degranulation (*e.g.*, neutrophils, mast cells). There are data to support that the inhibitory signal

from FcγRIIb can dominate that of activatory signals (Proulx, 2010, Clinical Immunology 135:422-429).

[0165] FcRn has a crucial role in maintaining the long half-life of IgG in the serum of adults and children. The receptor binds IgG in acidified vesicles (pH<6.5) protecting the IgG molecule from degradation, and then releasing it at the higher pH of 7.4 in blood.

[0166] FcRn is unlike leukocyte Fc receptors, and instead, has structural similarity to MHC class I molecules. It is a heterodimer composed of a β₂-microglobulin chain, non-covalently attached to a membrane-bound chain that includes three extracellular domains. One of these domains, including a carbohydrate chain, together with β₂-microglobulin interacts with a site between the CH2 and CH3 domains of Fc. The interaction includes salt bridges made to histidine residues on IgG that are positively charged at pH<6.5. At higher pH, the His residues lose their positive charges, the FcRn-IgG interaction is weakened and IgG dissociates.

[0167] In one embodiment, a TBM of the disclosure comprises an Fc domain that binds to human FcRn.

[0168] In one embodiment, the Fc domain has an (e.g., one or two) Fc regions comprising a histidine residue at position 310, and preferably also at position 435. These histidine residues are important for human FcRn binding. In one embodiment, the histidine residues at positions 310 and 435 are native residues, *i.e.*, positions 310 and 435 are not modified. Alternatively, one or both of these histidine residues may be present as a result of a modification.

[0169] The TBMs of the disclosure may comprise one or more Fc regions that alter Fc binding to FcRn. The altered binding may be increased binding or decreased binding.

[0170] In one embodiment, the TBM comprises an Fc domain in which at least one (and optionally both) Fc regions comprises one or more modifications such that it binds to FcRn with greater affinity and avidity than the corresponding native immunoglobulin.

[0171] In one embodiment, the Fc region is modified by substituting the threonine residue at position 250 with a glutamine residue (T250Q).

[0172] In one embodiment, the Fc region is modified by substituting the methionine residue at position 252 with a tyrosine residue (M252Y)

[0173] In one embodiment, the Fc region is modified by substituting the serine residue at position 254 with a threonine residue (S254T).

[0174] In one embodiment, the Fc region is modified by substituting the threonine residue at position 256 with a glutamic acid residue (T256E).

[0175] In one embodiment, the Fc region is modified by substituting the threonine residue at position 307 with an alanine residue (T307A).

[0176] In one embodiment, the Fc region is modified by substituting the threonine residue at position 307 with a proline residue (T307P).

[0177] In one embodiment, the Fc region is modified by substituting the valine residue at position 308 with a cysteine residue (V308C).

[0178] In one embodiment, the Fc region is modified by substituting the valine residue at position 308 with a phenylalanine residue (V308F).

[0179] In one embodiment, the Fc region is modified by substituting the valine residue at position 308 with a proline residue (V308P).

[0180] In one embodiment, the Fc region is modified by substituting the glutamine residue at position 311 with an alanine residue (Q311A).

[0181] In one embodiment, the Fc region is modified by substituting the glutamine residue at position 311 with an arginine residue (Q311R).

[0182] In one embodiment, the Fc region is modified by substituting the methionine residue at position 428 with a leucine residue (M428L).

[0183] In one embodiment, the Fc region is modified by substituting the histidine residue at position 433 with a lysine residue (H433K).

[0184] In one embodiment, the Fc region is modified by substituting the asparagine residue at position 434 with a phenylalanine residue (N434F).

[0185] In one embodiment, the Fc region is modified by substituting the asparagine residue at position 434 with a tyrosine residue (N434Y).

[0186] In one embodiment, the Fc region is modified by substituting the methionine residue at position 252 with a tyrosine residue, the serine residue at position 254 with a threonine residue, and the threonine residue at position 256 with a glutamic acid residue (M252Y/S254T/T256E).

[0187] In one embodiment, the Fc region is modified by substituting the valine residue at position 308 with a proline residue and the asparagine residue at position 434 with a tyrosine residue (V308P/N434Y).

[0188] In one embodiment, the Fc region is modified by substituting the methionine residue at position 252 with a tyrosine residue, the serine residue at position 254 with a threonine residue, the threonine residue at position 256 with a glutamic acid residue, the histidine residue at position 433 with a lysine residue and the asparagine residue at position 434 with a phenylalanine residue (M252Y/S254T/T256E/H433K/N434F).

[0189] It will be appreciated that any of the modifications listed above may be combined to alter FcRn binding.

[0190] In one embodiment, the TBM comprises an Fc domain in which one or both Fc regions comprise one or more modifications such that the Fc domain binds to FcRn with lower affinity and avidity than the corresponding native immunoglobulin.

[0191] In one embodiment, the Fc region comprises any amino acid residue other than histidine at position 310 and/or position 435.

[0192] The TBM of the disclosure may comprise an Fc domain in which one or both Fc regions comprise one or more modifications which increase its binding to FcγRIIb. FcγRIIb is the only inhibitory receptor in humans and the only Fc receptor found on B cells.

[0193] In one embodiment, the Fc region is modified by substituting the proline residue at position 238 with an aspartic acid residue (P238D).

[0194] In one embodiment, the Fc region is modified by substituting the glutamic acid residue at position 258 with an alanine residue (E258A).

[0195] In one embodiment, the Fc region is modified by substituting the serine residue at position 267 with an alanine residue (S267A).

[0196] In one embodiment, the Fc region is modified by substituting the serine residue at position 267 with a glutamic acid residue (S267E).

[0197] In one embodiment, the Fc region is modified by substituting the leucine residue at position 328 with a phenylalanine residue (L328F).

[0198] In one embodiment, the Fc region is modified by substituting the glutamic acid residue at position 258 with an alanine residue and the serine residue at position 267 with an alanine residue (E258A/S267A).

[0199] In one embodiment, the Fc region is modified by substituting the serine residue at position 267 with a glutamic acid residue and the leucine residue at position 328 with a phenylalanine residue (S267E/L328F).

[0200] It will be appreciated that any of the modifications listed above may be combined to increase FcγRIIb binding.

[0201] In one embodiment of the disclosure, TBMs are provided comprising Fc domains which display decreased binding to FcγR.

[0202] In one embodiment TBM comprises an Fc domain in which one or both Fc regions comprise one or more modifications that decrease Fc binding to FcγR.

[0203] The Fc domain can be derived from IgG1.

[0204] In one embodiment, the Fc region is modified by substituting the leucine residue at position 234 with an alanine residue (L234A).

[0205] In one embodiment, the Fc region is modified by substituting the leucine residue at position 235 with an alanine residue (L235A).

[0206] In one embodiment, the Fc region is modified by substituting the glycine residue at position 236 with an arginine residue (G236R).

[0207] In one embodiment, the Fc region is modified by substituting the asparagine residue at position 297 with an alanine residue (N297A) or a glutamine residue (N297Q).

[0208] In one embodiment, the Fc region is modified by substituting the serine residue at position 298 with an alanine residue (S298A).

[0209] In one embodiment, the Fc region is modified by substituting the leucine residue at position 328 with an arginine residue (L328R).

[0210] In one embodiment, the Fc region is modified by substituting the leucine residue at position 234 with an alanine residue and the leucine residue at position 235 with an alanine residue (L234A/L235A).

[0211] In one embodiment, the Fc region is modified by substituting the phenylalanine residue at position 234 with an alanine residue and the leucine residue at position 235 with an alanine residue (F234A/L235A).

[0212] In one embodiment, the Fc region is modified by substituting the glycine residue at position 236 with an arginine residue and the leucine residue at position 328 with an arginine residue (G236R/L328R).

[0213] It will be appreciated that any of the modifications listed above may be combined to decrease FcγR binding.

[0214] In one embodiment a TBM of the present disclosure comprises an Fc domain in which one or both Fc regions comprise one or more modifications that decrease Fc binding to FcγRIIIa without affecting the Fc's binding to FcγRII.

[0215] In one embodiment, the Fc region is modified by substituting the serine residue at position 239 with an alanine residue (S239A).

[0216] In one embodiment, the Fc region is modified by substituting the glutamic acid residue at position 269 with an alanine residue (E269A).

[0217] In one embodiment, the Fc region is modified by substituting the glutamic acid residue at position 293 with an alanine residue (E293A).

[0218] In one embodiment, the Fc region is modified by substituting the tyrosine residue at position 296 with a phenylalanine residue (Y296F).

[0219] In one embodiment, the Fc region is modified by substituting the valine residue at position 303 with an alanine residue (V303A).

[0220] In one embodiment, the Fc region is modified by substituting the alanine residue at position 327 with a glycine residue (A327G).

[0221] In one embodiment, the Fc region is modified by substituting the lysine residue at position 338 with an alanine residue (K338A).

[0222] In one embodiment, the Fc region is modified by substituting the aspartic acid residue at position 376 with an alanine residue (D376A).

[0223] It will be appreciated that any of the modifications listed above may be combined to decrease FcγRIIIa binding.

6.3.1.2. Fc Domains with Altered Complement Binding

[0224] The TBM of the disclosure may comprise an Fc domain in which one or both Fc regions comprises one or more modifications that alter Fc binding to complement. Altered complement binding may be increased binding or decreased binding.

[0225] In one embodiment the Fc region comprises one or more modifications which decrease its binding to C1q. Initiation of the classical complement pathway starts with binding of hexameric C1q protein to the CH2 domain of antigen bound IgG and IgM.

[0226] In one embodiment the TBM of the disclosure comprises an Fc domain in which one or both Fc regions comprises one or more modifications to decrease Fc binding to C1q.

[0227] In one embodiment, the Fc region is modified by substituting the leucine residue at position 234 with an alanine residue (L234A).

[0228] In one embodiment, the Fc region is modified by substituting the leucine residue at position 235 with an alanine residue (L235A).

[0229] In one embodiment, the Fc region is modified by substituting the leucine residue at position 235 with a glutamic acid residue (L235E).

[0230] In one embodiment, the Fc region is modified by substituting the glycine residue at position 237 with an alanine residue (G237A).

[0231] In one embodiment, the Fc region is modified by substituting the lysine residue at position 322 with an alanine residue (K322A).

[0232] In one embodiment, the Fc region is modified by substituting the proline residue at position 331 with an alanine residue (P331A).

[0233] In one embodiment, the Fc region is modified by substituting the proline residue at position 331 with a serine residue (P331S).

[0234] In one embodiment, a TBM of the disclosure comprises an Fc domain derived from IgG4. IgG4 has a naturally lower complement activation profile than IgG1, but also weaker binding of FcγR. Thus, in one embodiment, the TBM comprises an IgG4 Fc domain and also comprises one or more modifications that increase FcγR binding.

[0235] It will be appreciated that any of the modifications listed above may be combined to reduce C1q binding.

6.3.1.3. Fc Domains with Altered Disulfide Architecture

[0236] The TBM of the disclosure can include an Fc domain comprising one or more modifications to create and/or remove a cysteine residue. Cysteine residues have an important role in the spontaneous assembly of Fc-based multispecific binding molecules, by forming disulfide bridges between individual pairs of polypeptide monomers. Thus, by altering the number and/or position of cysteine residues, it is possible to modify the structure of the TBM to produce a protein with improved therapeutic properties.

[0237] A TBM of the present disclosure can comprise an Fc domain in which one or both Fc regions, preferably both Fc regions, comprise a cysteine residue at position 309. In one embodiment, the cysteine residue at position 309 is created by a modification, *e.g.*, for an Fc domain derived from IgG1, the leucine residue at position 309 is substituted with a cysteine residue (L309C), for an Fc domain derived from IgG2, the valine residue at position 309 is substituted with a cysteine residue (V309C).

[0238] In one embodiment, the Fc region is modified by substituting the valine residue at position 308 with a cysteine residue (V308C).

[0239] In one embodiment, two disulfide bonds in the hinge region are removed by mutating a core hinge sequence CPPC (SEQ ID NO: 2) to SPPS (SEQ ID NO: 3).

6.3.1.4. Fc Domains with Altered Glycosylation

[0240] In certain aspects, TBMs with improved manufacturability are provided that comprise fewer glycosylation sites than a corresponding immunoglobulin. These proteins have less complex post translational glycosylation patterns and are thus simpler and less expensive to manufacture.

[0241] In one embodiment a glycosylation site in the CH2 domain is removed by substituting the asparagine residue at position 297 with an alanine residue (N297A) or a glutamine residue (N297Q). In addition to improved manufacturability, these aglycosyl mutants also reduce FcγR binding as described herein above.

6.3.1.5. Fc Heterodimerization

[0242] Many multispecific molecule formats entail dimerization between two Fc regions that, unlike a native immunoglobulin, are operably linked to non-identical antigen-binding domains

(or portions thereof, e.g., a VH or VH-CH1 of a Fab). Inadequate heterodimerization of two Fc regions to form an Fc domain has always been an obstacle for increasing the yield of desired multispecific molecules and represents challenges for purification. A variety of approaches available in the art can be used in for enhancing dimerization of Fc regions that might be present in the TBMs of the disclosure, for example as disclosed in EP 1870459A1; U.S. Pat. No. 5,582,996; U.S. Pat. No. 5,731,168; U.S. Pat. No. 5,910,573; U.S. Pat. No. 5,932,448; U.S. Pat. No. 6,833,441; U.S. Pat. No. 7,183,076; U.S. Patent Application Publication No. 2006204493A1; and PCT Publication No. WO2009/089004A1.

[0243] The present disclosure provides TBMs comprising Fc heterodimers, *i.e.*, Fc domains comprising heterologous, non-identical Fc regions. Heterodimerization strategies are used to enhance dimerization of Fc regions operably linked to different ABMs (or portions thereof, e.g., a VH or VH-CH1 of a Fab) and reduce dimerization of Fc regions operably linked to the same ABM or portion thereof. Typically, each Fc region in the Fc heterodimer comprises a CH3 domain of an antibody. The CH3 domains are derived from the constant region of an antibody of any isotype, class or subclass, and preferably of IgG (IgG1, IgG2, IgG3 and IgG4) class, as described in the preceding section.

[0244] Typically, the TBMs comprise other antibody fragments in addition to CH3 domains, such as, CH1 domains, CH2 domains, hinge domain, VH domain(s), VL domain(s), CDR(s), and/or antigen-binding fragments described herein. In some embodiments, the two hetero-polypeptides are two heavy chains forming a bispecific or multispecific molecules.

Heterodimerization of the two different heavy chains at CH3 domains give rise to the desired antibody or antibody-like molecule, while homodimerization of identical heavy chains will reduce yield of the desired antibody or molecule. In an exemplary embodiment, the two or more hetero-polypeptide chains comprise two chains comprising CH3 domains and forming the molecules of any of the multispecific molecule formats described above of the present disclosure. In an embodiment, the two hetero-polypeptide chains comprising CH3 domains comprise modifications that favor heterodimeric association of the polypeptides, relative to unmodified chains. Various examples of modification strategies are provided below in Table 2 and Sections 6.3.1.5.1 to 6.3.1.5.3.

TABLE 2 Fc Heterodimerization Strategies				
NO.	STRATEGY	CH3 DOMAIN 1	CH3 DOMAIN 2	REFERENCES
Fc 1	knobs-into-holes (Y-T)	T366Y	Y407T	Ridgway <i>et al.</i> , 1996, Protein Eng 9:617-21
Fc 2	knobs-into-holes (CW-CSAV)	S354C, T366W	Y349C, T366S, L368A, Y407V	Atwell <i>et al.</i> , 1997, J Mol Biol. 270(1):26-35; Merchant <i>et al.</i> , 1998, Nat Biotechnol 16:677-681

TABLE 2 Fc Heterodimerization Strategies				
NO.	STRATEGY	CH3 DOMAIN 1	CH3 DOMAIN 2	REFERENCES
Fc 3	HA-TF	S364H, F405A	Y349T, T394F	Moore <i>et al.</i> , 2011, MAb 3(6):546-57
Fc 4	ZW1 (VYAV-VLLW)	T350V, L351Y, F405A, Y407V	T350V, T366L, K392L, T394W	Von Kreudenstein <i>et al.</i> , 2013, MAb 5:646-54
Fc 5	CH3 charge pairs (DD-KK)	K392D, K409D	E356K, D399K	Gunasekaran <i>et al.</i> , 2010, J Biol Chem 285:19637-46
Fc 6	IgG1 hinge, CH3 charge pairs (EEE-RRR)	IgG1: D221E, P228E, L368E	IgG1: D221R, P228R, K409R	Strop <i>et al.</i> , 2012, J Mol Biol 420:204-19
Fc 7	IgG2 hinge, CH3 charge pairs (EEE-RRR)	IgG2: C223E, P228E, L368E	IgG2: C223R, E225R, P228R, K409R	Strop <i>et al.</i> , 2012, J Mol Biol 420:204-19
Fc 8	EW-RVT	K360E, K409W,	Q347R, D399V, F405T	Choi <i>et al.</i> , 2013, Mol Cancer Ther 12:2748-59
Fc 9	EW-RVTS-S	K360E, K409W, Y349C	Q347R, D399V, F405T, S354C	Choi <i>et al.</i> , 2015, Mol Immunol 65:377-83
Fc 10	Biclonic	366K (+351K)	351D or E or D at 349, 368, 349, or 349 + 355	Geuijen <i>et al.</i> , 2014, Journal of Clinical Oncology 32:suppl:560
Fc 11	DuoBody (L-R)	F405L	K409R	Labrijn <i>et al.</i> , 2013, Proc Natl Acad Sci USA 110:5145-50
Fc 12	SEEDbody	IgG/A chimera	IgG/A chimera	Davis <i>et al.</i> , 2010, Protein Eng Des Sel 23:195-202
Fc 13	BEAT	residues from TCR α interface	residues from TCR β interface	Moretti <i>et al.</i> , 2013, BMC Proceedings 7(Suppl 6):O9
Fc 14	7.8.60 (DMA-RRVV)	K360D, D399M, Y407A	E345R, Q347R, T366V, K409V	Leaver-Fey <i>et al.</i> , Structure 24:641-51
Fc 15	20.8.34 (SYMV-GDQA)	Y349S, K370Y, T366M, K409V	E356G, E357D, S364Q, Y407A	Leaver-Fey <i>et al.</i> , Structure 24:641-51
Fc 16	Skew variant 12757	None	none	Figure 34 of US 2016/0355600
Fc 17	Skew variant 12758	L368D, K370S	S364K	Figure 34 of US 2016/0355600
Fc 18	Skew variant 12759	L368D, K370S	S364K, E357L	Figure 34 of US 2016/0355600
Fc 19	Skew variant 12760	L368D, K370S	S364K, E357Q	Figure 34 of US 2016/0355600
Fc 20	Skew variant 12761	T411E, K360E, Q362E	D401K	Figure 34 of US 2016/0355600
Fc 21	Skew variant 12496	L368E, K370S	S364K	Figure 34 of US 2016/0355600
Fc 22	Skew variant 12511	K370S	S364K	Figure 34 of US 2016/0355600
Fc 23	Skew variant 12840	L368E, K370S	S364K, E357Q	Figure 34 of US 2016/0355600

TABLE 2 Fc Heterodimerization Strategies				
NO.	STRATEGY	CH3 DOMAIN 1	CH3 DOMAIN 2	REFERENCES
Fc 24	Skew variant 12841	K370S	S364K, E357Q	Figure 34 of US 2016/0355600
Fc 25	Skew variant 12894	L368E, K370S	S364K	Figure 34 of US 2016/0355600
Fc 26	Skew variant 12895	K370S	S364K	Figure 34 of US 2016/0355600
Fc 27	Skew variant 12896	L368E, K370S	S364K, E357Q	Figure 34 of US 2016/0355600
Fc 28	Skew variant 12901	K370S	S364K, E357Q	Figure 34 of US 2016/0355600
Fc 29	pl_ISO(-)	I199T, N203D, K274Q, R355Q, N384S, K392N, V397M, Q419E, DEL447		Figure 31 of US 2016/0355600
Fc 30	pl_(-)_isosteric_A	N208D, Q295E, N384D, Q418E, N421D		Figure 31 of US 2016/0355600
Fc 31	pl_(-)_isosteric_B	N208D, Q295E, Q418E, N421D		Figure 31 of US 2016/0355600
Fc 32	pl_ISO(+RR)	Q196K, I199T, P217R, P228R, N276K		Figure 31 of US 2016/0355600
Fc 33	pl_ISO(+)	Q196K, I199T, N276K		Figure 31 of US 2016/0355600
Fc 34	pl_(+) isosteric_A	E269Q, E272Q, E283Q, E357Q,		Figure 31 of US 2016/0355600
Fc 35	pl_(+) isosteric_B	E269Q, E272Q, E283Q		Figure 31 of US 2016/0355600
Fc 36	pl_(+) isosteric_E269Q, E272Q	E269Q, E272Q		Figure 31 of US 2016/0355600
Fc 37	pl_(+) isosteric_E 269Q, E283Q	E269Q, E283Q		Figure 31 of US 2016/0355600
Fc 38	pl_(+) isosteric_E272Q, E283Q	E272Q, E283Q		Figure 31 of US 2016/0355600
Fc 39	pl_(+) isosteric_E 269Q	E269Q		Figure 31 of US 2016/0355600
Fc 40	Heterodimerization	F405A	T394F	Figure 30A of US 2016/0355600
Fc 41	Heterodimerization	S364D	Y349K	Figure 30A of US 2016/0355600
Fc 42	Heterodimerization	S364E	L368K	Figure 30A of US 2016/0355600
Fc 43	Heterodimerization	S364E	Y349K	Figure 30A of US 2016/0355600
Fc 44	Heterodimerization	S364F	K370G	Figure 30A of US 2016/0355600
Fc 45	Heterodimerization	S364H	Y349K	Figure 30A of US 2016/0355600

TABLE 2 Fc Heterodimerization Strategies				
NO.	STRATEGY	CH3 DOMAIN 1	CH3 DOMAIN 2	REFERENCES
Fc 46	Heterodimerization	S364H	Y349T	Figure 30A of US 2016/0355600
Fc 47	Heterodimerization	S364Y	K370G	Figure 30A of US 2016/0355600
Fc 48	Heterodimerization	T411K	K370E	Figure 30A of US 2016/0355600
Fc 49	Heterodimerization	V397S, F405A	T394F	Figure 30A of US 2016/0355600
Fc 50	Heterodimerization	K370R, T411K	K370E, T411E	Figure 30A of US 2016/0355600
Fc 51	Heterodimerization	L351E, S364D	Y349K, L351K	Figure 30A of US 2016/0355600
Fc 52	Heterodimerization	L351E, S364E	Y349K, L351K	Figure 30A of US 2016/0355600
Fc 53	Heterodimerization	L351E, T366D	L351K, T366K	Figure 30A of US 2016/0355600
Fc 54	Heterodimerization	P395T, V397S, F405A	T394F	Figure 30A of US 2016/0355600
Fc 55	Heterodimerization	S364D, K370G	S364Y, K370R	Figure 30A of US 2016/0355600
Fc 56	Heterodimerization	S364D, T394F	Y349K, F405A	Figure 30A of US 2016/0355600
Fc 57	Heterodimerization	S364E, F405A	Y349K, T394F	Figure 30A of US 2016/0355600
Fc 58	Heterodimerization	S364E, F405S	Y349K, T394Y	Figure 30A of US 2016/0355600
Fc 59	Heterodimerization	S364E, T411E	Y349K, D401K	Figure 30A of US 2016/0355600
Fc 60	Heterodimerization	S364H, D401K	Y349T, T411E	Figure 30A of US 2016/0355600
Fc 61	Heterodimerization	S364H, F405A	Y349T, T394F	Figure 30A of US 2016/0355600
Fc 62	Heterodimerization	S364H, T394F	Y349T, F405A	Figure 30A of US 2016/0355600
Fc 63	Heterodimerization	Y349C, S364E	Y349K, S354C	Figure 30A of US 2016/0355600
Fc 64	Heterodimerization	L351E, S364D, F405A	Y349K, L351K, T394F	Figure 30A of US 2016/0355600
Fc 65	Heterodimerization	L351K, S364H, D401K	Y349T, L351E, T411E	Figure 30A of US 2016/0355600
Fc 66	Heterodimerization	S364E, T411E, F405A	Y349K, T394F, D401K	Figure 30A of US 2016/0355600
Fc 67	Heterodimerization	S364H, D401K, F405A	Y349T, T394F, T411E	Figure 30A of US 2016/0355600
Fc 68	Heterodimerization	S364H, F405A, T411E	Y349T, T394F, D401K	Figure 30A of US 2016/0355600
Fc 69	Heterodimerization	T411E, K360E, N390D	D401K	Figure 30C of US 2016/0355600

TABLE 2 Fc Heterodimerization Strategies				
NO.	STRATEGY	CH3 DOMAIN 1	CH3 DOMAIN 2	REFERENCES
Fc 70	Heterodimerization	T411E, Q362E, N390D	D401K	Figure 30C of US 2016/0355600
Fc 71	Heterodimerization	T411E, Q347R	D401K, K360D	Figure 30C of US 2016/0355600
Fc 72	Heterodimerization	T411E, Q347R	D401K, K360E	Figure 30C of US 2016/0355600
Fc 73	Heterodimerization	T411E, K360	D401K, Q347K	Figure 30C of US 2016/0355600
Fc 74	Heterodimerization	T411E, K360D	D401K, Q347R	Figure 30C of US 2016/0355600
Fc 75	Heterodimerization	T411E, K360E	D401K, Q347K	Figure 30C of US 2016/0355600
Fc 76	Heterodimerization	T411E, K360E	D401K, Q347R	Figure 30C of US 2016/0355600
Fc 77	Heterodimerization	T411E, S364K	D401K, K370S	Figure 30C of US 2016/0355600
Fc 78	Heterodimerization	T411E, K370S	D401K, S364K	Figure 30C of US 2016/0355600
Fc 79	Heterodimerization	Q347E	E357Q	Figure 30C of US 2016/0355600
Fc 80	Heterodimerization	Q347E	E357Q, Q362K	Figure 30C of US 2016/0355600
Fc 81	Heterodimerization	K360D, Q362E	Q347R	Figure 30C of US 2016/0355600
Fc 82	Heterodimerization	K360D, Q362E	D401K	Figure 30C of US 2016/0355600
Fc 83	Heterodimerization	K360D, Q362E	Q347R, D401K	Figure 30C of US 2016/0355600
Fc 84	Heterodimerization	K360E, Q362E	Q347R	Figure 30C of US 2016/0355600
Fc 85	Heterodimerization	K360E, Q362E	D401K	Figure 30C of US 2016/0355600
Fc 86	Heterodimerization	K360E, Q362E	Q347R, D401K	Figure 30C of US 2016/0355600
Fc 87	Heterodimerization	Q362E, N390D	D401K	Figure 30C of US 2016/0355600
Fc 88	Heterodimerization	Q347E, K360D	D401N	Figure 30C of US 2016/0355600
Fc 89	Heterodimerization	K360D	Q347R, N390K	Figure 30C of US 2016/0355600
Fc 90	Heterodimerization	K360D	N390K, D401N	Figure 30C of US 2016/0355600
Fc 91	Heterodimerization	K360E	Y349H	Figure 30C of US 2016/0355600
Fc 92	Heterodimerization	K370S, Q347E	S364K	Figure 30C of US 2016/0355600
Fc 93	Heterodimerization	K370S, E357L	S364K	Figure 30C of US 2016/0355600

TABLE 2				
Fc Heterodimerization Strategies				
NO.	STRATEGY	CH3 DOMAIN 1	CH3 DOMAIN 2	REFERENCES
Fc 94	Heterodimerization	K370S, E357Q	S364K	Figure 30C of US 2016/0355600
Fc 95	Heterodimerization	K370S, Q347E, E357L	S364K	Figure 30C of US 2016/0355600
Fc 96	Heterodimerization	K370S, Q347E, E357Q	S364K	Figure 30C of US 2016/0355600
Fc 97	Heterodimerization	L368D, K370S, Q347E	S364K	Figure 30D of US 2016/0355600
Fc 98	Heterodimerization	L368D, K370S, E357L	S364K	Figure 30D of US 2016/0355600
Fc 99	Heterodimerization	L368D, K370S, E357Q	S364K	Figure 30D of US 2016/0355600
Fc 100	Heterodimerization	L368D, K370S, Q347E, E357L	S364K	Figure 30D of US 2016/0355600
Fc 101	Heterodimerization	L368D, K370S, Q347E, E357Q	S364K	Figure 30D of US 2016/0355600
Fc 102	Heterodimerization	L368E, K370S, Q347E	S364K	Figure 30D of US 2016/0355600
Fc 103	Heterodimerization	L368E, K370S, E357L	S364K	Figure 30D of US 2016/0355600
Fc 104	Heterodimerization	L368E, K370S, E357Q	S364K	Figure 30D of US 2016/0355600
Fc 105	Heterodimerization	L368E, K370S, Q347E, E357L	S364K	Figure 30D of US 2016/0355600
Fc 106	Heterodimerization	L368E, K370S, Q347E, E357Q	S364K	Figure 30D of US 2016/0355600
Fc 107	Heterodimerization	L368D, K370T, Q347E	S364K	Figure 30D of US 2016/0355600
Fc 108	Heterodimerization	L368D, K370T, E357L	S364K	Figure 30D of US 2016/0355600
Fc 109	Heterodimerization	L368D, K370T, E357Q	S364K	Figure 30D of US 2016/0355600
Fc 110	Heterodimerization	L368D, K370T, Q347E, E357L	S364K	Figure 30D of US 2016/0355600
Fc 111	Heterodimerization	L368D, K370T, Q347E, E357Q	S364K	Figure 30D of US 2016/0355600
Fc 112	Heterodimerization	L368E, K370T, Q347E	S364K	Figure 30D of US 2016/0355600
Fc 113	Heterodimerization	L368E, K370T, E357L	S364K	Figure 30D of US 2016/0355600
Fc 114	Heterodimerization	L368E, K370T, E357Q	S364K	Figure 30D of US 2016/0355600
Fc 115	Heterodimerization	L368E, K370T, Q347E, E357L	S364K	Figure 30D of US 2016/0355600
Fc 116	Heterodimerization	L368E, K370T, Q347E, E357Q	S364K	Figure 30D of US 2016/0355600
Fc 117	Heterodimerization	T411E, Q362E	D401K, T411K	Figure 30D of US 2016/0355600

TABLE 2 Fc Heterodimerization Strategies				
NO.	STRATEGY	CH3 DOMAIN 1	CH3 DOMAIN 2	REFERENCES
Fc 118	Heterodimerization	T411E, N390D	D401K, T411K	Figure 30D of US 2016/0355600
Fc 119	Heterodimerization	T411E, Q362E	D401R, T411R	Figure 30D of US 2016/0355600
Fc 120	Heterodimerization	T411E, N390D	D401R, T411R	Figure 30D of US 2016/0355600
Fc 121	Heterodimerization	Y407T	T366Y	Figure 30D of US 2016/0355600
Fc 122	Heterodimerization	F405A	T394W	Figure 30D of US 2016/0355600
Fc 123	Heterodimerization	T366Y, F405A	T394W, Y407T	Figure 30D of US 2016/0355600
Fc 124	Heterodimerization	T366S, L368A, Y407V	T366W	Figure 30D of US 2016/0355600
Fc 125	Heterodimerization	T366S, L368A, Y407V, Y349C	T366W, S354C	Figure 30D of US 2016/0355600
Fc 126	Heterodimerization	K392D, K409D	E356K, D399K	Figure 30E of US 2016/0355600
Fc 127	Heterodimerization	K370D, K392D, K409D	E356K, E357K, D399K	Figure 30E of US 2016/0355600
Fc 128	Heterodimerization	I199T, N203D, K247Q, R355Q, N384S, K392N, V397M, Q419E, K447	Q196K, L99T, P217R, P228R, N276K	Figure 30E of US 2016/0355600
Fc 129	Heterodimerization	I199T, N203D, K247Q, R355Q, N384S, K392N, V397M, Q419E, K447	Q196K, L99T, N276K	Figure 30E of US 2016/0355600
Fc 130	Heterodimerization	N384S, K392N, V397M, Q419E	N276K	Figure 30E of US 2016/0355600
Fc 131	Heterodimerization	D221E, P228E, L368E	D221R, P228R, K409R	Figure 30E of US 2016/0355600
Fc 132	Heterodimerization	C220E, P228E, L368E	C220R, E224R, P228R, K409R	Figure 30E of US 2016/0355600
Fc 133	Heterodimerization	F405L	K409R	Figure 30E of US 2016/0355600
Fc 134	Heterodimerization	T366I, K392M, T394W	F405A, Y407V	Figure 30E of US 2016/0355600
Fc 135	Heterodimerization	T366V, K409F	L351Y, Y407A	Figure 30E of US 2016/0355600
Fc 136	Heterodimerization	T366A, K392E, K409F, T411E	D399R, S400R, Y407A	Figure 30E of US 2016/0355600
Fc 137	Heterodimerization	L351K	L351E	Figure 30E of US 2016/0355600
Fc 138	Heterodimerization	I199T, N203D, K247Q, R355Q, Q419E, K447	Q196K, L199T, P217R, P228R, N276K	Figure 30E of US 2016/0355600

TABLE 2 Fc Heterodimerization Strategies				
NO.	STRATEGY	CH3 DOMAIN 1	CH3 DOMAIN 2	REFERENCES
Fc 139	Heterodimerization	I199T, N203D, K247Q, R355Q, Q419E, K447	Q196K, I199T, N276K	Figure 30E of US 2016/0355600
Fc 140	Heterodimerization	I199T, N203D, K274Q, R355Q, N384S, K392N, V397M, Q419E DEL447		Figure 30E of US 2016/0355600
Fc 141	Heterodimerization	N208D, Q295E N384D, Q418E N421D		Figure 30E of US 2016/0355600
Fc 142	Heterodimerization	N208D, Q295E Q418E, N421D		Figure 30E of US 2016/0355600
Fc 143	Heterodimerization	Q196K, I199T P217R, P228R N276K		Figure 30E of US 2016/0355600
Fc 144	Heterodimerization	Q196K, I199T N276K		Figure 30E of US 2016/0355600
Fc 145	Heterodimerization	E269Q, E272Q E283Q, E357Q		Figure 30E of US 2016/0355600
Fc 146	Heterodimerization	E269Q, E272Q E283Q,		Figure 30E of US 2016/0355600
Fc 147	Heterodimerization	E269Q, E272Q		Figure 30E of US 2016/0355600
Fc 148	Heterodimerization	E269Q, E283Q		Figure 30E of US 2016/0355600
Fc 149	Heterodimerization	E272Q, E283Q		Figure 30E of US 2016/0355600
Fc 150	Heterodimerization	E269Q		Figure 30E of US 2016/0355600

6.3.1.5.1. Knob-in-hole (KIH)

[0245] TBMs of the disclosure may comprise one or more, *e.g.*, a plurality, of modifications to one or more of the constant domains of an Fc domain, *e.g.*, to the CH3 domains. In one example, a TBM of the present disclosure comprises two polypeptides that each comprise a heavy chain constant domain of an antibody, *e.g.*, a CH2 or CH3 domain. In an example, the two heavy chain constant domains, *e.g.*, the CH2 or CH3 domains of the TBM comprise one or more modifications that allow for a heterodimeric association between the two chains. In one aspect, the one or more modifications are disposed on CH2 domains of the two heavy chains. In one aspect, the one or more modifications are disposed on CH3 domains of at least two polypeptides of the TBM. In one aspect, the one or more modifications to a first polypeptide of the TBM comprising a heavy chain constant domain can create a “knob” and the one or more modifications to a second polypeptide of the TBM creates a “hole,” such that heterodimerization of the polypeptide of the TBM comprising a heavy chain constant domain causes the “knob” to

interface (e.g., interact, e.g., a CH2 domain of a first polypeptide interacting with a CH2 domain of a second polypeptide, or a CH3 domain of a first polypeptide interacting with a CH3 domain of a second polypeptide) with the “hole.” As the term is used herein, a “knob” refers to at least one amino acid side chain which projects from the interface of a first polypeptide of the TBM comprising a heavy chain constant domain and is therefore positionable in a compensatory “hole” in the interface with a second polypeptide of the TBM comprising a heavy chain constant domain so as to stabilize the heteromultimer, and thereby favor heteromultimer formation over homomultimer formation, for example. The knob may exist in the original interface or may be introduced synthetically (e.g. by altering nucleic acid encoding the interface). The preferred import residues for the formation of a knob are generally naturally occurring amino acid residues and are preferably selected from arginine (R), phenylalanine (F), tyrosine (Y) and tryptophan (W). Most preferred are tryptophan and tyrosine. In the preferred embodiment, the original residue for the formation of the protuberance has a small side chain volume, such as alanine, asparagine, aspartic acid, glycine, serine, threonine or valine.

[0246] A “hole” refers to at least one amino acid side chain which is recessed from the interface of a second polypeptide of the TBM comprising a heavy chain constant domain and therefore accommodates a corresponding knob on the adjacent interfacing surface of a first polypeptide of the TBM comprising a heavy chain constant domain. The hole may exist in the original interface or may be introduced synthetically (e.g. by altering nucleic acid encoding the interface). The preferred import residues for the formation of a hole are usually naturally occurring amino acid residues and are preferably selected from alanine (A), serine (S), threonine (T) and valine (V). Most preferred are serine, alanine or threonine. In the preferred embodiment, the original residue for the formation of the hole has a large side chain volume, such as tyrosine, arginine, phenylalanine or tryptophan.

[0247] In a preferred embodiment, a first CH3 domain is modified at residue 366, 405 or 407 to create either a “knob” or a “hole” (as described above), and the second CH3 domain that heterodimerizes with the first CH3 domain is modified at: residue 407 if residue 366 is modified in the first CH3 domain, residue 394 if residue 405 is modified in the first CH3 domain, or residue 366 if residue 407 is modified in the first CH3 domain to create a “hole” or “knob” complementary to the “knob” or “hole” of the first CH3 domain.

[0248] In another preferred embodiment, a first CH3 domain is modified at residue 366, and the second CH3 domain that heterodimerizes with the first CH3 domain is modified at residues 366, 368 and/or 407, to create a “hole” or “knob” complementary to the “knob” or “hole” of the first CH3 domain. In one embodiment, the modification to the first CH3 domain introduces a tyrosine (Y) residue at position 366. In an embodiment, the modification to the first CH3 is T366Y. In one embodiment, the modification to the first CH3 domain introduces a tryptophan

(W) residue at position 366. In an embodiment, the modification to the first CH3 is T366W. In some embodiments, the modification to the second CH3 domain that heterodimerizes with the first CH3 domain modified at position 366 (e.g., has a tyrosine (Y) or tryptophan (W) introduced at position 366, e.g., comprises the modification T366Y or T366W), comprises a modification at position 366, a modification at position 368 and a modification at position 407. In some embodiments, the modification at position 366 introduces a serine (S) residue, the modification at position 368 introduces an alanine (A), and the modification at position 407 introduces a valine (V). In some embodiments, the modifications comprise T366S, L368A and Y407V. In one embodiment the first CH3 domain of the multispecific molecule comprises the modification T366Y, and the second CH3 domain that heterodimerizes with the first CH3 domain comprises the modifications T366S, L368A and Y407V, or vice versa. In one embodiment the first CH3 domain of the multispecific molecule comprises the modification T366W, and the second CH3 domain that heterodimerizes with the first CH3 domain comprises the modifications T366S, L368A and Y407V, or vice versa.

[0249] Additional steric or “skew” (e.g., knob in hole) modifications are described in PCT publication no. WO2014/145806 (for example, Figure 3, Figure 4 and Figure 12 of WO2014/145806), PCT publication no. WO2014/110601, and PCT publication no. WO 2016/086186, WO 2016/086189, WO 2016/086196 and WO 2016/182751 the contents of which are incorporated herein in their entireties. An example of a KIH variant comprises a first constant chain comprising a L368D and a K370S modification, paired with a second constant chain comprising a S364K and E357Q modification.

[0250] Additional knob in hole modification pairs suitable for use in any of the multispecific molecules of the present disclosure are further described in, for example, WO1996/027011, and Merchant *et al.*, 1998, Nat. Biotechnol., 16:677-681, the contents of which are hereby incorporated by reference in their entirety.

[0251] In further embodiments, the CH3 domains may be additionally modified to introduce a pair of cysteine residues. Without being bound by theory, it is believed that the introduction of a pair of cysteine residues capable of forming a disulfide bond provide stability to heterodimerized TBMs comprising paired CH3 domains. In some embodiments, the first CH3 domain comprises a cysteine at position 354, and the second CH3 domain that heterodimerizes with the first CH3 domain comprises a cysteine at position 349. In some embodiments, the first CH3 domain comprises a cysteine at position 354 (e.g., comprises the modification S354C) and a tyrosine (Y) at position 366 (e.g., comprises the modification T366Y), and the second CH3 domain that heterodimerizes with the first CH3 domain comprises a cysteine at position 349 (e.g., comprises the modification Y349C), a serine at position 366 (e.g., comprises the modification T366S), an alanine at position 368 (e.g., comprises the modification L368A), and a valine at

position 407 (e.g., comprises the modification Y407V). In some embodiments, the first CH3 domain comprises a cysteine at position 354 (e.g., comprises the modification S354C) and a tryptophan (W) at position 366 (e.g., comprises the modification T366W), and the second CH3 domain that heterodimerizes with the first CH3 domain comprises a cysteine at position 349 (e.g., comprises the modification Y349C), a serine at position 366 (e.g., comprises the modification T366S), an alanine at position 368 (e.g., comprises the modification L368A), and a valine at position 407 (e.g., comprises the modification Y407V).

6.3.1.5.2. Alternative Knob and Hole: IgG Heterodimerization

[0252] Heterodimerization of polypeptide chains of a TBM comprising paired CH3 domains can be increased by introducing one or more modifications in a CH3 domain which is derived from the IgG1 antibody class. In an embodiment, the modifications comprise a K409R modification to one CH3 domain paired with F405L modification in the second CH3 domain. Additional modifications may also, or alternatively, be at positions 366, 368, 370, 399, 405, 407, and 409. Preferably, heterodimerization of polypeptides comprising such modifications is achieved under reducing conditions, e.g., 10-100 mM 2-MEA (e.g., 25, 50, or 100 mM 2-MEA) for 1-10, e.g., 1.5-5, e.g., 5, hours at 25-37C, e.g., 25C or 37C.

[0253] The amino acid replacements described herein can be introduced into the CH3 domains using techniques which are well known in the art (see, e.g., McPherson, ed., 1991, *Directed Mutagenesis: a Practical Approach*; Adelman *et al.*, 1983, *DNA*, 2:183).

[0254] The IgG heterodimerization strategy is further described in, for example, WO2008/119353, WO2011/131746, and WO2013/060867, the contents of which are hereby incorporated by reference in their entirety.

[0255] In any of the embodiments described in this Section, the CH3 domains can be additionally modified to introduce a pair of cysteine residues as described in Section 6.3.1.5.1.

6.3.1.5.3. Polar Bridge

[0256] Heterodimerization of polypeptide chains of TBMs comprising an Fc domain can be increased by introducing modifications based on the “polar-bridging” rationale, which is to make residues at the binding interface of the two polypeptide chains to interact with residues of similar (or complimentary) physical property in the heterodimer configuration, while with residues of different physical property in the homodimer configuration. In particular, these modifications are designed so that, in the heterodimer formation, polar residues interact with polar residues, while hydrophobic residues interact with hydrophobic residues. In contrast, in the homodimer formation, residues are modified so that polar residues interact with hydrophobic residues. The favorable interactions in the heterodimer configuration and the

unfavorable interactions in the homodimer configuration work together to make it more likely for Fc regions to form heterodimers than to form homodimers.

[0257] In an exemplary embodiment, the above modifications are generated at one or more positions of residues 364, 368, 399, 405, 409, and 411 of a CH3 domain.

[0258] In some embodiments, one or more modifications selected from S364L, T366V, L368Q, N399K, F405S, K409F and R411K are introduced into one of the two CH3 domains. One or more modifications selected from Y407F, K409Q and T411N can be introduced into the second CH3 domain.

[0259] In another embodiment, one or more modifications selected from a group consisting of S364L, T366V, L368Q, D399K, F405S, K409F and T411K are introduced into one CH3 domain, while one or more modifications selected from Y407F, K409Q and T411D are introduced into the second CH3 domain.

[0260] In one exemplary embodiment, the original residue of threonine at position 366 of one CH3 domain is replaced by valine, while the original residue of tyrosine at position 407 of the other CH3 domain is replaced by phenylalanine.

[0261] In another exemplary embodiment, the original residue of serine at position 364 of one CH3 domain is replaced by leucine, while the original residue of leucine at position 368 of the same CH3 domain is replaced by glutamine.

[0262] In yet another exemplary embodiment, the original residue of phenylalanine at position 405 of one CH3 domain is replaced by serine and the original residue of lysine at position 409 of this CH3 domain is replaced by phenylalanine, while the original residue of lysine at position 409 of the other CH3 domain is replaced by glutamine.

[0263] In yet another exemplary embodiment, the original residue of aspartic acid at position 399 of one CH3 domain is replaced by lysine, and the original residue of threonine at position 411 of the same CH3 domain is replaced by lysine, while the original residue of threonine at position 411 of the other CH3 domain is replaced by aspartic acid.

[0264] The amino acid replacements described herein can be introduced into the CH3 domains using techniques which are well known in the art (see, e.g., McPherson, ed., 1991, Directed Mutagenesis: a Practical Approach; Adelman *et al.*, 1983, DNA, 2:183). The polar bridge strategy is described in, for example, WO2006/106905, WO2009/089004 and K.Gunasekaran, *et al.* (2010) The Journal of Biological Chemistry, 285:19637-19646, the contents of which are hereby incorporated by reference in their entirety.

[0265] Additional polar bridge modifications are described in, for example, PCT publication no. WO2014/145806 (for example, Figure 6 of WO2014/145806), PCT publication no. WO2014/110601, and PCT publication no. WO 2016/086186, WO 2016/086189, WO

2016/086196 and WO 2016/182751 the contents of which are incorporated herein in their entireties. An example of a polar bridge variant comprises a constant chain comprising a N208D, Q295E, N384D, Q418E and N421D modification.

[0266] In any of the embodiments described herein, the CH3 domains may be additionally modified to introduce a pair of cysteine residues as described in Section 6.3.1.5.1.

[0267] Additional strategies for enhancing heterodimerization are described in, for example, WO2016/105450, WO2016/086186, WO2016/086189, WO2016/086196, WO2016/141378, and WO2014/145806, and WO2014/110601, the entire contents of each of which is hereby incorporated by reference in its entirety. Any of said strategies can be employed in a TBM described herein.

6.3.2. Hinge Regions

[0268] The TBMs of the disclosure can also comprise hinge regions, *e.g.*, connecting an antigen-binding module to an Fc region. The hinge region can be a native or a modified hinge region. Hinge regions are typically found at the N-termini of Fc regions.

[0269] A native hinge region is the hinge region that would normally be found between Fab and Fc domains in a naturally occurring antibody. A modified hinge region is any hinge that differs in length and/or composition from the native hinge region. Such hinges can include hinge regions from other species, such as human, mouse, rat, rabbit, shark, pig, hamster, camel, llama or goat hinge regions. Other modified hinge regions may comprise a complete hinge region derived from an antibody of a different class or subclass from that of the heavy chain Fc region. Alternatively, the modified hinge region may comprise part of a natural hinge or a repeating unit in which each unit in the repeat is derived from a natural hinge region. In a further alternative, the natural hinge region may be altered by converting one or more cysteine or other residues into neutral residues, such as serine or alanine, or by converting suitably placed residues into cysteine residues. By such means the number of cysteine residues in the hinge region may be increased or decreased. Other modified hinge regions may be entirely synthetic and may be designed to possess desired properties such as length, cysteine composition and flexibility.

[0270] A number of modified hinge regions have already been described for example, in U.S. Pat. No. 5,677,425, WO9915549, WO2005003170, WO2005003169, WO2005003170, WO9825971 and WO2005003171 and these are incorporated herein by reference.

[0271] Examples of suitable hinge sequences are shown in Table 3.

TABLE 3 Hinge Sequences			
Hinge Name	Hinge Description	Hinge Sequence	SEQ ID NO:
H1	Human IgA1	VPSTPPTPSPSTPPTSPSPS	4

TABLE 3 Hinge Sequences			
Hinge Name	Hinge Description	Hinge Sequence	SEQ ID NO:
H2	Human IgA2	VPPPPP	5
H3	Human IgD	ESPKAQASSVPTAQPQAEGSLAKATTAPATTRN TGRGGEEKKKKEKEKEEQEERETKTP	6
H4	Human IgG1	EPKSCDKTHTCPPCP	7
H5	Human IgG2	ERKCCVECP	8
H6	Human IgG3	ELKTPLGDTTHTCPRCPEPKSCDTPPPCPRCPE PKSCDTPPPCPRCPEPKSCDTPPPCPRCP	9
H7	Human IgG4	ESKYGPPCPSCP	10
H8	Human IgG4(P)	ESKYGPPCPPCP	11
H9	Engineered v1	CPPC	2
H10	Engineered v2	CPSC	12
H11	Engineered v3	CPRC	13
H12	Engineered v4	SPPC	14
H13	Engineered v5	CPPS	15
H14	Engineered v6	SPPS	3
H15	Engineered v7	DKTHTCAA	16
H16	Engineered v8	DKTHTCPPCPA	17
H17	Engineered v9	DKTHTCPPCPATCPPCPA	18
H18	Engineered v10	DKTHTCPPCPATCPPCPATCPPCPA	19
H19	Engineered v11	DKTHTCPPCPAGKPTLYNSLVMSDAGTCY	20
H20	Engineered v12	DKTHTCPPCPAGKPTHVNVSVVMAEVDGTCY	21
H21	Engineered v13	DKTHTCCVECPCPA	22
H22	Engineered v14	DKTHTCPRCPEPKSCDTPPPCPRCPA	23
H23	Engineered v15	DKTHTCPSCPA	24

[0272] In one embodiment, the heavy chain Fc region possesses an intact hinge region at its N-terminus.

[0273] In one embodiment the heavy chain Fc region and hinge region are derived from IgG4 and the hinge region comprises the modified sequence CPPC (SEQ ID NO: 2). The core hinge region of human IgG4 contains the sequence CPSC (SEQ ID NO: 12) compared to IgG1 which contains the sequence CPPC (SEQ ID NO: 2). The serine residue present in the IgG4 sequence leads to increased flexibility in this region, and therefore a proportion of molecules form disulfide bonds within the same protein chain (an intrachain disulfide) rather than bridging to the other heavy chain in the IgG molecule to form the interchain disulfide. (Angel *et al.*, 1993,

Mol Immunol 30(1):105-108). Changing the serine residue to a proline to give the same core sequence as IgG1 allows complete formation of inter-chain disulfides in the IgG4 hinge region, thus reducing heterogeneity in the purified product. This altered isotype is termed IgG4P.

6.3.3. ABM Linkers

[0274] In certain aspects, the present disclosure provides TBMs comprising at least three ABMs, wherein two or more components of an ABM (e.g., a VH and a VL of an scFv), two or more ABMs, or an ABM and a non-ABM domain (e.g., a dimerization domain such as an Fc region) are connected to one another by a peptide linker. Such linkers are referred to herein as “ABM linkers”, as opposed to the ADC linkers used to attach drugs to TBMs as described, for example, in Section 6.9.2.

[0275] A peptide linker can range from 2 amino acids to 60 or more amino acids, and in certain aspects a peptide linker ranges from 3 amino acids to 50 amino acids, from 4 to 30 amino acids, from 5 to 25 amino acids, from 10 to 25 amino acids or from 12 to 20 amino acids. In particular embodiments, a peptide linker is 2 amino acids, 3 amino acids, 4 amino acid, 5 amino acids, 6 amino acids, 7 amino acids, 8 amino acids, 9 amino acids, 10 amino acids, 11 amino acids, 12 amino acids, 13 amino acids, 14 amino acid, 15 amino acids, 16 amino acids, 17 amino acids, 18 amino acids, 19 amino acids, 20 amino acids, 21 amino acids, 22 amino acids, 23 amino acids, 24 amino acid, 25 amino acids, 26 amino acids, 27 amino acids, 28 amino acids, 29 amino acids, 30 amino acids, 31 amino acids, 32 amino acids, 33 amino acids, 34 amino acid, 35 amino acids, 36 amino acids, 37 amino acids, 38 amino acids, 39 amino acids, 40 amino acids, 41 amino acids, 42 amino acids, 43 amino acids, 44 amino acid, 45 amino acids, 46 amino acids, 47 amino acids, 48 amino acids, 49 amino acids, or 50 amino acids in length.

[0276] Charged and/or flexible linkers are particularly preferred.

[0277] Examples of flexible ABM linkers that can be used in the TBMs of the disclosure include those disclosed by Chen *et al.*, 2013, Adv Drug Deliv Rev. 65(10):1357–1369 and Klein *et al.*, 2014, Protein Engineering, Design & Selection 27(10):325–330. A particularly useful flexible linker is (GGGGS)*n* (SEQ ID NO: 25) (also referred to as (G4S)*n* (SEQ ID NO: 25)). In some embodiments, *n* is any number between 1 and 10, *i.e.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, and 10, or any range bounded by any two of the foregoing numbers, *e.g.*, 1 to 5, 2 to 5, 3 to 6, 2 to 4, 1 to 4, and so on and so forth.

[0278] Other examples of suitable TBM linkers for use in the TBMs of the present disclosure are shown in Table 4 below:

TABLE 4 ABM Linker Sequences

Linker Name	Linker Sequence	SEQ ID NO:
L1	ADAAP	26
L2	ADAAPTVSIFP	27
L3	ADAAPTVSIFPP	28
L4	AKTTAP	29
L5	AKTTAPSVYPLAP	30
L6	AKTTPKLEEGEFSEARV	31
L7	AKTTPKLGG	32
L8	AKTTPP	33
L9	AKTTPPSVTPLAP	34
L10	ASTKGP	35
L11	ASTKGPSVFPLAP	36
L12	ASTKGPSVFPLAPASTKGPSVFPLAP	37
L13	EGKSSGSGSESKST	38
L14	GEGESGEGESGEGES	39
L15	GEGESGEGESGEGESGEGES	40
L16	GEGGSGEGGS	41
L17	GENKVEYAPALMALS	42
L18	GEGSGGEGSGGEGS	43
L19	GGGESGGEGSGGEGS	44
L20	GGGESGGGESGGGES	45
L21	(GGGGS) _n (also referred to as (G4S) _n), wherein n can be 1-10.	46
L22	GGGGS	47
L23	GGGSGGGSGGGGS	1
L24	GGGSGGGSGGGSGGGGS	48
L25	GGGKSGGGKSGGGKS	49
L26	GGGKSGGKSGGKGS	50
L27	GGKSGGKSGGKGS	51
L28	GGSGG	52
L29	GGSGGGGSG	53
L30	GGSGGGGSGGGGS	54
L31	GHEAAVMQVQYPAS	55
L32	GKGGSGKGGSGKGS	56
L33	GKGKSGKGKSGKGKS	57
L34	GKGKSGKGKSGKGKSGKGKS	58

TABLE 4 ABM Linker Sequences		
Linker Name	Linker Sequence	SEQ ID NO:
L35	GKPGSGKPGSGKPGS	59
L36	GKPGSGKPGSGKPGSGKPGS	60
L37	GPAKELTPLKEAKVS	61
L38	GSAGSAAGSGEF	62
L39	IRPRAIGGSKPRVA	63
L40	KESGSVSSEQLAQFRSLD	64
L41	KTTPKLEEGERFSEAR	65
L42	QPKAAP	66
L43	QPKAAPSVTLFPP	67
L44	RADAAAA(G4S) ₄	68
L45	RADAAAAGGPGS	69
L46	RADAAP	70
L47	RADAAPTVS	71
L48	SAKTPP	72
L49	SAKTPPKLEEGERFSEARV	73
L50	SAKTPPKLGG	74
L51	STAGDTHLGGEDFD	75
L52	TVAAP	76
L53	TVAAPSVFIFPP	77
L54	TVAAPSVFIFPPTVAAPSVFIFPP	78

[0279] In various aspects, the disclosure provides a TBM which comprises one or more ABM linkers. Each of the ABM linkers can be range from 2 amino acids to 60 amino acids in length, preferably 4 to 30 amino acids, from 5 to 25 amino acids, from 10 to 25 amino acids or from 12 to 20 amino acids in length, optionally selected from Table 4 above. In particular embodiments, the TBM comprises two, three, four, five or six ABM linkers. The ABM linkers can be on one, two, three, four or even more polypeptide chains of the TBM.

6.4. Exemplary Trispecific Binding Molecules

[0280] Exemplary TBM configurations are shown in FIG. 1. FIG. 1A shows the components of the TBM configurations shown in FIGS. 1B-1Z. The scFv, Fab, non-immunoglobulin based ABM, and Fc each can have the characteristics described for these components in Sections 6.2 and 6.3. The components of the TBM configurations shown in FIG. 1 can be associated with each other by any of the means described in Sections 6.2 and 6.3 (e.g., by direct bonds, ABM

linkers, disulfide bonds, Fc domains with modified with knob in hole interactions, *etc.*). The orientations and associations of the various components shown in FIG. 1 are merely exemplary; as will be appreciated by skilled artisans, other orientations and associations may be suitable (*e.g.*, as described in Sections 6.2 and 6.3).

[0281] TBMs of the disclosure are not limited to the configurations shown in FIG. 1. Other configurations that may be used are known to those skilled in the art. See, *e.g.*, WO 2014/145806; WO 2017/124002; Liu *et al.*, 2017, Front Immunol. 8:38; Brinkmann & Kontermann, 2017, mAbs 9:2, 182-212; US 2016/0355600; Klein *et al.*, 2016, MABs 8(6):1010-20; and US 2017/0145116.

6.4.1. Exemplary Trivalent TBMs

[0282] The TBMs of the disclosure can be trivalent, *i.e.*, they have three antigen-binding domains, each of which binds one of CD2, a component of a TCR complex and TAA.

[0283] Exemplary trivalent TBM configurations are shown in FIGS. 1B through 1O and FIGS. 1V-1Z.

[0284] As depicted in FIGS. 1B-1K, 1O and 1V-1Z, a TBM can comprise two half antibodies, one comprising two ABMs and the other comprising one ABM, the two halves paired through an Fc domain.

[0285] In the embodiment of FIG. 1B, the first (or left) half antibody comprises an scFv and an Fc region, and the second (or right) half antibody comprises a Fab, an scFv and an Fc region. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0286] In the embodiment of FIG. 1C, the first (or left) half antibody comprises two Fab and an Fc region, and the second (or right) half antibody comprises a Fab and an Fc region. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0287] In the embodiment of FIG. 1D, the first (or left) half antibody comprises a Fab, an scFv and an Fc region, and the second (or right) half antibody comprises a Fab and an Fc region. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0288] In the embodiment of FIG. 1E, the first (or left) half antibody comprises an scFv and an Fc region, and the second (or right) half antibody comprises two Fab and an Fc region. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0289] In the embodiment of FIG. 1F, the first (or left) half antibody comprises an scFv, an Fc region, and a Fab, and the second (or right) half antibody comprises a Fab and an Fc region. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0290] In the embodiment of FIG. 1G, the first (or left) half antibody comprises an scFv and an Fc region, and the second (or right) half antibody comprises a Fab an Fc region, and an scFV. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0291] In the embodiment of FIG. 1H, the first (or left) half antibody comprises two Fab and an Fc region, and the second (or right) half antibody comprises a non-immunoglobulin based ABM and an Fc region. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0292] In the embodiment of FIG. 1I, the first (or left) half antibody comprises a Fab, an scFv, and an Fc region, and the second (or right) half antibody comprises a non-immunoglobulin based ABM and an Fc region. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0293] In the embodiment of FIG. 1J, the first (or left) half antibody comprises a Fab and an Fc region, and the second (or right) half antibody comprises an scFv, a non-immunoglobulin based ABM and an Fc region. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0294] In the embodiment of FIG. 1K, the first (or left) half antibody comprises an scFv and an Fc region, and the second (or right) half antibody comprises an scFv, an Fc region, and a second scFv. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0295] In the embodiment of FIG. 1N, the first (or left) half antibody comprises a Fab, an Fc region, and an scFv, and the second (or right) half antibody comprises a Fab, and an Fc region. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0296] In the embodiment of FIG. 1O, the first (or left) half antibody comprises a Fab, an Fc region, and a scFab, and the second (or right) half antibody comprises a Fab and an Fc region. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0297] In the embodiment of FIG. 1V, the first (or left) half antibody comprises a non-immunoglobulin based ABM, an Fab and an Fc region, and the second (or right) half antibody comprises an Fab and an Fc region. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0298] In the embodiment of FIG. 1W, the first (or left) half antibody comprises a non-immunoglobulin based ABM, an scFv and an Fc region, and the second (or right) half antibody

comprises an Fab and an Fc region. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0299] In the embodiment of FIG. 1X, the first (or left) half antibody comprises an scFv, an Fc region and a non-immunoglobulin based ABM on the C-terminal end of the Fc region, and the second (or right) half antibody comprises an Fab and an Fc region. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0300] In the embodiment of FIG. 1Y, the first (or left) half antibody comprises an scFv, an Fc region and an scFv on the C-terminal end of the Fc region, and the second (or right) half antibody comprises non-immunoglobulin based ABM and an Fc region. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0301] In the embodiment of FIG. 1Z, the first (or left) half antibody comprises an scFv, an Fc region and an Fab on the C-terminal end of the Fc region, and the second (or right) half antibody comprises non-immunoglobulin based ABM and an Fc region. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0302] Alternatively, as depicted in FIG. 1L, trivalent a TBM can comprise two half antibodies, each comprising one complete ABM and a portion of another ABM (one a VH, the other a VL). The two half antibodies are paired through an Fc domain, whereupon the VH and the VL associate to form a complete antigen-binding Fv domain.

[0303] The TBM can be a single chain, as shown in FIG. 1M. The TBM of FIG. 1M comprises three scFv domains connected through linkers.

[0304] In each of the configurations shown in FIGS. 1B-1O and 1V-Z, each of the domains designated X, Y, and Z represents a TCR ABM, a CD2 ABM, or a TAA ABM, although not necessarily in that order. In other words, X can be a TCR ABM, a CD2 ABM, or TAA ABM, Y can be a TCR ABM, a CD2 ABM, or a TAA ABM, and Z can be a CD2 ABM, a TCR ABM, or a TAA ABM, provided that the TBM comprises at least one TCR ABM, at least one CD2 ABM, and at least one TAA ABM.

[0305] Accordingly, the present disclosure provides a trivalent TBM as shown in any one of FIGS. 1B through 1O and 1V through Z, wherein X is a CD2 ABM, Y is a TCR ABM and Z is a TAA ABM (this configuration of ABMs designated as "T1" for convenience).

[0306] The present disclosure also provides a trivalent TBM as shown in any one of FIGS. 1B through 1O and 1V through Z, wherein X is a CD2 ABM, Y is a TAA ABM, and Z is a TCR ABM (this configuration of ABMs designated as "T2" for convenience).

[0307] The present disclosure further provides a trivalent TBM as shown in any one of FIGS. 1B through 1O and 1V through Z, wherein X is a TCR ABM, Y is a CD2 ABM, and Z is a TAA ABM (this configuration of ABMs designated as "T3" for convenience).

[0308] The present disclosure yet further provides a trivalent TBM as shown in any one of FIGS. 1B through 1O and 1V through Z, wherein X is a TCR ABM, Y is a TAA ABM, and Z is a CD2 ABM (this configuration of ABMs designated as “T4” for convenience).

[0309] The present disclosure yet further provides a trivalent TBM as shown in any one of FIGS. 1B through 1O and 1V through Z, wherein X is a TAA ABM, Y is a CD2 ABM, and Z is a TCR ABM (this configuration of ABMs designated as “T5” for convenience).

[0310] The present disclosure yet further provides a trivalent TBM as shown in any one of FIGS. 1B through 1O and 1V through Z, wherein X is a TAA ABM, Y is a TCR ABM, and Z is a CD2 ABM (this configuration of ABMs designated as “T6” for convenience).

6.4.2. Exemplary Tetravalent TBMs

[0311] The TBMs of the disclosure can be tetravalent, *i.e.*, they have four antigen-binding domains, one or two of which binds CD2, one or two of which binds a component of a TCR complex, and one or two of which binds TAA.

[0312] Exemplary tetravalent TBM configurations are shown in FIGS. 1P-1R.

[0313] As depicted in FIGS. 1P-1R, a tetravalent TBM can comprise two half antibodies, each comprising two complete ABMs, the two halves paired through an Fc domain.

[0314] In the embodiment of FIG. 1P, the first (or left) half antibody comprises a Fab, an Fc region, and a second Fab, and the second (or right) half antibody comprises a Fab, an Fc region, and a second Fab. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0315] In the embodiment of FIG. 1Q, the first (or left) half antibody comprises a Fab, an Fc region, and an scFv, and the second (or right) half antibody comprises a Fab, an Fc region, and an scFv. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0316] In the embodiment of FIG. 1R, the first (or left) half antibody comprises a Fab, an Fc region, and an scFv, and the second (or right) half antibody comprises an scFv, an Fc region, and a Fab. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0317] In the configuration shown in FIGS. 1P-1R, each of X, Y, Z, and A represent a TCR ABM, a CD2 ABM, or a TAA ABM, although not necessarily in that order, and provided that the TBM comprises at least one TCR ABM, one CD2 ABM, and one TAA ABM. Thus, the tetravalent ABMs of the disclosure will include two ABMs against one of a component of a TCR complex, CD2 and TAA. Preferably, a tetravalent TBM has two TAA ABMs.

[0318] Accordingly, in the present disclosure provides a tetravalent TBM as shown in any one of FIGS. 1P-1R, wherein X is a CD2 ABM, Y is a TCR ABM and both Z and A are TAA ABMs (this configuration of ABMs designated as “Tv 1” for convenience).

[0319] The disclosure further provides a tetravalent TBM as shown in any one of FIGS. 1P-1R, wherein X is a CD2 ABM, both Y and A are TAA ABMs, and Z is a TCR ABM (this configuration of ABMs designated as “Tv 2” for convenience).

[0320] The disclosure yet further provides a tetravalent TBM as shown in any one of FIGS. 1P-1R, wherein X is a TCR ABM, Y is a CD2 ABM, and both Z and A are TAA ABMs (this configuration of ABMs designated as “Tv 3” for convenience).

[0321] The disclosure further provides a tetravalent TBM as shown in any one of FIGS. 1P-1R, wherein, X is a TCR ABM, both Y and A are TAA ABMs, and Z is a CD2 ABM (this configuration of ABMs designated as “Tv 4” for convenience).

[0322] The disclosure further provides a tetravalent TBM as shown in any one of FIGS. 1P-1R, wherein both X and A are TAA ABMs, Y is a CD2 ABM, and Z is a TCR ABM (this configuration of ABMs designated as “Tv 5” for convenience).

[0323] The disclosure further provides a tetravalent TBM as shown in any one of FIGS. 1P-1R, wherein both X and A are TAA ABMs, Y is a TCR ABM, and Z is a CD2 ABM (this configuration of ABMs designated as “Tv 6” for convenience).

[0324] The disclosure further provides a tetravalent TBM as shown in any one of FIGS. 1P-1R, wherein X is a CD2 ABM, both Y and Z are CD2 ABMs, and Z is a TCR ABM (this configuration of ABMs designated as “Tv 7” for convenience).

[0325] The disclosure further provides a tetravalent TBM as shown in any one of FIGS. 1P-1R, wherein both X and Z are TAA ABMs, Y is a CD2 ABM, and A is a TCR ABM (this configuration of ABMs designated as “Tv 8” for convenience).

[0326] The disclosure further provides a tetravalent TBM as shown in any one of FIGS. 1P-1R, wherein X is a TCR ABM, both Y and A are TAA ABMs, and Z is a CD2 ABM (this configuration of ABMs designated as “Tv 9” for convenience).

[0327] The disclosure further provides a tetravalent TBM as shown in any one of FIGS. 1P-1R, wherein both X and Y are TAA ABMs, Z is a CD2 ABM, and A is a TCR ABM (this configuration of ABMs designated as “Tv 10” for convenience).

[0328] The disclosure further provides a tetravalent TBM as shown in any one of FIGS. 1P-1R, wherein both X and Z are TAA ABMs, Y is a TCR ABM, and A is a CD2 ABM (this configuration of ABMs designated as “Tv 11” for convenience).

[0329] The disclosure further provides a tetravalent TBM as shown in any one of FIGS. 1P-1R, wherein both X and Y are TAA ABMs, Z is a TCR ABM, and A is a CD2 ABM (this configuration of ABMs designated as “Tv 12” for convenience).

6.4.3. Exemplary Pentavalent TBMs

[0330] The TBMs of the disclosure can be pentavalent, *i.e.*, they have five antigen-binding domains, one, two, or three of which binds CD2, one, two, or three of which binds a component of a TCR complex, and one, two, or three of which binds TAA.

[0331] An exemplary pentavalent TBM configuration is shown in FIG. 1S.

[0332] As depicted in FIG. 1S, a pentavalent TBM can comprise two half antibodies, one of which comprises two complete ABMs and the other of which comprises one complete ABM, the two halves paired through an Fc domain.

[0333] In the embodiment of FIG. 1S, the first (or left) half antibody comprises a Fab, an scFv, and an Fc region, and the second (or right) half antibody comprises a Fab, an Fc region, and an scFv. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0334] In the configuration shown in FIG. 1S, each of X, Y, Z, A, and B represent a TCR ABM, a CD2 ABM, or a TAA ABM, although not necessarily in that order, and provided that the TBM comprises at least one TCR ABM, one CD2 ABM, and one TAA ABM. Thus, the pentavalent TBMs of the disclosure can include two ABMs against two of a component of a TCR complex, CD2 and TAA, or three ABMs against one of a component of a TCR complex, CD2 and TAA. Preferably, a pentavalent TBM has two or three TAA ABMs. In a specific embodiment, a pentavalent TBM has three TAA ABMs.

[0335] Accordingly, the present disclosure provides a pentavalent TBM as shown in FIG. 1S, wherein X, Y, Z, A, and B are ABMs directed to CD2, a component of a TCR complex, and TAA as shown in Table 5.

Table 5 ABM Permutations in Pentavalent TBMs					
Pentavalent Configuration	X	Y	Z	A	B
Pv 1	CD2	CD2	TCR	TAA	TAA
Pv 2	CD2	CD2	TAA	TCR	TAA
Pv 3	CD2	CD2	TAA	TAA	TCR
Pv 4	CD2	TCR	CD2	TAA	TAA
Pv 5	CD2	TAA	CD2	TCR	TAA
Pv 6	CD2	TAA	CD2	TAA	TCR
Pv 7	CD2	TCR	TAA	CD2	TAA
Pv 8	CD2	TAA	TCR	CD2	TAA
Pv 9	CD2	TAA	TAA	CD2	TCR

Table 5 ABM Permutations in Pentavalent TBMs					
Pentavalent Configuration	X	Y	Z	A	B
Pv 10	CD2	TCR	TAA	TAA	CD2
Pv 11	CD2	TAA	TCR	TAA	CD2
Pv 12	CD2	TAA	TAA	TCR	CD2
Pv 13	TCR	CD2	CD2	TAA	TAA
Pv 14	TAA	CD2	CD2	TCR	TAA
Pv 15	TAA	CD2	CD2	TAA	TCR
Pv 16	TCR	CD2	TAA	CD2	TAA
Pv 17	TAA	CD2	TCR	CD2	TAA
Pv 18	TAA	CD2	TAA	CD2	TCR
Pv 19	TCR	CD2	TAA	TAA	CD2
Pv 20	TAA	CD2	TCR	TAA	CD2
Pv 21	TAA	CD2	TAA	TCR	CD2
Pv 22	TCR	TAA	CD2	CD2	TAA
Pv 23	TAA	TCR	CD2	CD2	TAA
Pv 24	TAA	TAA	CD2	CD2	TCR
Pv 25	TCR	TAA	CD2	TAA	CD2
Pv 26	TAA	TCR	CD2	TAA	CD2
Pv 27	TAA	TAA	CD2	TCR	CD2
Pv P28	TCR	TAA	TAA	CD2	CD2
Pv 29	TAA	TCR	TAA	CD2	CD2
Pv 30	TAA	TAA	TCR	CD2	CD2
Pv 31	CD2	TCR	TCR	TAA	TAA
Pv 32	CD2	TCR	TAA	TCR	TAA
Pv 33	CD2	TCR	TAA	TAA	TCR
Pv 34	CD2	TAA	TCR	TCR	TAA
Pv 35	CD2	TAA	TCR	TAA	TCR
Pv 36	CD2	TAA	TAA	TCR	TCR
Pv 37	TCR	CD2	TCR	TAA	TAA
Pv 38	TCR	CD2	TAA	TCR	TAA
Pv 39	TCR	CD2	TAA	TAA	TCR
Pv 40	TAA	CD2	TCR	TCR	TAA
Pv 41	TAA	CD2	TCR	TAA	TCR
Pv 42	TAA	CD2	TAA	TCR	TCR
Pv 43	TCR	TCR	CD2	TAA	TAA
Pv 44	TCR	TAA	CD2	TCR	TAA
Pv 45	TCR	TAA	CD2	TAA	TCR
Pv 46	TAA	TCR	CD2	TCR	TAA
Pv 47	TAA	TCR	CD2	TAA	TCR
Pv 48	TAA	TAA	CD2	TCR	TCR
Pv 49	TCR	TCR	TAA	CD2	TAA
Pv 50	TCR	TAA	TCR	CD2	TAA

Table 5 ABM Permutations in Pentavalent TBMs					
Pentavalent Configuration	X	Y	Z	A	B
Pv 51	TCR	TAA	TAA	CD2	TCR
Pv 52	TAA	TCR	TCR	CD2	TAA
Pv 53	TAA	TCR	TAA	CD2	TCR
Pv 54	TAA	TAA	TCR	CD2	TCR
Pv 55	TCR	TCR	TAA	TAA	CD2
Pv 56	TCR	TAA	TCR	TAA	CD2
Pv 57	TCR	TAA	TAA	TCR	CD2
Pv 58	TAA	TCR	TCR	TAA	CD2
Pv 59	TAA	TCR	TAA	TCR	CD2
Pv 60	TAA	TAA	TCR	TCR	CD2
Pv 61	CD2	TCR	TAA	TAA	TAA
Pv 62	CD2	TAA	TCR	TAA	TAA
Pv 63	CD2	TAA	TAA	TCR	TAA
Pv 64	CD2	TAA	TAA	TAA	TCR
Pv 65	TCR	CD2	TAA	TAA	TAA
Pv 66	TAA	CD2	TCR	TAA	TAA
Pv 67	TAA	CD2	TAA	TCR	TAA
Pv 68	TAA	CD2	TAA	TAA	TCR
Pv 69	TCR	TAA	CD2	TAA	TAA
Pv 70	TAA	TCR	CD2	TAA	TAA
Pv 71	TAA	TAA	CD2	TCR	TAA
Pv 72	TAA	TAA	CD2	TAA	TCR
Pv 73	TCR	TAA	TAA	CD2	TAA
Pv 74	TAA	TCR	TAA	CD2	TAA
Pv 75	TAA	TAA	TCR	CD2	TAA
Pv 76	TAA	TAA	TAA	CD2	TCR
Pv 77	TCR	TAA	TAA	TAA	CD2
Pv 78	TAA	TCR	TAA	TAA	CD2
Pv 79	TAA	TAA	TCR	TAA	CD2
Pv 80	TAA	TAA	TAA	TCR	CD2

6.4.4. Exemplary Hexavalent TBMs

[0336] The TBMs of the disclosure can be hexavalent, *i.e.*, they have six antigen-binding domains, one, two, three, or four of which binds CD2, one, two, three, or four of which binds a component of a TCR complex, and one, two, three, or four of which binds TAA.

[0337] Exemplary hexavalent TBM configurations are shown in FIGS. 1T-1U.

[0338] As depicted in FIGS. 1T-1U, a pentavalent TBM can comprise two half antibodies, one of which comprises two complete ABMs and the other of which comprises one complete ABM, the two halves paired through an Fc domain.

[0339] In the embodiment of FIG. 1T, the first (or left) half antibody comprises a Fab, a second Fab, an Fc region, and an scFv, and the second (or right) half antibody comprises a Fab, a second Fab, an Fc region, and an scFv. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0340] In the embodiment of FIG. 1U, the first (or left) half antibody comprises a first Fv, a second Fv, a third Fv, and an Fc region, and the second (or right) half antibody comprises a first Fv, a second Fv, a third Fv, and an Fc region. The first and second half antibodies are associated through the Fc regions forming an Fc domain.

[0341] In the configuration shown in FIGS. 1T-1U, each of X, Y, Z, A, B, and C represent a TCR ABM, a CD2 ABM, or a TAA ABM, although not necessarily in that order, and provided that the TBM comprises at least one TCR ABM, one CD2 ABM, and one TAA ABM. Thus, the hexavalent TBMs of the disclosure can include (i) two ABMs against each of a component of a TCR complex, CD2 and TAA, (ii) three ABMs against one of a component of a TCR complex, CD2 and TAA, (iii) or four ABMs against one of a component of a TCR complex, CD2, and TAA. For example, a hexavalent ABM can include three ABMs against TAA, two ABMs against CD2 and one ABM against a component of a TCR complex. As another example, a hexavalent ABM can include three ABMs against TAA, two ABMs against a component of a TCR complex and one ABM against CD2. Preferably, a hexavalent TBM has two, three, four TAA ABMs. In a specific embodiment, a hexavalent TBM has three TAA ABMs. In other embodiments, a hexavalent TBM has four TAA ABMs.

[0342] Accordingly, in the present disclosure provides hexavalent TBMs as shown in any one of FIGS. 1T-1U, wherein X, Y, Z, A, B, and C are ABMs directed to CD2, a component of a TCR complex, and TAA as shown in Table 6.

Table 6 ABM Permutations in Hexavalent TBMs						
Hexavalent Configuration	X	Y	Z	A	B	C
Hv 1	CD2	CD2	TCR	TCR	TAA	TAA
Hv 2	CD2	CD2	TCR	TAA	TCR	TAA
Hv 3	CD2	CD2	TCR	TAA	TAA	TCR
Hv 4	CD2	CD2	TAA	TCR	TCR	TAA
Hv 5	CD2	CD2	TAA	TCR	TAA	TCR
Hv 6	CD2	CD2	TAA	TAA	TCR	TCR
Hv 7	CD2	TCR	CD2	TCR	TAA	TAA
Hv 8	CD2	TCR	CD2	TAA	TCR	TAA
Hv 9	CD2	TCR	CD2	TAA	TAA	TCR
Hv 10	CD2	TAA	CD2	TCR	TCR	TAA
Hv 11	CD2	TAA	CD2	TCR	TAA	TCR

Table 6 ABM Permutations in Hexavalent TBMs						
Hexavalent Configuration	X	Y	Z	A	B	C
Hv 12	CD2	TAA	CD2	TAA	TCR	TCR
Hv 13	CD2	TCR	TCR	CD2	TAA	TAA
Hv 14	CD2	TCR	TAA	CD2	TCR	TAA
Hv 15	CD2	TCR	TAA	CD2	TAA	TCR
Hv 16	CD2	TAA	TCR	CD2	TCR	TAA
Hv 17	CD2	TAA	TCR	CD2	TAA	TCR
Hv 18	CD2	TAA	TAA	CD2	TCR	TCR
Hv 19	CD2	TCR	TCR	TAA	CD2	TAA
Hv 20	CD2	TCR	TAA	TCR	CD2	TAA
Hv 21	CD2	TCR	TAA	TAA	CD2	TCR
Hv 22	CD2	TAA	TCR	TCR	CD2	TAA
Hv 23	CD2	TAA	TCR	TAA	CD2	TCR
Hv 24	CD2	TAA	TAA	TCR	CD2	TCR
Hv 25	CD2	TCR	TCR	TAA	TAA	CD2
Hv 26	CD2	TCR	TAA	TCR	TAA	CD2
Hv 27	CD2	TCR	TAA	TAA	TCR	CD2
Hv 28	CD2	TAA	TCR	TCR	TAA	CD2
Hv 29	CD2	TAA	TCR	TAA	TCR	CD2
Hv 30	CD2	TAA	TAA	TCR	TCR	CD2
Hv 31	TCR	CD2	CD2	TCR	TAA	TAA
Hv 32	TCR	CD2	CD2	TAA	TCR	TAA
Hv 33	TCR	CD2	CD2	TAA	TAA	TCR
Hv 34	TAA	CD2	CD2	TCR	TCR	TAA
Hv 35	TAA	CD2	CD2	TCR	TAA	TCR
Hv 36	TAA	CD2	CD2	TAA	TCR	TCR
Hv 37	TCR	CD2	TCR	CD2	TAA	TAA
Hv 38	TCR	CD2	TAA	CD2	TCR	TAA
Hv 39	TCR	CD2	TAA	CD2	TAA	TCR
Hv 40	TAA	CD2	TCR	CD2	TCR	TAA
Hv 41	TAA	CD2	TCR	CD2	TAA	TCR
Hv 42	TAA	CD2	TAA	CD2	TCR	TCR
Hv 43	TCR	CD2	TCR	TAA	CD2	TAA
Hv 44	TCR	CD2	TAA	TCR	CD2	TAA
Hv 45	TCR	CD2	TAA	TAA	CD2	TCR
Hv 46	TAA	CD2	TCR	TCR	CD2	TAA
Hv 47	TAA	CD2	TCR	TAA	CD2	TCR
Hv 48	TAA	CD2	TAA	TCR	CD2	TCR
Hv 49	TCR	CD2	TCR	TAA	TAA	CD2
Hv 50	TCR	CD2	TAA	TCR	TAA	CD2

Table 6 ABM Permutations in Hexavalent TBMs						
Hexavalent Configuration	X	Y	Z	A	B	C
Hv 51	TCR	CD2	TAA	TAA	TCR	CD2
Hv 52	TAA	CD2	TCR	TCR	TAA	CD2
Hv 53	TAA	CD2	TCR	TAA	TCR	CD2
Hv 54	TAA	CD2	TAA	TCR	TCR	CD2
Hv 55	TCR	TCR	CD2	CD2	TAA	TAA
Hv 56	TCR	TAA	CD2	CD2	TCR	TAA
Hv 57	TCR	TAA	CD2	CD2	TAA	TCR
Hv 58	TAA	TCR	CD2	CD2	TCR	TAA
Hv 59	TAA	TCR	CD2	CD2	TAA	TCR
Hv 60	TAA	TAA	CD2	CD2	TCR	TCR
Hv 61	TCR	TCR	CD2	TAA	CD2	TAA
Hv 62	TCR	TAA	CD2	TCR	CD2	TAA
Hv 63	TCR	TAA	CD2	TAA	CD2	TCR
Hv 64	TAA	TCR	CD2	TCR	CD2	TAA
Hv 65	TAA	TCR	CD2	TAA	CD2	TCR
Hv 66	TAA	TAA	CD2	TCR	CD2	TCR
Hv 67	TCR	TCR	CD2	TAA	TAA	CD2
Hv 68	TCR	TAA	CD2	TCR	TAA	CD2
Hv 69	TCR	TAA	CD2	TAA	TCR	CD2
Hv 70	TAA	TCR	CD2	TCR	TAA	CD2
Hv 71	TAA	TCR	CD2	TAA	TCR	CD2
Hv 72	TAA	TAA	CD2	TCR	TCR	CD2
Hv 73	TCR	TCR	TAA	CD2	CD2	TAA
Hv 74	TCR	TAA	TCR	CD2	CD2	TAA
Hv 75	TCR	TAA	TAA	CD2	CD2	TCR
Hv 76	TAA	TCR	TCR	CD2	CD2	TAA
Hv 77	TAA	TCR	TAA	CD2	CD2	TCR
Hv 78	TAA	TAA	TCR	CD2	CD2	TCR
Hv 79	TCR	TCR	TAA	CD2	TAA	CD2
Hv 80	TCR	TAA	TCR	CD2	TAA	CD2
Hv 81	TCR	TAA	TAA	CD2	TCR	CD2
Hv 82	TAA	TCR	TCR	CD2	TAA	CD2
Hv 83	TAA	TCR	TAA	CD2	TCR	CD2
Hv 84	TAA	TAA	TCR	CD2	TCR	CD2
Hv 85	TCR	TCR	TAA	TAA	CD2	CD2
Hv 86	TCR	TAA	TCR	TAA	CD2	CD2
Hv 87	TCR	TAA	TAA	TCR	CD2	CD2
Hv 88	TAA	TCR	TCR	TAA	CD2	CD2
Hv 89	TAA	TCR	TAA	TCR	CD2	CD2

Table 6 ABM Permutations in Hexavalent TBMs						
Hexavalent Configuration	X	Y	Z	A	B	C
Hv 90	TAA	TAA	TCR	TCR	CD2	CD2
Hv 91	CD2	TCR	TCR	TAA	TAA	TAA
Hv 92	CD2	TCR	TAA	TCR	TAA	TAA
Hv 93	CD2	TCR	TAA	TAA	TCR	TAA
Hv 94	CD2	TCR	TAA	TAA	TAA	TCR
Hv 95	CD2	TAA	TCR	TCR	TAA	TAA
Hv 96	CD2	TAA	TCR	TAA	TCR	TAA
Hv 97	CD2	TAA	TCR	TAA	TAA	TCR
Hv 98	CD2	TAA	TAA	TCR	TCR	TAA
Hv 99	CD2	TAA	TAA	TCR	TAA	TCR
Hv 100	CD2	TAA	TAA	TAA	TCR	TCR
Hv 101	TCR	CD2	TCR	TAA	TAA	TAA
Hv 102	TCR	CD2	TAA	TCR	TAA	TAA
Hv 103	TCR	CD2	TAA	TAA	TCR	TAA
Hv 104	TCR	CD2	TAA	TAA	TAA	TCR
Hv 105	TAA	CD2	TCR	TCR	TAA	TAA
Hv 106	TAA	CD2	TCR	TAA	TCR	TAA
Hv 107	TAA	CD2	TCR	TAA	TAA	TCR
Hv 108	TAA	CD2	TAA	TCR	TCR	TAA
Hv 109	TAA	CD2	TAA	TCR	TAA	TCR
Hv 110	TAA	CD2	TAA	TAA	TCR	TCR
Hv 111	TCR	TCR	CD2	TAA	TAA	TAA
Hv 112	TCR	TAA	CD2	TCR	TAA	TAA
Hv 113	TCR	TAA	CD2	TAA	TCR	TAA
Hv 114	TCR	TAA	CD2	TAA	TAA	TCR
Hv 115	TAA	TCR	CD2	TCR	TAA	TAA
Hv 116	TAA	TCR	CD2	TAA	TCR	TAA
Hv 117	TAA	TCR	CD2	TAA	TAA	TCR
Hv 118	TAA	TAA	CD2	TCR	TCR	TAA
Hv 119	TAA	TAA	CD2	TCR	TAA	TCR
Hv 120	TAA	TAA	CD2	TAA	TCR	TCR
Hv 121	TCR	TCR	TAA	CD2	TAA	TAA
Hv 122	TCR	TAA	TCR	CD2	TAA	TAA
Hv 123	TCR	TAA	TAA	CD2	TCR	TAA
Hv 124	TCR	TAA	TAA	CD2	TAA	TCR
Hv 125	TAA	TCR	TCR	CD2	TAA	TAA
Hv 126	TAA	TCR	TAA	CD2	TCR	TAA
Hv 127	TAA	TCR	TAA	CD2	TAA	TCR
Hv 128	TAA	TAA	TCR	CD2	TCR	TAA

Table 6 ABM Permutations in Hexavalent TBMs						
Hexavalent Configuration	X	Y	Z	A	B	C
Hv 129	TAA	TAA	TCR	CD2	TAA	TCR
Hv 130	TAA	TAA	TAA	CD2	TCR	TCR
Hv 131	TCR	TCR	TAA	TAA	CD2	TAA
Hv 132	TCR	TAA	TCR	TAA	CD2	TAA
Hv 133	TCR	TAA	TAA	TCR	CD2	TAA
Hv 134	TCR	TAA	TAA	TAA	CD2	TCR
Hv 135	TAA	TCR	TCR	TAA	CD2	TAA
Hv 136	TAA	TCR	TAA	TCR	CD2	TAA
Hv 137	TAA	TCR	TAA	TAA	CD2	TCR
Hv 138	TAA	TAA	TCR	TCR	CD2	TAA
Hv 139	TAA	TAA	TCR	TAA	CD2	TCR
Hv 140	TAA	TAA	TAA	TCR	CD2	TCR
Hv 141	TCR	TCR	TAA	TAA	TAA	CD2
Hv 142	TCR	TAA	TCR	TAA	TAA	CD2
Hv 143	TCR	TAA	TAA	TCR	TAA	CD2
Hv 144	TCR	TAA	TAA	TAA	TCR	CD2
Hv 145	TAA	TCR	TCR	TAA	TAA	CD2
Hv 146	TAA	TCR	TAA	TCR	TAA	CD2
Hv 147	TAA	TCR	TAA	TAA	TCR	CD2
Hv 148	TAA	TAA	TCR	TCR	TAA	CD2
Hv 149	TAA	TAA	TCR	TAA	TCR	CD2
Hv 150	TAA	TAA	TAA	TCR	TCR	CD2
Hv 151	CD2	CD2	TCR	TAA	TAA	TAA
Hv 152	CD2	CD2	TAA	TCR	TAA	TAA
Hv 153	CD2	CD2	TAA	TAA	TCR	TAA
Hv 154	CD2	CD2	TAA	TAA	TAA	TCR
Hv 155	CD2	TCR	CD2	TAA	TAA	TAA
Hv 156	CD2	TAA	CD2	TCR	TAA	TAA
Hv 157	CD2	TAA	CD2	TAA	TCR	TAA
Hv 158	CD2	TAA	CD2	TAA	TAA	TCR
Hv 159	CD2	TCR	TAA	CD2	TAA	TAA
Hv 160	CD2	TAA	TCR	CD2	TAA	TAA
Hv 161	CD2	TAA	TAA	CD2	TCR	TAA
Hv 162	CD2	TAA	TAA	CD2	TAA	TCR
Hv 163	CD2	TCR	TAA	TAA	CD2	TAA
Hv 164	CD2	TAA	TCR	TAA	CD2	TAA
Hv 165	CD2	TAA	TAA	TCR	CD2	TAA
Hv 166	CD2	TAA	TAA	TAA	CD2	TCR
Hv 167	CD2	TCR	TAA	TAA	TAA	CD2

Table 6 ABM Permutations in Hexavalent TBMs						
Hexavalent Configuration	X	Y	Z	A	B	C
Hv 168	CD2	TAA	TCR	TAA	TAA	CD2
Hv 169	CD2	TAA	TAA	TCR	TAA	CD2
Hv 170	CD2	TAA	TAA	TAA	TCR	CD2
Hv 171	TCR	CD2	CD2	TAA	TAA	TAA
Hv 172	TAA	CD2	CD2	TCR	TAA	TAA
Hv 173	TAA	CD2	CD2	TAA	TCR	TAA
Hv 174	TAA	CD2	CD2	TAA	TAA	TCR
Hv 175	TCR	CD2	TAA	CD2	TAA	TAA
Hv 176	TAA	CD2	TCR	CD2	TAA	TAA
Hv 177	TAA	CD2	TAA	CD2	TCR	TAA
Hv 178	TAA	CD2	TAA	CD2	TAA	TCR
Hv 179	TCR	CD2	TAA	TAA	CD2	TAA
Hv 180	TAA	CD2	TCR	TAA	CD2	TAA
Hv 181	TAA	CD2	TAA	TCR	CD2	TAA
Hv 182	TAA	CD2	TAA	TAA	CD2	TCR
Hv 183	TCR	CD2	TAA	TAA	TAA	CD2
Hv 184	TAA	CD2	TCR	TAA	TAA	CD2
Hv 185	TAA	CD2	TAA	TCR	TAA	CD2
Hv 186	TAA	CD2	TAA	TAA	TCR	CD2
Hv 187	TCR	TAA	CD2	CD2	TAA	TAA
Hv 188	TAA	TCR	CD2	CD2	TAA	TAA
Hv 189	TAA	TAA	CD2	CD2	TCR	TAA
Hv 190	TAA	TAA	CD2	CD2	TAA	TCR
Hv 191	TCR	TAA	CD2	TAA	CD2	TAA
Hv 192	TAA	TCR	CD2	TAA	CD2	TAA
Hv 193	TAA	TAA	CD2	TCR	CD2	TAA
Hv 194	TAA	TAA	CD2	TAA	CD2	TCR
Hv 195	TCR	TAA	CD2	TAA	TAA	CD2
Hv 196	TAA	TCR	CD2	TAA	TAA	CD2
Hv 197	TAA	TAA	CD2	TCR	TAA	CD2
Hv 198	TAA	TAA	CD2	TAA	TCR	CD2
Hv 199	TCR	TAA	TAA	CD2	CD2	TAA
Hv 200	TAA	TCR	TAA	CD2	CD2	TAA
Hv 201	TAA	TAA	TCR	CD2	CD2	TAA
Hv 202	TAA	TAA	TAA	CD2	CD2	TCR
Hv 203	TCR	TAA	TAA	CD2	TAA	CD2
Hv 204	TAA	TCR	TAA	CD2	TAA	CD2
Hv 205	TAA	TAA	TCR	CD2	TAA	CD2
Hv 206	TAA	TAA	TAA	CD2	TCR	CD2

Table 6 ABM Permutations in Hexavalent TBMs						
Hexavalent Configuration	X	Y	Z	A	B	C
Hv 207	TCR	TAA	TAA	TAA	CD2	CD2
Hv 208	TAA	TCR	TAA	TAA	CD2	CD2
Hv 209	TAA	TAA	TCR	TAA	CD2	CD2
Hv 210	TAA	TAA	TAA	TCR	CD2	CD2
Hv 211	CD2	TCR	TAA	TAA	TAA	TAA
Hv 212	CD2	TAA	TCR	TAA	TAA	TAA
Hv 213	CD2	TAA	TAA	TCR	TAA	TAA
Hv 214	CD2	TAA	TAA	TAA	TCR	TAA
Hv 215	CD2	TAA	TAA	TAA	TAA	TCR
Hv 216	TCR	CD2	TAA	TAA	TAA	TAA
Hv 217	TAA	CD2	TCR	TAA	TAA	TAA
Hv 218	TAA	CD2	TAA	TCR	TAA	TAA
Hv 219	TAA	CD2	TAA	TAA	TCR	TAA
Hv 220	TAA	CD2	TAA	TAA	TAA	TCR
Hv 221	TCR	TAA	CD2	TAA	TAA	TAA
Hv 222	TAA	TCR	CD2	TAA	TAA	TAA
Hv 223	TAA	TAA	CD2	TCR	TAA	TAA
Hv 224	TAA	TAA	CD2	TAA	TCR	TAA
Hv 225	TAA	TAA	CD2	TAA	TAA	TCR
Hv 226	TCR	TAA	TAA	CD2	TAA	TAA
Hv 227	TAA	TCR	TAA	CD2	TAA	TAA
Hv 228	TAA	TAA	TCR	CD2	TAA	TAA
Hv 229	TAA	TAA	TAA	CD2	TCR	TAA
Hv 230	TAA	TAA	TAA	CD2	TAA	TCR
Hv 231	TCR	TAA	TAA	TAA	CD2	TAA
Hv 232	TAA	TCR	TAA	TAA	CD2	TAA
Hv 233	TAA	TAA	TCR	TAA	CD2	TAA
Hv 234	TAA	TAA	TAA	TCR	CD2	TAA
Hv 235	TAA	TAA	TAA	TAA	CD2	TCR
Hv 236	TCR	TAA	TAA	TAA	TAA	CD2
Hv 237	TAA	TCR	TAA	TAA	TAA	CD2
Hv 238	TAA	TAA	TCR	TAA	TAA	CD2
Hv 239	TAA	TAA	TAA	TCR	TAA	CD2
Hv 240	TAA	TAA	TAA	TAA	TCR	CD2

6.5. TCR ABMs

The TBMs of the disclosure contain an ABM that specifically binds to a component of a TCR complex. The TCR is a disulfide-linked membrane-anchored heterodimeric protein normally

consisting of the highly variable alpha (α) and beta (β) chains expressed as part of a complex with the invariant CD3 chain molecules. T cells expressing this receptor are referred to as $\alpha\beta$ (or $\alpha\beta$) T cells, though a minority of T cells express an alternate receptor, formed by variable gamma (γ) and delta (δ) chains, referred as $\gamma\delta$ T cells.

[0343] In a preferred embodiment, TBMs of the disclosure contain an ABM that specifically binds to CD3.

6.5.1. CD3 ABMs

[0344] The TBMs of the disclosure can contain an ABM that specifically binds to CD3. The term "CD3" refers to the cluster of differentiation 3 co-receptor (or co-receptor complex, or polypeptide chain of the co-receptor complex) of the T cell receptor. The amino acid sequence of the polypeptide chains of human CD3 are provided in NCBI Accession P04234, P07766 and P09693. CD3 proteins may also include variants. CD3 proteins may also include fragments. CD3 proteins also include post-translational modifications of the CD3 amino acid sequences. Post-translational modifications include, but are not limited to, N-and O-linked glycosylation.

[0345] In some embodiments, a TBM of the disclosure can comprise an ABM which is an anti-CD3 antibody (e.g., as described in US 2016/0355600, WO 2014/110601, and WO 2014/145806, the contents of which are hereby incorporated by reference) or an antigen-binding domain thereof. Exemplary anti-CD3 VH, VL, and scFV sequences that can be used in TBM of the disclosure are provided in Table 7A.

TABLE 7A CD3 Binders – Variable domain sequences			
Binding Domain	Chain	Sequence	SEQ ID NO:
CD3-1	VH	QVQLQQSGAELARPGASVKMSCKASGYTFTRYTMHWWKQRPQGQ LEWIGYINPSRGYTNYNQKFQDKATLTDDKSSSTAYMQLSSLTSEDS AVYYCARYYDDHYCLDYWGQGTTTLTVSS	79
	VL	QIVLTQSPAIMSASPGEKVTMTCSASSSVSYMNWYQQKSGTSPKR WIYDTSKLASGVPAHFRGSGSGTSYSLTISGMEAEDAATYYCQQWS SNPFTFGSGTKLEIN	80
CD3-2	VH	EVQLVESGGGLVQPKGSLKLSAASGFTFNTYAMNWWRQAPGKGL EWWARIRSKYNNYATYYADSVKDRFTISRDDSQSILYLQMNNLKTED TAMYYCVRHGNFGNSYVSWFAYWGQGTLTVSA	81
	VL	QAVVTQESALTTSPGETVTLTCSRSTGAVTTSNYANWWQEKPDHLF TGLIGGTNKRAPGVPARFSGSLIGDKAALTITGAQTEDEAIYFCALWY SNLWWFGGGTKLTVL	82
CD3-3	VH	QVQLQQSGAELARPGASVKMSCKASGYTFTSYTMHWWKQRPQGQ LEWIGYINPSSGYTKYNQKFQDKATLTADKSSSTAYMQLSSLTSEDS AVYYCARWQDYDVYFDYWGQGTTTLTVSS	83
	VL	QIVLSQSPAILSASPGEKVTMTCSRASSSVSYMHWYQQKPGSSPKPW IYATSNLASGVPARFSGSGSGTSYSLTISRVEAEDAATYYCQQWSSN	84

TABLE 7A CD3 Binders – Variable domain sequences			
Binding Domain	Chain	Sequence	SEQ ID NO:
		PPTFGGGTKLETK	
CD3-4	VH	QVQLQQSGAELARPGASVKMSCKASGYTFTRYTMHWWKQRPGQG LEWIGYINPSRGYTNYNQKFKDKATLTDDKSSSTAYMQLSSLTSEDS AVYYCARYYDDHYCLDYWGQGTTTLTVSS	79
	VL	QIVLTQSPAISASPGKEKVTMTCRASSSVSYMNWYQQKSGTSPKR WIYDTSKVASGVPYRFSGSGSGTSYSLTSSMEADAATYYCQQWS SNPLTFGSGTKLEIN	85
CD3-5	VH	QVQLVQSGGGVVPGRSLRLSCKASGYTFTRYTMHWWRQAPGKG LEWIGYINPSRGYTNYNQKVKDRFTISRDN SKNTAFLQMDSL RPEDT GVYFCARYYDDHYCLDYWGQGTPVTVSS	86
	VL	DIQMTQSPSSLSASVGDRTITCSASSSVSYMNWYQQTPGKAPKR WIYDTSKLASGVPSRFSGSGSGTDYFTISLQPEDATYYCQQWSS NPFTFGQGTKLQIT	87
CD3-6	VH	QVQLVESGGGVVPGRSLRLSCAASGFKFSGYGMHWWRQAPGKG LEWVAWIWYDGSKKYYVDSVKGRFTISRDN SKNTLYLQMNSLRAED TAVYYCARQMGYWHFDLWGRGTLTVSS	88
	VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLA WYQQKPGQAPRLL IYDASNRATGIPARFSGSGSGTDFTLTISLLEPEDFAVYYCQQR SNW PPLTFGGGKVEIK	89
CD3-7	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWWRQAPGKGL EWWGRIRSKYNNYATYYADSVKDRFISRDDSKNSLYLQMNSLKTED TAVYYCVRHGNFGNSYVSWFAYWGQGT LTVTVSS	90
	VL	QAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTSNYANWWQQKPGQA PRGLIGGTNKRAPWTPARFSGSLLGGKAALIGAQA EADYYCALW YSNLWWFGGGTKLTVL	91
CD3-8	VH	DIKLQQSGAELARPGASVKMSCKTSGYTFTRYTMHWWKQRPGQGL EWIGYINPSRGYTNYNQKFKDKATLTDDKSSSTAYMQLSSLTSEDSA VYYCARYYDDHYCLDYWGQGTTTLTVSS	92
	VL	DIQLTQSPAISASPGKEKVTMTCRASSSVSYMNWYQQKSGTSPKR WIYDTSKVASGVPYRFSGSGSGTSYSLISSMEADAATYYCQQWSS NPLTFGAGTKLELK	93
CD3-9	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWWRQAPGKGL EWWARIRSKYNNYATYYADSVKDRFISRDDSKNSLYLQMNSLKTEDT AVYYCVRHGNFGNSYVSWFAYWGQGT LTVTVSS	94
	VL	QAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTSNYANWWQQKPGQA PRGLIGGTNKRAPWTPARFSGSLLGGKAALIGAQA EADYYCALW YSNLWWFGGGTKLTVL	91
CD3-10	VH	EVKLLESGGGLVQPKGSLKLSAASGFTFNTYAMNWWRQAPGKGL EWWARIRSKYNNYATYYADSVKDRFTISRDDSQSILYLQMNNLKTED	95

TABLE 7A CD3 Binders – Variable domain sequences			
Binding Domain	Chain	Sequence	SEQ ID NO:
		TAMYYCVRHGNFGNSYVSWFAYWGQGLTVTVSA	
	VL	QAVVTQESALTTSPGETVTLTCSRSTGAVTTSNYANWWQEKPDHLF TGLIGGTNKRAPGVPARFSGSLIGDKAALTITGAQTEDEAIYFCALWY SNLWWFGGGTKLTVL	82
CD3-11	VH	EVQLVESGGGLVQPGGSLKLSCAASGFTFNSYAMNWRQAPGKGL EWWARIRSKYNNYATYYADSVKGRFTISRDDSKNTAYLQMNNLKTE DTAVYYCVRHGNFGNSYVSWWAYWGQGLTVTVSS	96
	VL	QTVVTQEPLSLTVSPGGTVTLTCGSSTGAVTSGNYPNWWQQKPGQA PRGLIGGTKFLAPGTPQRFSGSLLGGKAALTLSGVQPEDEAEYYCVL WYSNRWWFGGGTKLTVL	97
CD3-12	VH	EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWRQAPGKGL EWWARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTE DTAVYYCVRHGNFGNSYISYWAYWGQGLTVTVSS	98
	VL	QTVVTQEPLSLTVSPGGTVTLTCGSSTGAVTSGNYPNWWQQKPGQA PRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCVL WYSNRWWFGGGTKLTVL	99
CD3-13	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTRYTMHWWRQAPGQGL EWMGYINPSRGYTNYNQKFKDRVTMTTDTSTAYMELSRLRSDDT AVYYCARYYDDHYCLDYWGQGLTVTVSS	100
	VL	EIVLTQSPATLSLSPGERATLSCSASSSVSYMNWYQQKPGQAPRLLI YDTSKLASGVPAHFRGSGSGTDFTLTISSLEPEDFAVYYCQQWSSN PFTFGQGTKVEIK	101
CD3-14	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWRQAPGKGL EWWSRIRSKYNNYATYYADSVKDRFTISRDDSKNTLYLQMNSLRAED TAVYYCARHGNFGNSYVSWFAYWGQGTMTVTVSS	102
	VL	QAVVTQEPLSLTVSPGGTVTLTCRSSTGAVTTSNYANWWQQKPGQA PRGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCA LWYSNLWWFGGGTKLTVL	103
CD3-15	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWRQAPGKGL EWWGRIRSKYNNYATYYADSVKDRFTISRDDSKNSLYLQMNSLKTE DTAVYYCVRHGNFGNSYVSWFAYWGQGLTVTVSS	104
	VL	QAVVTQEPLSLTVSPGGTVTLTCRSSTGAVTTSNYANWWQEKPGQA PRGLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCAL WYSNLWWFGGGTKLTVL	105
CD3-16	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWRQAPGKGL EWWGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAE DTAVYYCVRHGNFGNSYVSWFAYWGQGLTVTVSS	106
	VL	QAVVTQEPLSLTVSPGGTVTLTCGSSTGAVTTSNYANWWQQKPGQA PRGLIGGTNKRAPGVPARFSGSLLGGKAALTLSGAQPEDEAEYYCA	107

TABLE 7A CD3 Binders – Variable domain sequences			
Binding Domain	Chain	Sequence	SEQ ID NO:
		LWYSNLWWFGGGTKLTVL	
CD3-17	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWWRQAPGKGL EWWGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAE DTAVYYCVRHGNFGDSYVSWFAYWGQGTLLTVSS	108
	VL	QAVVTQEPSLTVSPGGTVTLTCSSTGAVTTSNYANWWQKPGKS PRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCAL WYSNHWWFGGGTKLTVL	109
CD3-18	VH	QVQLVQSGGGVVPGRSLRLSCKASGYTFTRYTMHWVRQAPGKG LEWIGYINPSRGYTNYNQKVKDRFTISRDN SKNTAFLQMDSL RPEDT GVYFCARYYDDHYCLDYWGQGTPTVTVSS	86
	VL	DIQMTQSPSSLSASVGDRTITCSASSSVSYMNWYQQTPGKAPKR WIYDTSKLASGVPSRFSGSGSGTDYFTFISLQPEDATYYCQQWSS NPFTFGQGT	110
CD3-19	VH	QVQLVQSGGGVVPGRSLRLSCKASGYTFTRYTMHWVRQAPGKG LEWIGYINPSRGYTNYNQKVKDRFTISRDN SKNTAFLQMDSL RPEDT GVYFCARYYDDHYSLDYWGQGTPTVTVSS	111
	VL	DIQMTQSPSSLSASVGDRTITCSASSSVSYMNWYQQTPGKAPKR WIYDTSKLASGVPSRFSGSGSGTDYFTFISLQPEDATYYCQQWSS NPFTFGQGT	110
CD3-20	VH	EVQLQQSGPELVKPGASMKISCKASGYSTGYTMNWWKQSHGKNL EWMGLINPYKGVSTYNQKFKDKATLTVDKSSSTAYMELLSTSEDSA VYYCARSGYYGDSWDYFDVWGQGTLLTVFS	112
	VL	DIQMTQTTSSLSASLGDRVTISCRASQDIRNYLNWYQQKPDGTVKLL IYYTSRLHSGVPSKFSFGSGSGTDYSLTISNLEQEDIATYFCQQGNTLP WTFAGGKLEIK	113
CD3-21	VH	EVQLVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWWRQASGKGL EWWGRIRSKYNNYATYYADSVKDRFTISRDDSKSTLYLQMNSLKTED TAVYYCVRHGNFGNSYVSWFAYWGQGTLLTVSS	114
	VL	QAVVTQEPSLTVSPGGTVTLTCSRSTGAVTTSNYANWWQKPGQA PRGLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQPEDEAEYFCA LWYSNLWWFGGGTKLTVL	115
	scFv	EVQLVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWWRQASGKGL EWWGRIRSKYNNYATYYADSVKDRFTISRDDSKSTLYLQMNSLKTED TAVYYCVRHGNFGNSYVSWFAYWGQGTLLTVSSGGGGSGGGGSG GGGSGGGGSQAVVTQEPSLTVSPGGTVTLTCSRSTGAVTTSNYAN WWQKPGQAPRGLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQ PEDEAEYFCALWYSNLWWFGGGTKLTVL	116
CD3-22	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWWRQAPGKGL EWWGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAE DTAVYYCVRHGNFGDSYVSWFAYWGQGTLLTVSS	108

TABLE 7A CD3 Binders – Variable domain sequences			
Binding Domain	Chain	Sequence	SEQ ID NO:
	VL	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWWQQKPGKS PRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCAL WYSNHHWWFGGGTKLTVL	109
	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWRQAPGKGL EWWGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAE DTAVYYCVRHGNFGDSYVSWFAYWGQGTLLTVSSGKPGSGKPGS GKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYAN WWQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQP EDEADYYCALWYSNHHWWFGGGTKLTVL	117
CD3-23	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWRQAPGKGL EWWGRIRSKANNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAE DTAVYYCVRHGNFGDSYVSWFAYWGQGTLLTVSS	118
	VL	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWWQQKPGKS PRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCAL WYSNHHWWFGGGTKLTVL	109
	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWRQAPGKGL EWWGRIRSKANNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAE DTAVYYCVRHGNFGDSYVSWFAYWGQGTLLTVSSGKPGSGKPGS GKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYAN WWQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQP EDEADYYCALWYSNHHWWFGGGTKLTVL	119
CD3-24	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWRQAPGKGL EWWGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAE DTAVYYCVRHGNFGDEYVSWFAYWGQGTLLTVSS	120
	VL	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWWQQKPGKS PRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCAL WYSNHHWWFGGGTKLTVL	109
	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWRQAPGKGL EWWGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAE DTAVYYCVRHGNFGDEYVSWFAYWGQGTLLTVSSGKPGSGKPGS GKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYAN WWQQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQP EDEADYYCALWYSNHHWWFGGGTKLTVL	121
CD3-25	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWRQAPGKGL EWWGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAE DTAVYYCVRHGNFGDPYVSWFAYWGQGTLLTVSS	122
	VL	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWWQQKPGKS PRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCAL WYSNHHWWFGGGTKLTVL	109
	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWRQAPGKGL EWWGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAE DTAVYYCVRHGNFGDPYVSWFAYWGQGTLLTVSSGKPGSGKPGS	123

TABLE 7A CD3 Binders – Variable domain sequences			
Binding Domain	Chain	Sequence	SEQ ID NO:
		GKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYAN WWQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQP EDEADYYCALWYSNHWFGGGTKLTVL	
CD3-26	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWRQAPGKGL EWWGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAE DTAVYYCVRHGNFGDSYVSWFDYWGQGTLLTVSS	124
	VL	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWWQKPGKS PRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCAL WYSNHWFGGGTKLTVL	109
	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWRQAPGKGL EWWGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAE DTAVYYCVRHGNFGDSYVSWFDYWGQGTLLTVSSGKPGSGKPGS GKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYAN WWQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQP EDEADYYCALWYSNHWFGGGTKLTVL	125
CD3-27	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWRQAPGKGL EWWGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAE DTAVYYCVRHGNFGDSYVSWFAYWGQGTLLTVSS	126
	VL	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWWQKPGKS PRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQPEDEADYYCAL WYSNHWFGGGTKLTVL	109
	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMSWRQAPGKGL EWWGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAE DTAVYYCVRHGNFGDSYVSWFAYWGQGTLLTVSSGKPGSGKPGS GKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYAN WWQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQP EDEADYYCALWYSNHWFGGGTKLTVL	127
CD3-28	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWRQAPGKGL EWWGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAE DTAVYYCVRHGNFGNSYVSWFAYWGQGTLLTVSS	106
	VL	QAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWWQKPGQA PRGLIGGTNKRAPGVPARFSGSLLGGKAALTLSGAQPEDEAEYYCA LWYNSNLWFGGGTKLTVL	107
	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWRQAPGKGL EWWGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAE DTAVYYCVRHGNFGNSYVSWFAYWGQGTLLTVSSGGGGSGGGGS GGGGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYANWWQQ KPGQAPRGLIGGTNKRAPGVPARFSGSLLGGKAALTLSGAQPEDEA EYYCALWYNSNLWFGGGTKLTVLGSHHHHHH	128

[0346] CDR sequences for a number of CD3 binders as defined by the Kabat numbering scheme (Kabat *et al*, 1991, Sequences of Proteins of Immunological Interest, 5th Ed. Public

Health Service, National Institutes of Health, Bethesda, Md.), Chothia numbering scheme (Al-Lazikani *et al.*, 1997, J. Mol. Biol 273:927-948), and a combination of Kabat and Chothia numbering are provided in Tables 7B-7D, respectively.

TABLE 7B							
CD3 Binders – CDR sequences according to Kabat numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
CD3-1	VH	RYTMH	129	YINPSRGYTNYNQK FKD	149	YYDDHYCLDY	173
	VL	SASSSVSYM N	130	DTSKLAS	150	QQWSSNPFT	174
CD3-2	VH	TYAMN	131	RIRSKYNNYATYYA DSVKD	151	HGNFGNSYVSW FAY	175
	VL	RSSTGAVTT SNYAN	132	GTNKRAP	152	ALWYSNLWW	176
CD3-3	VH	SYTMH	133	YINPSSGYTKYNQK FKD	153	WQDYDVYFDY	177
	VL	RASSSVSYM H	134	ATSNLAS	154	QQWSSNPPT	178
CD3-4	VH	RYTMH	129	YINPSRGYTNYNQK FKD	149	YYDDHYCLDY	173
	VL	RASSSVSYM N	135	DTSKVAS	155	QQWSSNPLT	179
CD3-5	VH	RYTMH	129	YINPSRGYTNYNQK VKD	156	YYDDHYCLDY	173
	VL	SASSSVSYM N	130	DTSKLAS	150	QQWSSNPFT	174
CD3-6	VH	GYGMH	136	VIWYDGSKKYYVDS VKG	157	QMGYWHFDL	180
	VL	RASQSVSSY LA	137	DASNRAT	158	QQRSNWPPLT	181
CD3-7	VH	TYAMN	131	RIRSKYNNYATYYA D	159	VRHGNFGNSYV SWFAY	182
	VL	RSSTGAVTT SNYAN	132	GTNKRAP	152	ALWYSNLWW	176
CD3-8	VH	RYTMH	129	YINPSRGYTNYNQK FKD	149	YYDDHYCLDY	173
	VL	RASSSVSYM N	135	DTSKVAS	155	QQWSSNPLT	179
CD3-9	VH	TYAMN	131	RIRSKYNNYATYYA D	159	VRHGNFGNSYV SWFAY	182

TABLE 7B							
CD3 Binders – CDR sequences according to Kabat numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	VL	RSSTGAVTT SNYAN	132	GTNKRAP	152	ALWYSNLWW	176
CD3-10	VH	TYAMN	131	RIRSKYNNYATYYA DSVKD	151	HGNFGNSYVSW FAY	175
	VL	RSSTGAVTT SNYAN	132	GTNKRAP	152	ALWYSNLWW	176
CD3-11	VH	SYAMN	138	RIRSKYNNYATYYA DSVKG	160	HGNFGNSYVSW WAY	183
	VL	GSSTGAVTS GNYPN	139	GTKFLAP	161	VLWYSNRWW	184
CD3-12	VH	KYAMN	140	RIRSKYNNYATYYA DSVKD	151	HGNFGNSYISY WAY	185
	VL	GSSTGAVTS GNYPN	139	GTKFLAP	161	VLWYSNRWW	184
CD3-13	VH	RYTMH	129	YINPSRGYTNYNQK FKD	149	YYDDHYCLDY	173
	VL	SASSSVSYM N	130	DTSKLAS	150	QQWSSNPFT	174
CD3-14	VH	TYAMN	131	RIRSKYNNYATYYA DSVKD	151	HGNFGNSYVSW FAY	175
	VL	RSSTGAVTT SNYAN	132	GTNKRAP	152	ALWYSNLWW	176
CD3-15	VH	TYAMN	131	RIRSKYNNYATYYA DSVKD	151	HGNFGNSYVSW FAY	175
	VL	RSSTGAVTT SNYAN	132	GTNKRAP	152	ALWYSNLWW	176
CD3-16	VH	TYAMN	131	RIRSKYNNYATYYA DSVKG	160	HGNFGNSYVSW FAY	175
	VL	GSSTGAVTT SNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-17	VH	TYAMN	131	RIRSKYNNYATYYA DSVKG	160	HGNFGDSYVSW FAY	186
	VL	GSSTGAVTT SNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-18	VH	RYTMH	129	YINPSRGYTNYNQK VKD	156	YYDDHYCLDY	173
	VL	SASSSVSYM N	130	DTSKLAS	150	QQWSSNPFT	174
CD3-19	VH	RYTMH	129	YINPSRGYTNYNQK	156	YYDDHYSLDY	188

TABLE 7B							
CD3 Binders – CDR sequences according to Kabat numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
				VKD			
	VL	SASSSVSYM N	130	DTSKLAS	150	QQWSSNPFT	174
CD3-20	VH	GYTMN	142	LINPYKGVSTYNQKF KD	162	SGYYGDSDWYF DV	189
	VL	RASQDIRNY LN	143	YTSRLH	163	QQGNTLPWT	190
CD3-21	VH	TYAMN	131	RIRSKYNNYATYYA DSVKD	151	HGNFGNSYVSW FAY	175
	VL	RSSTGAVTT SNYAN	132	GTNKRAP	152	ALWYSNLWW	176
CD3-22	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-23	VH	TYAMN	131	RIRSKANNYATYY ADSVKG	164	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-24	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDEYVS WFAY	191
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-25	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDPYVS WFAY	192
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-26	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFDY	193
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-27	VH	TYAMS	144	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-28	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175

TABLE 7B CD3 Binders – CDR sequences according to Kabat numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-29	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-30	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-31	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-32	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-33	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-34	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-35	VH	TYAMH	145	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-36	VH	TYAMS	144	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-37	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175

TABLE 7B CD3 Binders – CDR sequences according to Kabat numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-38	VH	TYAMN	131	RIRSKANNYYATY YADSVKG	165	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-39	VH	TYAMN	131	RIRSKANSYATYY ADSVKG	166	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-40	VH	TYAMN	131	RIRSKYNNYATAY ADSVKG	167	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-41	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-42	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-43	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-44	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-45	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-46	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175

TABLE 7B CD3 Binders – CDR sequences according to Kabat numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-47	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-48	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-49	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-50	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-51	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGQSYVS WFAY	194
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-52	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-53	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFDY	195
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-54	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-55	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175

TABLE 7B CD3 Binders – CDR sequences according to Kabat numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-56	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-57	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-58	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-59	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-60	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT SSNYAN	146	GTNKRAP	152	ALWYSNLWW	176
CD3-61	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT SGHYAN	147	GTNKRAP	152	ALWYSNLWW	176
CD3-62	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	DTNKRAP	168	ALWYSNLWW	176
CD3-63	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNNRAP	169	ALWYSNLWW	176
CD3-64	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175

TABLE 7B CD3 Binders – CDR sequences according to Kabat numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	VL	GSSTGAVT TSNYAN	141	GTNKRAS	170	ALWYSNLWW	176
CD3-65	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTSNKHS	171	ALWYSNLWW	176
CD3-66	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-67	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-68	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-69	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-70	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-71	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-72	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-73	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175

TABLE 7B CD3 Binders – CDR sequences according to Kabat numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	LLWYSNLWW	196
CD3-74	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-75	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-76	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	RSSTGAVT TSNYAN	132	GTNKRAP	152	ALWYSNLWW	176
CD3-77	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	KSSTGAVT TSNYAN	148	GTNKRAP	152	ALWYSNLWW	176
CD3-78	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-79	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-80	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-81	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-82	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175

TABLE 7B CD3 Binders – CDR sequences according to Kabat numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-83	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-84	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-85	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-86	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-87	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-88	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-89	VH	TYAMN	131	RIRSKANNYATYY ADSVKG	164	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-90	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFDY	193
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-91	VH	TYAMS	144	RIRSKANNYATYY ADSVKG	164	HGNFGDSYVS WFDY	193

TABLE 7B CD3 Binders – CDR sequences according to Kabat numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-92	VH	TYAMN	131	RIRSNGGYSTYYA DSVKG	172	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-93	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-94	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-95	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-96	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-97	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-98	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-99	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-100	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186

TABLE 7B CD3 Binders – CDR sequences according to Kabat numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-101	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-102	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-103	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-104	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-105	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-106	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-107	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-108	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-109	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186

TABLE 7B CD3 Binders – CDR sequences according to Kabat numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-110	VH	TYAMN	131	RIRSKYNNTATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-111	VH	TYAMN	131	RIRSKYNNTATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-112	VH	TYAMN	131	RIRSKYNNTATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-113	VH	TYAMN	131	RIRSKYNNTATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-114	VH	TYAMN	131	RIRSKYNNTATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-115	VH	TYAMN	131	RIRSKYNNTATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-116	VH	TYAMN	131	RIRSKYNNTATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-117	VH	TYAMN	131	RIRSKYNNTATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-118	VH	TYAMN	131	RIRSKYNNTATYY ADSVKG	160	HGNFGNSYVS WFAY	175

TABLE 7B CD3 Binders – CDR sequences according to Kabat numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-119	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-120	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-121	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-122	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-123	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-124	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-125	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-126	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-127	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYVS WFAY	175

TABLE 7B							
CD3 Binders – CDR sequences according to Kabat numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187
CD3-128	VH	TYAMN	131	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYVS WFAY	186
	VL	GSSTGAVT TSNYAN	141	GTNKRAP	152	ALWYSNHWW	187

TABLE 7C							
CD3 Binders – CDR sequences according to Chothia numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
CD3-1	VH	GYTFTRY	197	NPSRGY	210	YYDDHYCLDY	173
	VL	SSSVSY	198	DTS	211	WSSNPF	222
CD3-2	VH	GFTFNTY	199	RSKYNN YA	212	HGNFGNSYVS WFAY	175
	VL	STGAVTTSNY	200	GTN	213	WYSNLW	223
CD3-3	VH	GYTFTSY	201	NPSSGY	214	WQDYDVYFDY	177
	VL	SSSVSY	198	ATS	215	WSSNPP	224
CD3-4	VH	GYTFTRY	197	NPSRGY	210	YYDDHYCLDY	173
	VL	SSSVSY	198	DTS	211	WSSNPL	225
CD3-5	VH	GYTFTRY	197	NPSRGY	210	YYDDHYCLDY	173
	VL	SSSVSY	198	DTS	211	WSSNPF	222
CD3-6	VH	GFKFSGY	202	WYDGSK	216	QMGYWHFDL	180
	VL	SQSVSSY	203	DAS	217	RSNWPPL	226
CD3-7	VH	GFTFSTY	204	RSKYNN YAT	218	HGNFGNSYVS WFA	227
	VL	STGAVTTSNY	200	GTN	213	WYSNLW	223
CD3-8	VH	GYTFTRY	197	NPSRGY	210	YYDDHYCLDY	173
	VL	SSSVSY	198	DTS	211	WSSNPL	225
CD3-9	VH	GFTFNTY	199	RSKYNN YAT	218	HGNFGNSYVS WFA	227

TABLE 7C							
CD3 Binders – CDR sequences according to Chothia numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	VL	STGAVTTSNY	200	GTN	213	WYSNLW	223
CD3-10	VH	GFTFNTY	199	RSKYNNYA	212	HGNFGNSYVS WFAY	175
	VL	STGAVTTSNY	200	GTN	213	WYSNLW	223
CD3-11	VH	GFTFNSY	205	RSKYNNYA	212	HGNFGNSYVS WWAY	183
	VL	STGAVTSGNY	206	GTK	219	WYSNRW	228
CD3-12	VH	GFTFNKY	207	RSKYNNYA	212	HGNFGNSYISY WAY	185
	VL	STGAVTSGNY	206	GTK	219	WYSNRW	228
CD3-13	VH	GYTFTRY	197	NPSRGY	210	YYDDHYCLDY	173
	VL	SSSVSY	198	DTS	211	WSSNPF	222
CD3-14	VH	GFTFSTY	204	RSKYNNYA	212	HGNFGNSYVS WFAY	175
	VL	STGAVTTSNY	200	GTN	213	WYSNLW	223
CD3-15	VH	GFTFNTY	199	RSKYNNYA	212	HGNFGNSYVS WFAY	175
	VL	STGAVTTSNY	200	GTN	213	WYSNLW	223
CD3-16	VH	GFTFNTY	199	RSKYNNYA	212	HGNFGNSYVS WFAY	175
	VL	STGAVTTSNY	200	GTN	213	WYSNLW	223
CD3-17	VH	GFTFSTY	204	RSKYNNYA	212	HGNFGDSYVS WFAY	186
	VL	STGAVTTSNY	200	GTN	213	WYSNHW	229
CD3-18	VH	GYTFTRY	197	NPSRGY	210	YYDDHYCLDY	173
	VL	SSSVSY	198	DTS	211	WSSNPF	222
CD3-19	VH	GYTFTRY	197	NPSRGY	210	YYDDHYSLDY	188
	VL	SSSVSY	198	DTS	211	WSSNPF	222
CD3-20	VH	GYSFTGY	208	NPYKGV	220	SGYYGDSDWY FDV	189

TABLE 7C							
CD3 Binders – CDR sequences according to Chothia numbering scheme							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
	VL	SQDIRNY	209	YTS	221	GNTLPW	230
CD3-21	VH	GFTFNTY	199	RSKYNNYA	212	HGNFGNSYVS WFAY	175
	VL	RSSTGAVTTS NYAN	132	GTNKRA P	152	ALWYSNLWW	176

TABLE 7D							
CD3 Binders – CDR sequences according to combination of Kabat and Chothia numbering schemes							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
CD3-1	VH	GYTFTRYTM H	231	YINPSRGYTNYN QKFKD	149	YYDDHYCLDY	173
	VL	SASSSVSYM N	130	DTSKLAS	150	QQWSSNPFT	174
CD3-2	VH	GFTFNTYAM N	232	RIRSKYNNYATYY ADSVKD	151	HGNFGNSYV SWFAY	175
	VL	RSSTGAVTT SNYAN	132	GTNKRAP	152	ALWYSNLWW	176
CD3-3	VH	GYTFTSYTM H	233	YINPSSGYTKYN QKFKD	153	WQDYDVYFD Y	177
	VL	RASSSVSYM H	134	ATSNLAS	154	QQWSSNPPT	178
CD3-4	VH	GYTFTRYTM H	231	YINPSRGYTNYN QKFKD	149	YYDDHYCLDY	173
	VL	RASSSVSYM N	135	DTSKVAS	155	QQWSSNPLT	179
CD3-5	VH	GYTFTRYTM H	231	YINPSRGYTNYN QKVVD	156	YYDDHYCLDY	173
	VL	SASSSVSYM N	130	DTSKLAS	150	QQWSSNPFT	174
CD3-6	VH	GKFSGYGM H	234	VIWYDGSKKYYV DSVKG	157	QMGYWHFDL	180
	VL	RASQSVSSY	137	DASNRAT	158	QQRSNWPPL	181

TABLE 7D CD3 Binders – CDR sequences according to combination of Kabat and Chothia numbering schemes							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		LA				T	
CD3-7	VH	GFTFSTYAMN	235	RIRSKYNNTYATYYADSVK	239	HGNFGNSYVSWFAY	175
	VL	RSSTGAVTTSNYAN	132	GTNKRAP	152	ALWYSNLWW	176
CD3-8	VH	GYTFTRYTMH	231	YINPSRGYTNYNQKFKD	149	YYDDHYCLDY	173
	VL	RASSSVSYM	135	DTSKVAS	155	QQWSSNPLT	179
CD3-9	VH	GFTFNTYAMN	232	RIRSKYNNTYATYYADSVK	239	HGNFGNSYVSWFAY	175
	VL	RSSTGAVTTSNYAN	132	GTNKRAP	152	ALWYSNLWW	176
CD3-10	VH	GFTFNTYAMN	232	RIRSKYNNTYATYYADSVKD	151	HGNFGNSYVSWFAY	175
	VL	RSSTGAVTTSNYAN	132	GTNKRAP	152	ALWYSNLWW	176
CD3-11	VH	GFTFNSYAMN	236	RIRSKYNNTYATYYADSVK	160	HGNFGNSYVSWWAY	183
	VL	GSSTGAVTS	139	GTKFLAP	161	VLWYSNRWW	184
CD3-12	VH	GFTFNKYAMN	237	RIRSKYNNTYATYYADSVKD	151	HGNFGNSYISYWAY	185
	VL	GSSTGAVTS	139	GTKFLAP	161	VLWYSNRWW	184
CD3-13	VH	GYTFTRYTMH	231	YINPSRGYTNYNQKFKD	149	YYDDHYCLDY	173
	VL	SASSSVSYM	130	DTSKLAS	150	QQWSSNPFT	174
CD3-14	VH	GFTFSTYAMN	235	RIRSKYNNTYATYYADSVKD	151	HGNFGNSYVSWFAY	175
	VL	RSSTGAVTTSNYAN	132	GTNKRAP	152	ALWYSNLWW	176
CD3-15	VH	GFTFNTYAM	232	RIRSKYNNTYATYY	151	HGNFGNSYV	175

TABLE 7D CD3 Binders – CDR sequences according to combination of Kabat and Chothia numbering schemes							
Binding Domain	Chain	CDR1	SEQ ID NO:	CDR2	SEQ ID NO:	CDR3	SEQ ID NO:
		N		ADSVKD		SWFAY	
	VL	RSSTGAVTT SNYAN	132	GTNKRAP	152	ALWYSNLWW	176
CD3-16	VH	GFTFNTYAM N	232	RIRSKYNNYATYY ADSVKG	160	HGNFGNSYV SWFAY	175
	VL	GSSTGAVTT SNYAN	141	GTNKRAP	152	ALWYSNLWW	176
CD3-17	VH	GFTFSTYAM N	235	RIRSKYNNYATYY ADSVKG	160	HGNFGDSYV SWFAY	186
	VL	GSSTGAVTT SNYAN	141	GTNKRAP	152	ALWYSNHWV	187
CD3-18	VH	GYTFTRYTM H	231	YINPSRGYTNYN QKVVD	156	YYDDHYCLDY	173
	VL	SASSSVSYM N	130	DTSKLAS	150	QQWSSNPFT	174
CD3-19	VH	GYTFTRYTM H	231	YINPSRGYTNYN QKVVD	156	YYDDHYSLDY	188
	VL	SASSSVSYM N	130	DTSKLAS	150	QQWSSNPFT	174
CD3-20	VH	GYSFTGYTM N	238	LINPYKGVSTYNQ KFKD	162	SGYYGDSDW YFDV	189
	VL	RASQDIRNYL N	143	YTSRLHS	240	QQGNTLPWT	190

[0347] In some embodiments, a TBM of the disclosure can comprise a CD3 ABM which comprises the CDRs of any of CD3-1 to CD3-128 as defined by Kabat numbering (e.g., as set forth in Table 7B). In other embodiments, a TBM of the disclosure can comprise a CD3 ABM which comprises the CDRs of any of CD3-1 to CD3-128 as defined by Chothia numbering (e.g., as set forth in Table 7C). In yet other embodiments, a TBM of the disclosure can comprise a CD3 ABM which comprises the CDRs of any of CD3-1 to CD3-128 as defined by a combination of Kabat and Chothia numbering (e.g., as set forth in Table 7D).

[0348] In some embodiments, a CD3 ABM comprises the CDR sequences of CD3-1. In some embodiments, a CD3 ABM comprises the CDR sequences of CD3-2. In some embodiments, a

[illegible]

[illegible]

[illegible]

[0349] A TBM of the disclosure can comprise the complete heavy and light variable sequences of any of CD3-1 to CD3-128. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-1. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-1. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-2. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-3. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-4. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-5. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-6. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-7. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-8. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-9. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-10. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-11. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-12. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-13. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-14. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-15. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-16. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-17. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-18. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-19. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-20. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-21. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-22. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-23. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-24. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-25. In

some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-26. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-27. In some embodiments, a TBM of the disclosure comprises a CD3 ABM which comprises the VH and VL sequences of CD3-28.

6.5.2. TCR- α/β ABMs

[0350] The TBMs of the disclosure can contain an ABM that specifically binds to the TCR- α chain, the TCR- β chain, or the TCR- $\alpha\beta$ dimer. Exemplary anti-TCR- α/β antibodies are known in the art (see, e.g., US 2012/0034221; Borst *et al.*, 1990, Hum Immunol. 29(3):175-88 (describing antibody BMA031), the contents of each of which are incorporated herein by reference). The VH, VL, and Kabat CDR sequences of antibody BMA031 as described in US 2012/0034221 are provided in Table 8.

Table 8 BMA031 sequences		
Domain	Sequence	SEQ ID NO:
BMA031 CDR-H1	KASGYKFTSYVMH	241
BMA031 CDR-H2	YINPYNDVTKYNEKFK	242
BMA031 CDR-H3	GSYYDYDGFVY	243
BMA031 CDR-L1	SATSSVSYMH	244
BMA031 CDR-L2	DTSKLAS	150
BMA031 CDR-L3	QQWSSNPLT	179
BMA031 VH	EVQLQQSGPELVKPGASVKMSCKASGYKFTSYVMHWWKQKPGQGLE WIGYINPYNDVTKYNEKFKGKATLTSDKSSSTAYMELSSLTSEDSAVH YCARGSYDYDGFVYWGQGTLVTVSA	245
BMA031 VL	QIVLTQSPAISASPGEKVTMTCSATSSVSYMHWWYQQKSGTSPKRWI YDTSKLASGVPARFSGSGGTSYSLTISSMEAEDAATYYCQQWSSNP LTFGAGTKLELK	246

[0351] In an embodiment, a TCR ABM can comprise the CDR sequences of antibody BMA031. In other embodiments, a TCR ABM can comprise the VH and VL sequences of antibody BMA031.

6.5.3. TCR- γ/δ ABMs

[0352] The TBMs of the disclosure can contain an ABM that specifically binds to the TCR- γ chain, the TCR- δ chain, or the TCR- $\gamma\delta$ dimer. Exemplary anti-TCR- γ/δ antibodies are known in the art (see, e.g., US Pat. No. 5,980,892 (describing δ TCS1, produced by the hybridoma deposited with the ATCC as accession number HB 9578), the contents of which are incorporated herein by reference).

6.6. CD2 ABMs

6.6.1. Immunoglobulin-Based CD2 ABMs

[0353] In some embodiments, a TBM of the disclosure can comprise a ABM which is an anti-CD2 antibody or an antigen-binding domain thereof. Exemplary anti-CD2 antibodies are known in the art (see, e.g., US 6,849,258, CN102827281A, US 2003/0139579 A1, and US 5,795,572). Table 9 provides exemplary CDR, VH, and VL sequences that can be included in anti-CD2 antibodies or antigen-binding fragments thereof, for use in TBMs of the disclosure.

TABLE 9 Immunoglobulin Based CD2 Binders			
Name	Domain	Sequence	SEQ ID NO:
CD2-1	CDR-H1	EYYMY (Rat Lo-CD2a = BTI-322 from Fig. 33 of USP 6,849,258)	247
CD2-1	CDR-H2	RIDPEDGSIDYVEKFKK (Rat Lo-CD2a = BTI-322 from Fig. 33 of USP 6,849,258)	248
CD2-1	CDR-H3	GKFNYRFAY (Rat Lo-CD2a = BTI-322 from Fig. 33 of USP 6,849,258)	249
CD2-1	CDR-L1	RSSQSLLHSSGNTYLN (Rat Lo-CD2a = BTI-322 from Fig. 31 of USP 6,849,258)	250
CD2-1	CDR-L2	LVSLES (Rat Lo-CD2a = BTI-322 from Fig. 31 of USP 6,849,258)	251
CD2-1	CDR-L3	QFTHYPYT (Rat Lo-CD2a = BTI-322 from Fig. 31 of USP 6,849,258)	252
CD2-1	VH	EVQLQQSGPELQRPASVKLSCKASGYIFTEYYMYWVKQR PKQGLELVGRIDPEDGSIDYVEKFKKKATLTADTSSNTAYM QLSSLTSEDATYFCARGKFNYRFAYWGQGTLLTVSS (SEQ ID NO:100 of USP 6,849,258)	253
CD2-1	VL	DVLTQTPTLLATIGQSVSISCRSSQSLLHSSGNTYLNWLL QRTGQSPQPLIYLVSKLESGVPSNRFSGSGSGTDFTLKISGV EAEDLGVIYCMQFTHYPYTFGAGTKLELK (Rat Lo-CD2a Vk from SEQ ID NO:92, without signal sequence as shown in Fig. 31 of USP 6,849,258)	254
hu1CD2-1	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTEYYMYWVRQ APGQGLELMGRIDPEDGSIDYVEKFKKKVTLTADTSSSTAY	255

TABLE 9 Immunoglobulin Based CD2 Binders			
Name	Domain	Sequence	SEQ ID NO:
		MELSSLTSDDTAVYYCARGKFNYRFAYWGQGTLVTVSS (SEQ ID NO:101 of USP 6,849,258)	
	VL	DVVMTQSPPSLLVTLGQPASISCRSSQSLLHSSGNTYLNWL LQRPGQSPQPLIYLVSKLESGVPDRFSGSGSGTDFTLKISG VEAEDVGVYYCMQFTHYPYTFGQGTKLEIK (SEQ ID NO:96 of USP 6,849,258)	256
hu2CD2-1	VH	EVQLQQSGPELQRPGLASVKLSCKASGYIFTEYYMYWVKQR PKQGLELVGRIDPEDGSIDYVEKFKKKATLTADTSSNTAYM QLSSLTSEDATYFCARGKFNYRFAYWGQGTLVTVSS (Vh of MEDI-507; SEQ ID NO:105 of USP 6,849,258)	257
	VL	DVVMTQSPPSLLVTLGQPASISCRSSQSLLHSSGNTYLNWL LQRPGQSPQPLIYLVSKLESGVPDRFSGSGSGTDFTLKISG VEAEDVGVYYCMQFTHYPYTFGQGTKLEIK (SEQ ID NO:96 of USP 6,849,258)(same as hu1CD2-1)	256

[0354] In some embodiments, a CD2 ABM comprises the CDR sequences of CD2-1 (SEQ ID NOS: 247-252). In some embodiments, a CD2 ABM comprises the heavy and light chain variable sequences of CD2-1 (SEQ ID NOS: 253-254). In some embodiments, a CD2 ABM comprises the heavy and light chain variable sequences of hu1CD2-1 (SEQ ID NOS: 255-256). In some embodiments, a CD2 ABM comprises the heavy and light chain variable sequences of hu2CD2-1 (SEQ ID NOS: 257 and 256, respectively).

[0355] In other embodiments, a CD2 ABM can comprise the CDR sequences of antibody 9D1 produced by the hybridoma deposited with the Chinese Culture Collection Committee General Microbiology Center on May 16, 2012 with accession no. CGMCC 6132, and which is described in CN102827281A. In other embodiments, a CD2 ABM can comprise the CDR sequences of antibody LO-CD2b produced by the hybridoma deposited with the American Type Culture Collection on June 22, 1999 with accession no. PTA-802, and which is described in US 2003/0139579 A1. In yet other embodiments, a CD2 ABM can comprise the CDR sequences of the CD2 SFv-Ig produced by expression of the construct cloned in the recombinant *E. coli* deposited with the ATCC on April 9, 1993 with accession no. 69277, and which is described in US 5,795,572.

[0356] In other embodiments, a CD2 ABM can comprise the VH and VL sequences of antibody 9D1. In other embodiments, a CD2 ABM can comprise the VH and VL sequences of antibody LO-CD2b. In yet other embodiments, a CD2 ABM can comprise the VH and VL sequences of

the CD2 SFv-Ig produced by expression of the construct cloned in the recombinant *E. coli* having ATCC accession no. 69277.

6.6.2. CD58-based CD2 ABMs

[0357] In certain aspects the present disclosure provides a TBM comprising a CD2 ABM which is a ligand. The CD2 ABM specifically binds to human CD2, whose natural ligand is CD58, also known as LFA-3. CD58/LFA-3 proteins are glycoproteins that are expressed on the surfaces of a variety of cell types (Dustin *et al.*, 1991, Annu. Rev. Immunol. 9:27) and play roles in mediating T-cell interactions with APCs in both antigen-dependent and antigen-independent manners (Wallner *et al.*, 1987, J. Exp. Med. 166:923). Accordingly, in certain aspects, the CD2 ABM is a CD58 moiety. As used herein, a CD58 moiety comprises an amino acid sequence comprising at least 70% sequence identity to a CD2-binding portion of CD58, *e.g.*, at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to a CD2-binding portion of CD58. The sequence of human CD58 has the Uniprot identifier P19256 (www.uniprot.org/uniprot/P19256). It has been established that CD58 fragments containing amino acid residues 30-123 of full length CD58 (*i.e.*, the sequence designated as CD58-4 in Table 10 below) are sufficient for binding to CD2. Wang *et al.*, 1999, Cell 97:791-803. Accordingly, in certain aspects, a CD58 moiety comprises an amino acid sequence comprising at least 70% sequence identity to amino acids 30-123 of CD58, *e.g.*, at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to the amino acid sequence designated CD58-4.

[0358] The interactions between CD58 and CD2 have been mapped through x-ray crystallography and molecular modeling. The substitution of residues E25, K29, K30, K32, D33, K34, E37, D84 and K87 (with numbering referring to the in the mature polypeptide) reduces binding to CD2. Ikemizu *et al.*, 1999, Proc. Natl. Acad. Sci. USA 96:4289-94. Accordingly, in preferred embodiments the CD58 moiety of the disclosure retains the wild type residues at E25, K29, K30, K32, D33, K34, E37, D84 and K87.

[0359] In contrast, the following substitutions (with numbering referring to the full length polypeptide) did not impact binding to CD2: F29S; V37K; V49Q; V86K; T113S; and L121G. Accordingly, a CD58 moiety of the disclosure can include one, two, three, four, five or all six of the foregoing substitutions.

[0360] Exemplary CD58 moieties are provided in Table 10 below:

TABLE 10 CD58 sequences			
Name	Description	Sequence	SEQ ID NO:

TABLE 10 CD58 sequences			
Name	Description	Sequence	SEQ ID NO:
CD58-1	Full length CD58, including signal sequence	MVAGSDAGRA LGVLSVVCLL HCFGFISCF S QQIYGVVYGN VTFHVPSNVP LKEVLWKKQK DKVAELENSE FRAFSSFKNR VYLDTVSGSL TIYNLTSSDE DEYEMESPNI TDTMKFFLYV LESLPSPTLT CALTNGSIEV QCMIPHEHNS HRGLIMYSWD CPMEQCKRNS TSIYFKMEND LPQKIQCTLS NPLFNTTSSI ILTTCIPSSG HSRHRYALIP IPLAVITTCI VLYMNGILKC DRKPDRTNSN	258
CD58-2	Extracellular domain of CD58, corresponding to amino acids 29-215 of CD58 (WT)	FS QQIYGVVYGN VTFHVPSNVP LKEVLWKKQK DKVAELENSE FRAFSSFKNR VYLDTVSGSL TIYNLTSSDE DEYEMESPNI TDTMKFFLYV LESLPSPTLT CALTNGSIEV QCMIPHEHNS HRGLIMYSWD CPMEQCKRNS TSIYFKMEND LPQKIQCTLS NPLFNTTSSI ILTTCIPSSG HSRHR	259
CD58-3	Extracellular domain of CD58, corresponding to amino acids 29-215 of CD58 (with permitted substitutions)	BS QQIYGVJYGN VTFHVPSNOP LKEVLWKKQK DKVAELENSE FRAFSSFKNR VYLDTVSGSL TIYNLTSSDE DEYEMESPNI TDXMKFFLYV ZESLPSPTLT CALTNGSIEV QCMIPHEHNS HRGLIMYSWD CPMEQCKRNS TSIYFKMEND LPQKIQCTLS NPLFNTTSSI ILTTCIPSSG HSRHR B = F or S J = V or K O = V or Q U = V or K X = T or S Z = L or G	260
CD58-4	Amino acids 30-123 (WT)	S QQIYGVVYGN VTFHVPSNVP LKEVLWKKQK DKVAELENSE FRA	261
CD58-5	Amino acids 30-123 (with permitted substitutions)	S QQIYGVJYGN VTFHVPSNOP LKEVLWKKQK DKVAELENSE FRA J = V or K O = V or Q	262

6.6.3. CD48-based CD2 ABMs

[0361] In certain aspects the present disclosure provides a TBM comprising a CD2 ABM which is CD48 moiety. As used herein, a CD48 moiety comprises an amino acid sequence comprising at least 70% sequence identity to a CD2-binding portion of CD48, e.g., at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity to a CD2-

binding portion of CD48. The sequence of human CD48 has the Uniprot identifier P09326 (www.uniprot.org/uniprot/P09326), which includes a signal peptide (amino acids 1-26) and a GPI anchor (amino acids 221-243). In certain aspects, a CD48 moiety comprises an amino acid sequence comprising at least 70% sequence identity (e.g., at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity) to the amino acid sequence of consisting of amino acids 27-220 of Uniprot identifier P09326. Human CD48 has an Ig-like C2-type I domain (amino acids 29-127 of Uniprot identifier P09326) and a Ig-like C2 type 2 domain (amino acids 132-212 of Uniprot identifier P09326). Accordingly, in some embodiments, a CD48 moiety comprises an amino acid sequence comprising at least 70% sequence identity (e.g., at least 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identity) to the amino acid sequence of consisting of amino acids 29-212 of Uniprot identifier P09326, to the C2-type I domain (amino acids 29-127 of Uniprot identifier P09326) and/or to the Ig-like C2 type 2 domain (amino acids 132-212 of Uniprot identifier P09326). A CD48 moiety can in some embodiments comprise one or more natural variants relative to the sequence of Uniprot identifier P09326. For example, a CD48 moiety can include a E102Q substitution. As another example, a CD48 moiety can comprise an amino acid sequence corresponding to a CD-48 isoform or a CD2 binding portion thereof, e.g., the isoform having Uniprot identifier P09326-2 or a CD2 binding portion thereof.

6.7. Tumor-Associated Antigen ABMs

[0362] The TBMs of the disclosure comprise at least one ABMs that bind specifically to a tumor-associated antigen (TAA). Preferably, the TAA is a human TAA. The antigen may or may not be present on normal cells. In certain embodiments, the TAA is preferentially expressed or upregulated on tumor cells as compared to normal cells. In other embodiments, the TAA is a lineage marker.

[0363] It is anticipated that any type of tumor and any type of TAA may be targeted by the TBMs of the disclosure. Exemplary types of cancers that may be targeted include acute lymphoblastic leukemia, acute myelogenous leukemia, biliary cancer, B-cell leukemia, B-cell lymphoma, biliary cancer, bone cancer, brain cancer, breast cancer, triple-negative breast cancer, cervical cancer, Burkitt lymphoma, chronic lymphocytic leukemia, chronic myelogenous leukemia, colorectal cancer, endometrial cancer, esophageal cancer, gall bladder cancer, gastric cancer, gastrointestinal tract cancer, glioma, hairy cell leukemia, head and neck cancer, Hodgkin's lymphoma, liver cancer, lung cancer, medullary thyroid cancer, melanoma, multiple myeloma, ovarian cancer, non-Hodgkin's lymphoma, pancreatic cancer, prostate cancer, pulmonary tract cancer, renal cancer, sarcoma, skin cancer, testicular cancer, urothelial cancer,

and other urinary bladder cancers. However, the skilled artisan will realize that TAAs are known for virtually any type of cancer.

[0364] Exemplary TAAs for which a TBM of the disclosure can be created include ABCF1; ACVR1; ACVR1B; ACVR2; ACVR2B; ACVRL1; ADORA2A; ADRB3; Aggrecan; AGR2; AICDA; AIF1; AIG1; AKAP1; AKAP2; ALK; AMH; AMHR2; ANGPT1; ANGPT2; ANGPTL3; ANGPTL4; ANPEP; APC; APOC1; AR; AZGP1 (zinc-a-glycoprotein); B7.1; B7.2; BAD; BAFF; BAG1; BAI1; BCL2; BCL6; BDNF; BLNK; BLR1 (MDR15); BlyS; BMP1; BMP2; BMP3B (GDF10); BMP4; BMP6; BMP8; BMPR1A; BMPR1B; BMPR2; BPAG1 (plectin); BRCA1; C19orf10 (IL27w); C3; C4A; C5; C5R1; Cadherin 17; CANT1; CASP1; CASP4; CAV1; CCBP2 (D6/JAB61); CCL1 (1-309); CCL11 (eotaxin); CCL13 (MCP-4); CCL15 (MIP-1d); CCL16 (HCC-4); CCL17 (TARC); CCL18 (PARC); CCL19 (MIP-3b); CCL2 (MCP-1); MCAF; CCL20 (MIP-3a); CCL21 (MIP-2); SLC; exodus-2; CCL22 (MDC/STC-1); CCL23 (MPIF-1); CCL24 (MPIF-2/eotaxin-2); CCL25 (TECK); CCL26 (eotaxin-3); CCL27 (CTACK/ILC); CCL28; CCL3 (MIP-1a); CCL4 (MIP-1b); CCL5 (RANTES); CCL7 (MCP-3); CCL8 (mcp-2); CCNA1; CCNA2; CCND1; CCNE1; CCNE2; CCR1 (CKR1/HM145); CCR2 (mcp-1RB/RA); CCR3 (CKR3/CMKBR3); CCR4; CCR5 (CMKBR5/ChemR13); CCR6 (CMKBR6/CKR-L3/STRL22/DRY6); CCR7 (CKR7/EBI1); CCR8 (CMKBR8/TER1/CKR-L1); CCR9 (GPR-9-6); CCRL1 (VSHK1); CCRL2 (L-CCR); CD164; CD19; CD1C; CD20; CD200; CD-22; CD24; CD28; CD3; CD37; CD38; CD3E; CD3G; CD3Z; CD4; CD32b; CD40; CD40L; CD44; CD45RB; CD52; CD69; CD72; CD74; CD79A; CD79B; CD8; CD80; CD81; CD83; CD86; CD97; CD179a; CDH1 (E-cadherin); CDH10; CDH12; CDH13; CDH18; CDH19; CDH20; CDH5; CDH7; CDH8; CDH9; CDK2; CDK3; CDK4; CDK5; CDK6; CDK7; CDK9; CDKN1A (p21Wap1/Cip1); CDKN1B (p27Kip1); CDKN1C; CDKN2A (p16INK4a); CDKN2B; CDKN2C; CDKN3; CEBPB; CER1; CHGA; CHGB; Chitinase; CHST10; CKLFSF2; CKLFSF3; CKLFSF4; CKLFSF5; CKLFSF6; CKLFSF7; CKLFSF8; CLDN3; CLDN6; CLDN7 (claudin-7); CLN3; CLU (clusterin); CMKLR1; CMKOR1 (RDC1); CNR1; COL18A1; COL1A1; COL4A3; COL6A1; CR2; CRP; CSF1 (M-CSF); CSF2 (GM-CSF); CSF3 (GCSF); CTLA4; CTNNB1 (b-catenin); CTSB (cathepsin B); CX3CL1 (SCYD1); CX3CR1 (V28); CXCL1 (GRO1); CXCL10(IP-10); CXCL11 (1-TAC/IP-9); CXCL12 (SDF1); CXCL13; CXCL14; CXCL16; CXCL2 (GRO2); CXCL3 (GRO3); CXCL5 (ENA-78/LIX); CXCL6 (GCP-2); CXCL9 (MIG); CXCR3 (GPR9/CKR-L2); CXCR4; CXCR6 (TYMSTR/STRL33/Bonzo); CYB5; CYC1; CYSLTR1; CGRP; C1q; C1r; C1; C4a; C4b; C2a; C2b; C3a; C3b; DAB2IP; DES; DKFZp451J0118; DNCL1; DPP4; E-selectin; E2F1; ECGF1; EDG1; EFNA1; EFNA3; EFNB2; EGF; EGFR; EGFRvIII; ELAC2; ENG; ENO1; ENO2; ENO3; EPHB4; EPO; ERBB2 (Her-2); EREG; ERK8; ESR1; ESR2; F3 (TF); Factor VII; Factor IX; Factor V; Factor VIIa; Factor Factor X; Factor XII; Factor XIII; FADD; FasL; FASN; FCER1A; FCER2; Fc gamma receptor; FCGR3A; FCRL5; FGF; FGF1 (aFGF); FGF10; FGF11; FGF12; FGF12B; FGF13; FGF14; FGF16; FGF17; FGF18; FGF19; FGF2 (bFGF); FGF20; FGF21; FGF22; FGF23; FGF3 (int-2);

FGF4 (HST); FGF5; FGF6 (HST-2); FGF7 (KGF); FGF8; FGF9; FGFR3; FIGF (VEGFD); FIL1 (EPSILON); FIL1 (ZETA); FLJ12584; FLJ25530; FLRT1 (fibronectin); FLT1; Folate receptor alpha; Folate receptor beta; FOS; FOSL1 (FRA-1); Fucosyl GM1; FY (DARC); GABRP (GABAa); GAGEB1; GAGEC1; GALNAC4S-6ST; GATA3; GDF5; GFI1; GGT1; GM-CSF; GloboH; GNAS1; GNRH1; GPNMB; GPR2 (CCR10); GPR20; GPR31; GPR44; GPR64; GPR81 (FKSG80); GPRC5D; GRCC10 (C10); GRP; GSN (Gelsolin); GSTP1; glycoprotein (gP) IIb/IIIa; HAVCR1; HAVCR2; HDAC4; HDAC5; HDAC7A; HDAC9; Her2; HER3; HGF; HIF1A; HIP1; histamine and histamine receptors; HLA-A; HLA-DRA; HM74; HMGB1; HMOX1; HMWMAA; HUMCYT2A; ICEBERG; ICOSL; ID2; IFN- α ; IFNA1; IFNA2; IFNA4; IFNA5; IFNA6; IFNA7; IFNB1; IFN- γ ; IFNW1; IGBP1; IGF1; IGF1R; IGF2; IGFBP2; IGFBP3; IGFBP6; IL-1; IL- α ; IL-1- β ; IL10; IL10RA; IL10RB; IL11; IL11RA; IL-12; IL12A; IL12B; IL12RB1; IL12RB2; IL13; IL13RA1; IL13RA2; IL14; IL15; IL15RA; IL16; IL17; IL17B; IL17C; IL17R; IL18; IL18BP; IL18R1; IL18RAP; IL19; IL1A; IL1B; IL1F10; IL1F5; IL1F6; IL1F7; IL1F8; IL1F9; IL1HY1; IL1R1; IL1R2; IL1RAP; IL1RAPL1; IL1RAPL2; IL1RL1; IL1RL2; IL1RN; IL2; IL20; IL20RA; IL21R; IL22; IL22R; IL22RA2; IL23; IL24; IL25; IL26; IL27; IL28A; IL28B; IL29; IL2RA; IL2RB; IL2RG; IL3; IL30; IL3RA; IL4; IL4R; IL5; IL5RA; IL6; IL6R; IL6ST (glycoprotein 130); IL7; IL7R; IL8; IL8RA; IL8RB; IL8RB; IL9; IL9R; ILK; INHA; INHBA; INSL3; INSL4; IRAK1; IRAK2; ITGA1; ITGA2; ITGA3; ITGA6 (α 6 integrin); ITGAV; ITGB3; ITGB4 (β 4 integrin); JAG1; JAK1; JAK3; JUN; K6HF; KAI1; KDR; KITLG; KLF5 (GC Box BP); KLF6; KLK10; KLK12; KLK13; KLK14; KLK15; KLK3; KLK4; KLK5; KLK6; KLK9; KRT1; KRT19 (Keratin 19); KRT2A; KRTHB6 (hair-specific type II keratin); L-selectin; LAMAS; LEP (leptin); Lingo-p75; Lingo-Troy; LRP6; LPS; LTA (TNF-b); LTB; LTB4R (GPR16); LTB4R2; LTBR; LY6K; LYPD8; MACMARCKS; MAG or Omgp; MAP2K7 (c-Jun); MDK; mesothelin; MIB1; midkine; MIF; MIP-2; MKI67 (Ki-67); MMP2; MMP9; MS4A1; MSMB; MT3 (metallothionein-III); MTSS1; MUC1 (mucin); MYC; MYD88; NCK2; neurocan; NKG2D; NFKB1; NFKB2; NGF; NGFB (NGF); NGFR; NgR-Lingo; NgR-Nogo66 (Nogo); NgR-p75; NgR-Troy; NME1 (NM23A); NOX5; NPPB; NR0B1; NR0B2; NR1D1; NR1D2; NR1H2; NR1H3; NR1H4; NR1I2; NR1I3; NR2C1; NR2C2; NR2E1; NR2E3; NR2F1; NR2F2; NR2F6; NR3C1; NR3C2; NR4A1; NR4A2; NR4A3; NR5A1; NR5A2; NR6A1; NRP1; NRP2; NT5E; NTN4; NY-BR-1; o-acetyl-GD2; ODZ1; OPRD1; OR51E2; P2RX7; PANX3; PAP; PART1; PATE; PAWR; PCA3; PCNA; PDGFA; PDGFB; PECAM1; PF4 (CXCL4); PGE2; PGF; PGR; phosphacan; PIAS2; PIK3CG; PLAC1; plasminogen activator; PLAU (uPA); PLG; PLXDC1; polysialic acid; PPBP (CXCL7); PPID; PR1; PRKCQ; PRKD1; PRL; PROC; Protein C; PROK2; PSAP; PSCA; PTAFR; PTEN; PTGS2 (COX-2); PTN; RAC2 (p21Rac2); RAGE; RARB; RGS1; RGS13; RGS3; RNF110 (ZNF144); ROBO2; SIO0A2; SCGB1D2 (lipophilin B); SCGB2A1 (mammaglobin 2); SCGB2A2 (mammaglobin 1); SCYE1 (endothelial Monocyte-activating cytokine); SDF2; SERPINA1; SERPINA3; SERPINB5 (maspin); SERPINE1 (PAI-1); SERPINF1; SHBG; SLA2; SLC2A2; SLC33A1; SLC34A2; SLC39A6; SLC43A1; SLIT2;

SLITRK6; SPP1; SPRR1B (Spr1); ST6GAL1; STAB1; STAT6; STEAP; STEAP2; substance P; TACSTD2; TB4R2; TBX21; TCP10; TDGF1; TEK; TEM1/CD248; TEM7R; TGFA; TGFB1; TGFB111; TGFB2; TGFB3; TGFBI; TGFB1; TGFB2; TGFB3; TH1L; THBS1 (thrombospondin-1); THBS2; THBS4; THPO; TIE (Tie-1); TIMP3; tissue factor; TLR10; TLR2; TLR3; TLR4; TLR5; TLR6; TLR7; TLR8; TLR9; TNF; TNF- α ; TNFAIP2 (B94); TNFAIP3; TNFRSF11A; TNFRSF1A; TNFRSF1B; TNFRSF21; TNFRSF5; TNFRSF6 (Fas); TNFRSF7; TNFRSF8; TNFRSF9; TNFSF10 (TRAIL); TNFSF11 (TRANCE); TNFSF12 (APO3L); TNFSF13 (April); TNFSF13B; TNFSF14 (HVEM-L); TNFSF15 (VEGI); TNFSF18; TNFSF4 (OX40 ligand); TNFSF5 (CD40 ligand); TNFSF6 (FasL); TNFSF7 (CD27 ligand); TNFSF8 (CD30 ligand); TNFSF9 (4-1BB ligand); TOLLIP; Toll-like receptors; TOP2A (topoisomerase α); TP53; TPM1; TPM2; TRADD; TRAF1; TRAF2; TRAF3; TRAF4; TRAF5; TRAF6; TREM1; TREM2; TRPC6; TSHR; TSLP; TWEAK; thrombomodulin; thrombin; UPK2; VEGF; VEGFB; VEGFC; versican; VHL C5; VLA-4; XCL1 (lymphotactin); XCL2 (SCM-1b); XCR1 (GPR5/CCXCR1); YY1; and ZFPM2.

[0365] In some embodiments, the TAA is ADRB3. In some embodiments, the TAA is AKAP-4. In some embodiments, the TAA is ALK. In some embodiments, the TAA is androgen receptor. In some embodiments, the TAA is B7H3. In some embodiments, the TAA is BCMA. In some embodiments, the TAA is BORIS. In some embodiments, the TAA is BST2. In some embodiments, the TAA is Cadherin17. In some embodiments, the TAA is CAIX. In some embodiments, the TAA is CD171. In some embodiments, the TAA is CD179a. In some embodiments, the TAA is CD19. In some embodiments, the TAA is CD20. In some embodiments, the TAA is CD22. In some embodiments, the TAA is CD24. In some embodiments, the TAA is CD30. In some embodiments, the TAA is CD300LF. In some embodiments, the TAA is CD32b. In some embodiments, the TAA is CD33. In some embodiments, the TAA is CD38. In some embodiments, the TAA is CD44v6. In some embodiments, the TAA is CD72. In some embodiments, the TAA is CD79a. In some embodiments, the TAA is CD79b. In some embodiments, the TAA is CD97. In some embodiments, the TAA is CEA. In some embodiments, the TAA is CLDN6. In some embodiments, the TAA is CLEC12A. In some embodiments, the TAA is CLL-1. In some embodiments, the TAA is CS-1. In some embodiments, the TAA is CXORF61. In some embodiments, the TAA is Cyclin B1. In some embodiments, the TAA is CYP1B1. In some embodiments, the TAA is EGFR. In some embodiments, the TAA is EGFRvIII. In some embodiments, the TAA is EMR2. In some embodiments, the TAA is EPCAM. In some embodiments, the TAA is EphA2. In some embodiments, the TAA is EphB2. In some embodiments, the TAA is ERBB2. In some embodiments, the TAA is ERG (TMPRSS2 ETS fusion gene). In some embodiments, the TAA is ETV6-AML. In some embodiments, the TAA is FAP. In some embodiments, the TAA is FCAR. In some embodiments, the TAA is FCRL5. In

some embodiments, the TAA is FLT3. In some embodiments, the TAA is FLT3. In some embodiments, the TAA is folate receptor alpha. In some embodiments, the TAA is folate receptor beta. In some embodiments, the TAA is Fos-related antigen 1. In some embodiments, the TAA is fucosyl GM1. In some embodiments, the TAA is GD2. In some embodiments, the TAA is GD2. In some embodiments, the TAA is GD3. In some embodiments, the TAA is GloboH. In some embodiments, the TAA is GM3. In some embodiments, the TAA is gp100Tn. In some embodiments, the TAA is GPC3. In some embodiments, the TAA is GPNMB. In some embodiments, the TAA is GPR20. In some embodiments, the TAA is GPRC5D. In some embodiments, the TAA is GPR64. In some embodiments, the TAA is HAVCR1. In some embodiments, the TAA is HER3. In some embodiments, the TAA is HMWMAA. In some embodiments, the TAA is hTERT. In some embodiments, the TAA is Igf-I receptor. In some embodiments, the TAA is IGLL1. In some embodiments, the TAA is IL-11Ra. In some embodiments, the TAA is IL-13Ra2. In some embodiments, the TAA is KIT. In some embodiments, the TAA is LAIR1. In some embodiments, the TAA is LCK. In some embodiments, the TAA is LewisY. In some embodiments, the TAA is LILRA2. In some embodiments, the TAA is LMP2. In some embodiments, the TAA is LRP6. In some embodiments, the TAA is LY6K. In some embodiments, the TAA is LY75. In some embodiments, the TAA is LYPD8. In some embodiments, the TAA is MAD-CT-1. In some embodiments, the TAA is MAD-CT-2. In some embodiments, the TAA is mesothelin. In some embodiments, the TAA is ML-IAP. In some embodiments, the TAA is MUC1. In some embodiments, the TAA is MYCN. In some embodiments, the TAA is NA17. In some embodiments, the TAA is NCAM. In some embodiments, the TAA is NKG2D. In some embodiments, the TAA is NY-BR-1. In some embodiments, the TAA is o-acetyl-GD2. In some embodiments, the TAA is OR51E2. In some embodiments, the TAA is OY-TES1. In some embodiments, the TAA is a p53 mutant. In some embodiments, the TAA is PANX3. In some embodiments, the TAA is PAX3. In some embodiments, the TAA is PAX5. In some embodiments, the TAA is PDGFR-beta. In some embodiments, the TAA is PLAC1. In some embodiments, the TAA is polysialic acid. In some embodiments, the TAA is PRSS21. In some embodiments, the TAA is PSCA. In some embodiments, the TAA is RhoC. In some embodiments, the TAA is ROR1. In some embodiments, the TAA is a sarcoma translocation breakpoint protein. In some embodiments, the TAA is SART3. In some embodiments, the TAA is SLC34A2. In some embodiments, the TAA is SLC39A6. In some embodiments, the TAA is sLe. In some embodiments, the TAA is SLITRK6. In some embodiments, the TAA is sperm protein 17. In some embodiments, the TAA is SSEA-4. In some embodiments, the TAA is SSX2. In some embodiments, the TAA is TAAG72. In some embodiments, the TAA is TAARP. In some embodiments, the TAA is TACSTD2. In some embodiments, the TAA is TEM1/CD248. In some embodiments, the TAA is TEM7R. In some embodiments, the TAA is TGS5. In some

embodiments, the TAA is Tie 2. In some embodiments, the TAA is Tn Ag. In some embodiments, the TAA is TSHR. In some embodiments, the TAA is tyrosinase. In some embodiments, the TAA is UPK2. In some embodiments, the TAA is VEGFR2. In some embodiments, the TAA is WT1. In some embodiments, the TAA is XAGE1.

[0366] A TAA ABM can comprise, for example, a ligand- or an antibody-based moiety. For example, in the case of BCMA as a TAA, the ABM can be APRIL, the BCMA ligand, or a portion thereof that binds BCMA, or an anti-BCMA antibody or an antigen-binding fragment thereof. Ligands and antibodies that bind to TAAs are well-known in the art. In the case of antibody-based moieties, the anti-TAA antibody or antigen-binding fragment can comprise, for example, the CDR sequences of an antibody set forth in Table 11. In some embodiments, the anti-TAA antibody or antigen-binding domain thereof has the heavy and light chain variable region sequences of an antibody set forth in Table 11.

TABLE 11	
Exemplary Anti-Tumor-Associated Antigen Antibodies	
Target	Examples of Antibody Name and/or Reference(s) and/or Source
ALK	antibodies described in e.g., Mino-Kenudson <i>et al.</i> , 2010, Clin Cancer Res 16(5):1561-1571
B7H3	MGA271 (Macrogenics)
BCMA	Any BCMA antibody described in WO2012163805, WO200112812, or WO2003062401.
CAIX	Antibody clone 303123 (R&D Systems)
CD123	US8,852,551; EP2426148; WO2014138819; WO2016028896; WO2014130635
CD171	Hong <i>et al.</i> , 2014, J Immunother 37(2):93-104 .
CD19	WO2014031687; WO2012079000; WO2014153270; US Pat. No. 7,741,465; the CD19 binder of Yescarta or Blinatumomab
CD20	Rituximab, Ofatumumab, Ocrelizumab, Veltuzumab, or GA101
CD22	Haso <i>et al.</i> , 2013, Blood, 121(7): 1165-1174; Wayne <i>et al.</i> , 2010, Clin Cancer Res 16(6): 1894-1903; Kato <i>et al.</i> , 2013, Leuk Res 37(1):83-88; Creative BioMart (creativebiomart.net): MOM-18047-S(P).
CD24	Maliar <i>et al.</i> , Gastroenterology 143(5):1375-1384 (2012)
CD30	Any CD30 antibody described in US7090843 B1, or EP0805871
CD33	Bross <i>et al.</i> , 2001, Clin Cancer Res 7(6):1490-1496 (Gemtuzumab Ozogamicin, hP67.6), Caron <i>et al.</i> , 1992, Cancer Res 52(24):6761-6767 (Lintuzumab, HuM195), Lapusan <i>et al.</i> , 2012, Invest New Drugs 30(3):1121-1131 (AVE9633), Aigner <i>et al.</i> , 2013, Leukemia 27(5): 1107-1115 (AMG330, CD33 BiTE), Dutour <i>et al.</i> , 2012, Adv Hematol 2012:683065, or Pizzitola <i>et al.</i> , 2014, Leukemia doi:10.1038/Lue.2014.62.

TABLE 11 Exemplary Anti-Tumor-Associated Antigen Antibodies	
Target	Examples of Antibody Name and/or Reference(s) and/or Source
CD38	Daratumumab (see, e.g., Groen <i>et al.</i> , 2010, Blood 116(21):1261-1262; MOR202 (see, e.g., US Pat. No. 8,263,746); or any CD38 antibody described in US Pat. No. 8,362,211.
CD44v6	Casucci <i>et al.</i> , 2013, Blood 122(20):3461-3472.
CD97	antibodies described in, e.g., US Pat. No. 6,846,911; de Groot <i>et al.</i> , 2009, J Immunol 183(6):4127-4134; antibody from R&D:MAB373
CEA	Chmielewski <i>et al.</i> , 2012, Gastroenterology 143(4):1095-1107.
CLDN6	WO2015069794; IMAB027, mAb, Ganymed Pharmaceuticals
CLL-1	PE-CLL1-hu Cat# 353604 (BioLegend); and PE-CLL1 (CLEC12A) Cat# 562566 (BD); WO 2014/051433 A1; US 2016/0368994 A1; US 2013/0295118 A1; US Pat. No. 8,536,310 B2; Lu <i>et al.</i> , 2014, Angewandte Chemie International Edition 53(37):9841-9845; Leong <i>et al.</i> , 2017, Blood 129(5):609-618
CS1	Elotuzumab (BMS), see e.g., Tai <i>et al.</i> , 2008, Blood 112(4):1329-37; Tai <i>et al.</i> , 2007, Blood. 110(5):1656-63.
EGFR	Cetuximab, panitumumab, zalutumumab, nimotuzumab, or matuzumab
EGFRvIII	WO2012138475; WO2014130657
EPCAM	MT110, EpCAM-CD3 bispecific Ab (see, e.g., clinicaltrials.gov/ct2/show/NCT00635596); Edrecolomab; 3622W94; ING-1; or adecatumumab (MT201).
EphA2	Yu <i>et al.</i> , 2014, Mol Ther 22(1):102-111.
Ephrin B2	Abengozar <i>et al.</i> , 2012, Blood 119(19):4565-4576.
ERBB2 (Her2/neu)	Trastuzumab or pertuzumab.
FAP	Ostermann <i>et al.</i> , 2008, Clinical Cancer Research 14:4584-4592 (FAP5), US Pat. Publication No. 2009/0304718; sibrotuzumab (see e.g., Hofheinz <i>et al.</i> , 2003, Oncology Research and Treatment 26(1):44-48); and Tran <i>et al.</i> , 2013, J Exp Med 210(6):1125-1135.
FLT3	Any FLT3 antibody described in WO2011076922, US Pat. No. 5777084, EP0754230, or US20090297529.
Folate receptor alpha	IMGN853, or any folate receptor alpha antibody described in US20120009181; US Pat. No. 4851332, LK26: US Pat No. 5952484.
Folate receptor beta	antibodies described in, e.g., US20100297138 ; WO2007/067992
GD2	Mujoo <i>et al.</i> , Cancer Res. 47(4):1098-1104 (1987); Cheung <i>et al.</i> , Cancer Res 45(6):2642-2649 (1985), Cheung <i>et al.</i> , J Clin Oncol 5(9):1430-1440 (1987), Cheung <i>et al.</i> , J Clin Oncol 16(9):3053-3060 (1998), Handgretinger <i>et al.</i> , Cancer

TABLE 11 Exemplary Anti-Tumor-Associated Antigen Antibodies	
Target	Examples of Antibody Name and/or Reference(s) and/or Source
	Immunol Immunother 35(3):199-204 (1992); mAb 14.18, 14G2a, ch14.18, hu14.18, 3F8, hu3F8, 3G6, 8B6, 60C3, 10B8, ME36.1, or 8H9 (see e.g., WO2012033885, WO2013040371, WO2013192294, WO2013061273, WO2013123061, WO2013074916, and WO201385552). Any GD2 antibody described in US Publication No.: 20100150910 or PCT Publication No.: WO 2011160119.
GD3	Any GD3 antibody described in US Pat. No. 7253263; US Pat. No. 8,207,308; US 20120276046; EP1013761; WO2005035577; or US Pat. No. 6437098.
GloboH	VK9; Kudryashov <i>et al.</i> , 1998, Glycoconj J.15(3):243-9; Lou <i>et al.</i> , 2014, Proc Natl Acad Sci USA 111(7):2482-2487; MBr1: Bremer <i>et al.</i> , 1984, J Biol Chem 259:14773–14777.
gp100	HMB45, NKIbetaB, or any anti-gp100 antibody described in WO2013165940, or US20130295007
GPRC5D	R&Dsystems: FAB6300A; Lifespan Biosciences: LS-A4180
HMWMAA	antibodies described in, e.g., Kmiecik <i>et al.</i> , 2014, Oncoimmunology 3(1):e27185 (PMID: 24575382) (mAb9.2.27); US Pat. No. 6528481; WO2010033866; US 20140004124
IGF-I receptor	Any IGF-I receptor antibody described in US8344112 B2; EP2322550 A1; WO 2006/138315, or PCT/US2006/022995.
IL-11Ra	Abcam (cat# ab55262) or Novus Biologicals (cat# EPR5446)
IL-13Ra2	Any IL-13Ra2 antibody described in WO2008/146911, WO2004087758, or WO2004087758
KIT	Any KIT antibody described in US7915391, US20120288506
KLRG2	ab121563 (Abcam); B-12 or sc-514346 (Santa Cruz); HPA018199 (Sigma Aldrich)
LewisY	Kelly <i>et al.</i> , Cancer Biother Radiopharm 23(4):411-423 (2008) (hu3S193 Ab (scFvs)); Dolezal <i>et al.</i> , Protein Engineering 16(1):47-56 (2003) (NC10 scFv)
LMP2	Any LMP2 antibody described in US 7,410,640 or US 2005/0129701
LRP6	WO2009064944, WO2009056634, WO2011119661, WO2011138392, WO2011138391, WO2013067355, WO2014029752, WO2017093478
Mesothelin	Any mesothelin antibody described in US 20110262448, US 2012/0107933 or US 9,719,996
MUC1	SAR566658
NCAM	2-2B: MAB5324 (EMD Millipore)
NY-BR-1	antibodies described in, e.g., Jager <i>et al.</i> , 2007, Appl Immunohistochem Mol Morphol 15(1):77-83

TABLE 11 Exemplary Anti-Tumor-Associated Antigen Antibodies	
Target	Examples of Antibody Name and/or Reference(s) and/or Source
o-acetyl-GD2	8B6
PDGFR-beta	Abcam ab32570
PLAC1	antibodies described in, e.g., Ghods <i>et al.</i> , 2013, Biotechnol Appl Biochem doi:10.1002/bab.1177
Polysialic acid	antibodies described in e.g., Nagae <i>et al.</i> , 2013, J Biol Chem 288(47):33784-33796
PRSS21	Any PRSS21 antibody described in US Pat. No.: 8,080,650.
PSCA	Morgenroth <i>et al.</i> , Prostate 67(10):1121-1131 (2007) (scFv 7F5); Nejatollahi <i>et al.</i> , J of Oncology 2013(2013), article ID 839831 (scFv C5-II); or any PSCA antibody described in US Pat Publication No. 20090311181.
PSMA	Parker <i>et al.</i> , Protein Expr Purif 89(2):136-145 (2013), US 20110268656 (J591 ScFv); Frigerio <i>et al.</i> , European J Cancer 49(9):2223-2232 (2013) (scFvD2B); WO 2006125481 (mAbs 3/A12, 3/E7 and 3/F11) or single chain antibody fragments (scFv A5 and D7).
ROR1	Hudecek <i>et al.</i> , Clin Cancer Res 19(12):3153-3164 (2013); or any ROR1 antibody described in WO 2011159847 or US20130101607.
SSEA-4	MC813 (Cell Signaling)
TAG72	Hombach <i>et al.</i> , Gastroenterology 113(4):1163-1170 (1997) or Abcam ab691.
TEM1/CD248	antibodies described in, e.g., Marty <i>et al.</i> , 2006, Cancer Lett 235(2):298-308; Zhao <i>et al.</i> , 2011, J Immunol Methods 363(2):221-232
Tn	Brooks <i>et al.</i> , PNAS 107(22):10056-10061 (2010); Stone <i>et al.</i> , OncoImmunology 1(6):863-873(2012); any Tn antibody described in US8,440,798
TSHR	antibodies described in, e.g., Marty <i>et al.</i> , 2006, Cancer Lett 235(2):298-308; Zhao <i>et al.</i> , 2011, J Immunol Methods 363(2):221-232
Tyrosinase	Any tyrosinase antibody described in US Pat. No. 5843674 or US19950504048.
VEGFR2	Chinnasamy <i>et al.</i> , J Clin Invest 120(11):3953-3968 (2010).

6.7.1. BCMA

[0367] In certain aspects, the present disclosure provides a TBM in which ABM3 BCMA is a tumor necrosis family receptor (TNFR) member expressed on cells of the B-cell lineage. BCMA expression is the highest on terminally differentiated B cells that assume the long lived plasma cell fate, including plasma cells, plasmablasts and a subpopulation of activated B cells and memory B cells. BCMA is involved in mediating the survival of plasma cells for maintaining long-term humoral immunity. The expression of BCMA has been recently linked to a number of cancers, autoimmune disorders, and infectious diseases. Cancers with increased expression

of BCMA include some hematological cancers, such as multiple myeloma, Hodgkin's and non-Hodgkin's lymphoma, various leukemias, and glioblastoma.

[0368] TBMs comprising a ABM that binds to BCMA can comprise, for example, an anti-BCMA antibody or an antigen-binding domain thereof. The anti-BCMA antibody or antigen-binding domain thereof can comprise, for example, CDR, VH, VL, or scFv sequences set forth in Tables 12A-12G.

TABLE 12A			
BCMA Binders – Variable domain and scFv sequences			
Antibody	Domain	Sequence	SEQ ID NO.
BCMA-1	VH	EVQLVESGGGLVQPGGSLRLSCAVSGFALSNGTHMSWVRRAPGK GLEWWSGIVYSGSTYYAASVKGRFTISRDNRSNTLYLQMNSLRPE DTAIYYCSAHGGESDVWGQGTITVTVSS	263
	VL	DIQLTQSPSSLSASVGDRTITCRASQSISSYLNWYQQKPGKAPKL LIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQSY STPYTFGQGTKEIK	264
	scFv	EVQLVESGGGLVQPGGSLRLSCAVSGFALSNGTHMSWVRRAPGK GLEWWSGIVYSGSTYYAASVKGRFTISRDNRSNTLYLQMNSLRPE DTAIYYCSAHGGESDVWGQGTITVTVSSASGGGGSGGRASGGGG SDIQLTQSPSSLSASVGDRTITCRASQSISSYLNWYQQKPGKAPK LLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQS YSTPYTFGQGTKEIK	265
BCMA-2	VH	QVQLVESGGGLVQPGSLRLSCAASGFTFSNYAMSWVRQAPGK GLGWWSGISRSGENTYYADSVKGRFTISRDNRSNTLYLQMNSLRD EDTAVYYCARSPAHYYGMDVWGQGTITVTVSS	266
	VL	DIVLTQSPGTLSPGERATLSCRASQSISSFLAWYQQKPGQAP RLLIYGASRRATGIPDRFSGSGSGTDFTLTISRLEPEDSAVYYCQQ YHSSPSWTFGQGTKEIK	267
	scFv	QVQLVESGGGLVQPGSLRLSCAASGFTFSNYAMSWVRQAPGK GLGWWSGISRSGENTYYADSVKGRFTISRDNRSNTLYLQMNSLRD EDTAVYYCARSPAHYYGMDVWGQGTITVTVSSASGGGGSGGRA SGGGGSDIVLTQSPGTLSPGERATLSCRASQSISSFLAWYQQ KPGQAPRLLIYGASRRATGIPDRFSGSGSGTDFTLTISRLEPEDSA VYYCQQYHSSPSWTFGQGTKEIK	268
BCMA-3	VH	QVQLVESGGGLVQPGSLRLSCAASGFTFDDYAMHWVRQAPGK GLEWWSGISWNSGSGYADSVKGRFTISRDNKNSLYLQMNSLRA EDTALYYCSVHSFLAYWGQGTITVTVSS	269
	VL	DIVMTQTPLSLPVTGPGEASISCRSSQSLLHSNGYNYLDWYLQKP GQSPQLLIYLGNSRASGVDPDRFSGSGSGTDFTLKISRVEAEDVGV YYCMQALQTPYTFGQGTKEIK	270
	scFv	QVQLVESGGGLVQPGSLRLSCAASGFTFDDYAMHWVRQAPGK GLEWWSGISWNSGSGYADSVKGRFTISRDNKNSLYLQMNSLRA EDTALYYCSVHSFLAYWGQGTITVTVSSASGGGGSGGRASGGGG SDIVMTQTPLSLPVTGPGEASISCRSSQSLLHSNGYNYLDWYLQKP GQSPQLLIYLGNSRASGVDPDRFSGSGSGTDFTLKISRVEAEDVGV YYCMQALQTPYTFGQGTKEIK	271
BCMA-4	VH	EVQLLES GGGLVQPGGSLRLSCAVSGFALSNGTHMSWVRRAPGK GLEWWSGIVYSGSTYYAASVKGRFTISRDNRSNTLYLQMNSLRPE DTAIYYCSAHGGESDVWGQGTITVTVSS	272
	VL	DIVMTQTPLSLSVTPGQPASISCKSSQSLLRNDGKTPLYWYLQKA GQPPQLLIYEVS NRFS GPDRFSGSGSGTDFTLKISRVEAEDVGA YYCMQNIQFPSPFGG GTKEIK	273
	scFv	EVQLLES GGGLVQPGGSLRLSCAVSGFALSNGTHMSWVRRAPGK GLEWWSGIVYSGSTYYAASVKGRFTISRDNRSNTLYLQMNSLRPE DTAIYYCSAHGGESDVWGQGTITVTVSSASGGGGSGGRASGGGG	274

TABLE 12A BCMA Binders – Variable domain and scFv sequences			
Antibody	Domain	Sequence	SEQ ID NO.
		SDIVMTQTPLSLSVTPGQPASISCKSSQSLLRNDGKTPLYWYLQKA GQPPQLLIYEVS NRFSGVPDRFSGSGSGTDFTLKISRVEAEDVGA YYCMQNIQFPSFGGGTKLEIK	
BCMA-5	VH	QVQLVQSGAEVRKTGASVKVSCKASGYIFDNFGINWVRQAPGQG LEWMGWINPKNNNTNYAQKFQGRVTITADESTNTAYMEVSSLRS EDTAVYYCARGPYYYQSYMVDVWGQGTMTVTSS	275
	VL	DIVMTQTPLSLPVTGPGEPAISCRSSQSLLHSNGYNYLNWYLQKP GQSPQLLIYLGSKRASGVDPDRFSGSGSGTDFTLHITRVGAEDVGV YYCMQALQTPYTFGQGTKEIK	276
	scFv	QVQLVQSGAEVRKTGASVKVSCKASGYIFDNFGINWVRQAPGQG LEWMGWINPKNNNTNYAQKFQGRVTITADESTNTAYMEVSSLRS EDTAVYYCARGPYYYQSYMVDVWGQGTMTVTSSASGGGGSGGR ASGGGGSDIVMTQTPLSLPVTGPGEPAISCRSSQSLLHSNGYNYL NWYLQKPGQSPQLLIYLGSKRASGVDPDRFSGSGSGTDFTLHITRV GAEDVGVYYCMQALQTPYTFGQGTKEIK	277
BCMA-6	VH	QVQLQESGGGLVQPGGSLRLSCAASGFTFSSDAMTWVRQAPGK GLEWWSVISGSGGTTYADSVKGRFTISRDN SKNTLYLQMNSLRA EDTAVYYCAKLDSSGYYYARGPRYWGGGTLTVSS	278
	VL	DIQLTQSPSSLSASVGDRTITCRASQSISSYLNWYQQKPGKAPKL LIYGASTLASGVPARFSGSGSGTHFTLTINSLQSEDSATYYCQQSY KRASFGQGTKEIK	279
	scFv	QVQLQESGGGLVQPGGSLRLSCAASGFTFSSDAMTWVRQAPGK GLEWWSVISGSGGTTYADSVKGRFTISRDN SKNTLYLQMNSLRA EDTAVYYCAKLDSSGYYYARGPRYWGGGTLTVSSASGGGGSG GRASGGGGSDIQLTQSPSSLSASVGDRTITCRASQSISSYLNWY QQKPGKAPKLLIYGASTLASGVPARFSGSGSGTHFTLTINSLQSED SATYYCQQSYKRASFGQGTKEIK	280
BCMA-7	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFSNYGITWVRQAPGQG LEWMGWISAYNGNTNYAQKFQGRVTMTNRTSISTAYMELSSLRS EDTAVYYCARGPYYYMDVWGKGTMTVTSS	281
	VL	EIVMTQSPLSLPVTGPGEPAISCRSSQSLLYSNGYNYVDWYLQKP GQSPQLLIYLGSNRASGVDPDRFSGSGSGTDFKLQISRVEAEDVGII YCMQGRQFPYSFGQGTKEIK	282
	scFv	QVQLVQSGAEVKKPGASVKVSCKASGYTFSNYGITWVRQAPGQG LEWMGWISAYNGNTNYAQKFQGRVTMTNRTSISTAYMELSSLRS EDTAVYYCARGPYYYMDVWGKGTMTVTSSASGGGGSGGRAS GGGGSEIVMTQSPLSLPVTGPGEPAISCRSSQSLLYSNGYNYVDW YLQKPGQSPQLLIYLGSNRASGVDPDRFSGSGSGTDFKLQISRVEA EDVGIIYCMQGRQFPYSFGQGTKEIK	283
BCMA-8	VH	EVQLLETGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGK GLEWWSGIVYSGSTYYAASVKGRFTISRDN SRNTLYLQMNSLRPE DTAIYYCSAHGGESDVWGQGTITVTSS	284
	VL	EIVLTQSPATLSVSPGESATLSCRASQSVSSNLAWYQQKPGQAPR LLIYGASTRASGIPDRFSGSGSGTDFTLTISLQAEDVAVYYCQQY GSSLTFGGGTKVEIK	285
	scFv	EVQLLETGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGK GLEWWSGIVYSGSTYYAASVKGRFTISRDN SRNTLYLQMNSLRPE DTAIYYCSAHGGESDVWGQGTITVTSSASGGGGSGGRASGGGG SEIVLTQSPATLSVSPGESATLSCRASQSVSSNLAWYQQKPGQAP RLLIYGASTRASGIPDRFSGSGSGTDFTLTISLQAEDVAVYYCQQ YGSSLTFGGGTKVEIK	286
BCMA-9	VH	EVQLVETGGGLVQPGGSLRLSCAVSGFALSNHGMSWVRRAPGK GLEWWSGIVYSGSTYYAASVKGRFTISRDN SRNTLYLQMNSLRPE DTAIYYCSAHGGESDVWGQGTITVTSS	287
	VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSKLAWYQQKPGQAP RLLMYGASIRATGIPDRFSGSGSGTEFTLTISLEPEDFAVYYCQQ	288

TABLE 12A BCMA Binders – Variable domain and scFv sequences			
Antibody	Domain	Sequence	SEQ ID NO.
		YGSSSWTFGQGTKVEIK	
	scFv	EVQLVETGGGLVQPGGSLRLSCAVSGFALSNGTHMSWVRRAPGK GLEWWSGIVYSGSTYYAASVKGRFTISRDNRSNTLYLQMNSLRPE DTAIYYCSAHGGESDVWGQGTITVTVSSASGGGGSGGRASGGGG SEIVMTQSPATLSVSPGERATLSCRASQSVSSKLAWYQQKPGQA PRLMYGASIRATGIPDRFSGSGSGTEFTLTISSELPEDFAVYYCQ QYGSSSWTFGQGTKVEIK	289
BCMA-10	VH	EVQLVETGGGVVQPGGSLRLSCAVSGFALSNGTHMSWVRRAPGK GLEWWSGIVYSGSTYYAASVKGRFTISRDNRSNTLYLQMNSLRPE DTAIYYCSAHGGESDVWGQGTITVTVSS	290
	VL	EIVLTQSPGTLSPGERATLSCRASQSVGSTNLAWYQQKPGQAP RLLIYDASNRATGIPDRFSGGGSGTDFTLTISRLEPEDFAVYYCQQ YGSSPPWTFGQGTKVEIK	291
	scFv	EVQLVETGGGVVQPGGSLRLSCAVSGFALSNGTHMSWVRRAPGK GLEWWSGIVYSGSTYYAASVKGRFTISRDNRSNTLYLQMNSLRPE DTAIYYCSAHGGESDVWGQGTITVTVSSASGGGGSGGRASGGGG SEIVLTQSPGTLSPGERATLSCRASQSVGSTNLAWYQQKPGQA PRLLIYDASNRATGIPDRFSGGGSGTDFTLTISRLEPEDFAVYYCQ QYGSSPPWTFGQGTKVEIK	292
BCMA-11	VH	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKG LEWWSYISSSGSTIYYADSVKGRFTISRDNKNSLYLQMNSLRAED TAVYYCARESGDGMVDVWGQGTITVTVSS	293
	VL	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPK LLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQS YTLAFGQGTGVDIK	294
	scFv	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKG LEWWSYISSSGSTIYYADSVKGRFTISRDNKNSLYLQMNSLRAED TAVYYCARESGDGMVDVWGQGTITVTVSSASGGGGSGGRASGGG GSDIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKA PKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQ QSYTLAFGQGTGVDIK	295
BCMA-12	VH	QVQLVQSGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKG LEWWSYISSSGNTIYYADSVKGRFTISRDNKNSLYLQMNSLRAED TAVYYCARSTMVREDYWGQGTITVTVSS	296
	VL	DIVLTQSPSLPVTLGQPASISCKSSSESLVHNSGKTYLNWFHQRPG QSPRRLIYEVSNRDSGVPDRFTGSGSGTDFTLKISRVEAEDVGVY YCMQGTHWPGTFGQGTKEIK	297
	scFv	QVQLVQSGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKG LEWWSYISSSGNTIYYADSVKGRFTISRDNKNSLYLQMNSLRAED TAVYYCARSTMVREDYWGQGTITVTVSSASGGGGSGGRASGGG GSDIVLTQSPSLPVTLGQPASISCKSSSESLVHNSGKTYLNWFHQR PGQSPRRLIYEVSNRDSGVPDRFTGSGSGTDFTLKISRVEAEDVG VYYCMQGTHWPGTFGQGTKEIK	298
BCMA-13	VH	QVQLVESGGGLVQPGGSLRLSCAVSGFALSNGTHMSWVRRAPGK GLEWWSGIVYSGSTYYAASVKGRFTISRDNRSNTLYLQMNSLRPE DTAIYYCSAHGGESDVWGQGTITVTVSS	299
	VL	DIRLTQSPSPLSASVGDRVTITCQASEDINKFLNWYHQTGKAPKL LIYDASTLQTGVPSRFSGSGSGTDFTLTINSLQPEDIGTYCQQYE SLPLTFGGGTKEIK	300
	scFv	QVQLVESGGGLVQPGGSLRLSCAVSGFALSNGTHMSWVRRAPGK GLEWWSGIVYSGSTYYAASVKGRFTISRDNRSNTLYLQMNSLRPE DTAIYYCSAHGGESDVWGQGTITVTVSSASGGGGSGGRASGGGG SDIRLTQSPSPLSASVGDRVTITCQASEDINKFLNWYHQTGKAPK LIYDASTLQTGVPSRFSGSGSGTDFTLTINSLQPEDIGTYCQQY ESLPLTFGGGTKEIK	301
BCMA-14	VH	EVQLVETGGGLVQPGGSLRLSCAVSGFALSNGTHMSWVRRAPGK	287

TABLE 12A BCMA Binders – Variable domain and scFv sequences			
Antibody	Domain	Sequence	SEQ ID NO.
		GLEWWSGIVYSGSTYYAASVKGRFTISRDNRSRNTLYLQMNSLRPE DTAIYYCSAHGGESDVWGQGTDTVSS	
	VL	ETTLTQSPATLSVSPGERATLSCRASQSVGSNLAWYQQKPGQGP RLLIYGASTRATGIPARFSGSGSGTEFTLTISLQPEDFAVYYCQQY NDWLPVTFGQGTKVEIK	302
	scFv	EVQLVETGGGLVQPGGSLRLSCAVSGFALSNGTHMSWRRAPGK GLEWWSGIVYSGSTYYAASVKGRFTISRDNRSRNTLYLQMNSLRPE DTAIYYCSAHGGESDVWGQGTDTVSSASGGGGSGGRASGGGG SETTLTQSPATLSVSPGERATLSCRASQSVGSNLAWYQQKPGQG PRLIYGASTRATGIPARFSGSGSGTEFTLTISLQPEDFAVYYCQQ YNDWLPVTFGQGTKVEIK	303
BCMA-15	VH	EVQLVESGGGLVQPGGSLRLSCAVSGFALSNGTHMSWRRAPGK GLEWWSGIVYSGSTYYAASVKGRFTISRDNRSRNTLYLQMNSLRPE DTAIYYCSAHGGESDVWGQGTDTVSS	263
	VL	EIVLTQSPGTLSLSPGERATLSCRASQSIGSSSLAWYQQKPGQAP RLLMYGASSRASGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQ QYAGSPPTFGQGTKVEIK	304
	scFv	EVQLVESGGGLVQPGGSLRLSCAVSGFALSNGTHMSWRRAPGK GLEWWSGIVYSGSTYYAASVKGRFTISRDNRSRNTLYLQMNSLRPE DTAIYYCSAHGGESDVWGQGTDTVSSASGGGGSGGRASGGGG SEIVLTQSPGTLSLSPGERATLSCRASQSIGSSSLAWYQQKPGQA PRLMYGASSRASGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQ QYAGSPPTFGQGTKVEIK	305
BCMA-16	VH	QVQLQESGPGLVKPSSETLSLTCTVSGGSISSSYYYWGWRQPPGK GLEWGSIIYSGSAYYNPSLKSRTISVDTSKNQFSLRLSSVTAAD TAVYYCARHWQEWPDADFIDWGQGTMTVSS	306
	VL	ETTLTQSPAFMSATPGDKVIISCKASQDIDDAMNWWYQQKPGEAPL FIIQSATSPVPGIPPRFSGSGFGTDFSLTINNIESEDAAYYFCLQHD NFPLTFGQGTKLEIK	307
	scFv	QVQLQESGPGLVKPSSETLSLTCTVSGGSISSSYYYWGWRQPPGK GLEWGSIIYSGSAYYNPSLKSRTISVDTSKNQFSLRLSSVTAAD TAVYYCARHWQEWPDADFIDWGQGTMTVSSGGGGSGGGGSGG GGSETTLTQSPAFMSATPGDKVIISCKASQDIDDAMNWWYQQKPG EAPLFIIQSATSPVPGIPPRFSGSGFGTDFSLTINNIESEDAAYYFCLQ HDNFPLTFGQGTKLEIK	308
BCMA-17	VH	QVNLRESGPALVKPTQTLTLCTFSGFSLRTSGMCMVSWIRQPPGK ALEWLARIDWDEDKFYSTSLKTRLTISKDTSDNQVLRMTNMDPA DTATYYCARSGAGGTSATAFDIWGPMTMTVSS	309
	VL	DIQMTQSPSSLSASVGDRVTITCRASQDIYNNLAWFQLKPGSAPR SLMYAANKSQSGVPSRFSGSASGTDFTLTISLQPEDFATYYCQH YYRFPYSFGQGTKLEIK	310
	scFv	VNLRESGPALVKPTQTLTLCTFSGFSLRTSGMCMVSWIRQPPGKA LEWLARIDWDEDKFYSTSLKTRLTISKDTSDNQVLRMTNMDPAD TATYYCARSGAGGTSATAFDIWGPMTMTVSSGGGGSGGGGSGG GGSDIQMTQSPSSLSASVGDRVTITCRASQDIYNNLAWFQLKPG SAPRSLMYAANKSQSGVPSRFSGSASGTDFTLTISLQPEDFATY YCQHYRFPYSFGQGTKLEIK	311
BCMA-18	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMNWVRQAPGK GLEWSSISSSSSYYADSVKGRFTISRDNKNSLYLQMNSLRAE DTAVYYCAKTIAAVYAFDIWGQGTDTVSS	312
	VL	EIVLTQSPSLPVTPEEPASISCRSSQSLLSNGYNYLDWYLQKPG QSPQLLIYLGSNRASGVPRFSGSGSGTDFTLKISRVEAEDVGVY YCMQALQTPYTFGQGTKLEIK	313
	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMNWVRQAPGK GLEWSSISSSSSYYADSVKGRFTISRDNKNSLYLQMNSLRAE	314

TABLE 12A BCMA Binders – Variable domain and scFv sequences			
Antibody	Domain	Sequence	SEQ ID NO.
		DTAVYYCAKTIAAVYAFDIWGQGTITVTVSSGGGGSGGGGSGGGG SEIVLTQSPLSLPVTPEEPASISCRSSQSLHNSNGYNYLDWYLQKP GQSPQLLIYLGSRASGVPDRFSGSGSGTDFTLKISRVEAEDVGV YYCMQALQTPYTFGQGTKLEIK	
BCMA-19	VH	EVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKG LEWWSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAED TAVYYCARDLRGAFDIWGQGTMTVTVSS	315
	VL	SYVLTQSPSVSAAPGYTATISCGGNNIGTKSVHWYQQKPGQAPLL VIRDDSVRPSKIPGRFSGSNSGNMATLTISGVQAGDEADFCYQVW DSDSEHVVFGGGTKLTVL	316
	scFv	EVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMSWIRQAPGKG LEWWSYISSSGSTIYYADSVKGRFTISRDNAKNSLYLQMNSLRAED TAVYYCARDLRGAFDIWGQGTMTVTVSSGGGGSGGGGSGGGGSS YVLTQSPSVSAAPGYTATISCGGNNIGTKSVHWYQQKPGQAPLLVI RDDSVRPSKIPGRFSGSNSGNMATLTISGVQAGDEADFCYQVWD SDSEHVVFGGGTKLTVL	317
BCMA-20	VH	QVQLVQSGAEVKKPGASVKVCKPSGTYTTSYIHWRRAPGQG LEWMGMINPSGGVTAYSQTLQGRVTMTSDTSSSTVYMESSLRS EDTAMYYCAREGSGSGWYFDWGRGTLTVTVSS	318
	VL	SYVLTQPPSVSVSPGQTASITCSGDGLSKKYVSWYQQKAGQSPV VLISRDKERPSGIPDRFSGSNSADTATLTISGTQAMDEADYYCQA WDDTTVVFGGGTKLTVL	319
	scFv	QVQLVQSGAEVKKPGASVKVCKPSGTYTTSYIHWRRAPGQG LEWMGMINPSGGVTAYSQTLQGRVTMTSDTSSSTVYMESSLRS EDTAMYYCAREGSGSGWYFDWGRGTLTVTVSSGGGGSGGGGSS GGGGSSYVLTQPPSVSVSPGQTASITCSGDGLSKKYVSWYQQKA GQSPVVLISRDKERPSGIPDRFSGSNSADTATLTISGTQAMDEADY YCQAWDDTTVVFGGGTKLTVL	320
BCMA-21	VH	QVQLQESGPGLVKPSQTLSTCTVSGGSISSGGYYWSWIRQHPG KGLEWIGYIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAAD TAVYYCARAGIAARLRGAFDIWGQGTMTVTVSS	321
	VL	DIVMTQSPSSVSASVGDRVIITCRASQGIRNWLAWYQQKPGKAPN LLIYAASNLQSGVPSRFSGSGSGADFTLTISLQPEDVATYYCQKY NSAPFTFGPGTKVDIK	322
	scFv	QVQLQESGPGLVKPSQTLSTCTVSGGSISSGGYYWSWIRQHPG KGLEWIGYIYYSGSTYYNPSLKSRTISVDTSKNQFSLKLSSVTAAD TAVYYCARAGIAARLRGAFDIWGQGTMTVTVSSGGGGSGGGGSG GGGSDIVMTQSPSSVSASVGDRVIITCRASQGIRNWLAWYQQKPG KAPNLLIYAASNLQSGVPSRFSGSGSGADFTLTISLQPEDVATYY CQKYNSAPFTFGPGTKVDIK	323
BCMA-22	VH	QVQLVQSGAEVKKPGSSVKVCKASGGTFSSYAIWVRQAPGQG LEWMGGIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRSED TAVYYCARRGGYQLLRWDVGLLRSAFDIWGQGTMTVTVSS	324
	VL	SYVLTQPPSVSVAPGQTARITCGGNNIGSKSVHWYQQKPGQAPV LVLYGKNNRPSGVPDRFSGSRSGTTASLTITGAQAEDEADYYCSS RDSSGDHLRVFGTGKVTVL	325
	scFv	QVQLVQSGAEVKKPGSSVKVCKASGGTFSSYAIWVRQAPGQG LEWMGGIPIFGTANYAQKFQGRVTITADESTSTAYMELSSLRSED TAVYYCARRGGYQLLRWDVGLLRSAFDIWGQGTMTVTVSSGGGG SGGGGSGGGGSSYVLTQPPSVSVAPGQTARITCGGNNIGSKSVH WYQQKPGQAPVLVLYGKNNRPSGVPDRFSGSRSGTTASLTITGA QAEDEADYYCSSRDSSGDHLRVFGTGKVTVL	326
BCMA-23	VH	EVQLQQSGPGLVKPSQTLSTCAISGDSVSSNSAAWNWIRQSPSR GLEWLGRTYRYSKYFYAISLKSRIINPDTSKNQFSLQLKSVTPE DTAVYYCARSSPEGLFLYWFDPWGQGTMTVTVSS	327
	VL	SSELTQDPAVSVALGQTIRITCQGDLSGNYATWYQQKPGQAPVL	328

TABLE 12A BCMA Binders – Variable domain and scFv sequences			
Antibody	Domain	Sequence	SEQ ID NO.
		VIYGTNNRPSGIPDRFSASSSGNTASLTITGAQAEDEADYYCNSRDSSGHLLFGTGTKVTVL	
	ScFv	EVQLQQSGPGLVKPSQTLSTCAISGDSVSSNSAAWNWIRQSPSRGLEWLGRTYYRSKWYSFYAISLKSRIINPDTSKNQFSLQLKSVTPEDTAVYYCARSSPEGLFLYWFDPWGQGTTLTVSSGGDGSGGGSGGGSSSELTQDPAVSVALGQTIRITCQGDSLGNYYATWYQQKPQQAPVLVIYGTNNRPSGIPDRFSASSSGNTASLTITGAQAEDEADYYCNSRDSSGHLLFGTGTKVTVL	329
BCMA-24	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKLEWWSAISGSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKVEGSGSLDYWGQGTTLTVSS	330
	VL	EIVMTQSPGTLSPGERATLSCRASQSVSSAYLAWYQQKPGQPRLISGASTRATGIPDRFGSGSGTDFTLTISRLEPEDFAVYYCQHYGSSFNSSSLFTFGQGTRLEIK	331
	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKLEWWSAISGSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKVEGSGSLDYWGQGTTLTVSSGGGGSGGGGSGGGSEIVMTQSPGTLSPGERATLSCRASQSVSSAYLAWYQQKPGQPRLISGASTRATGIPDRFGSGSGTDFTLTISRLEPEDFAVYYCQHYGSSFNSSSLFTFGQGTRLEIK	332
	VH	EVQLVETGGGLVQPGGSLRLSCAASGITFSRYPMWVRQAPGKGLEWWSGISDSGVSTYYADSAKGRFTISRDN SKNTLFLQMSSLRDEDTAVYYCVTRAGSEASDIWGQGTMTVSS	333
BCMA-25	VL	EIVLTQSPATLSLSPGERATLSCRASQSVSNLAWYQQKPGQAPRLIYDASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAIYYCQQFGTSSGLTFGGGTKLEIK	334
	scFv	EVQLVETGGGLVQPGGSLRLSCAASGITFSRYPMWVRQAPGKGLEWWSGISDSGVSTYYADSAKGRFTISRDN SKNTLFLQMSSLRDEDTAVYYCVTRAGSEASDIWGQGTMTVSSGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCRASQSVSNLAWYQQKPGQAPRLIYDASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAIYYCQQFGTSSGLTFGGGTKLEIK	335
BCMA-26	VH	QVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKLEWWSAISGSGGSTYYADSVKGRFTISRDN AKNSLYLQMNSLRAEDTAIYYCARATYKRELRYYYGMDVWGQGTMTVSS	336
	VL	EIVMTQSPGTVSLSPGERATLSCRASQSVSSSFLAWYQQKPGQAPRLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDSAVYYCQYHSSPSWTFGQGTRLEIK	337
	scFv	QVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKLEWWSAISGSGGSTYYADSVKGRFTISRDN AKNSLYLQMNSLRAEDTAIYYCARATYKRELRYYYGMDVWGQGTMTVSSGGGGSGGGGSGGGGSEIVMTQSPGTVSLSPGERATLSCRASQSVSSSFLAWYQQKPGQAPRLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDSAVYYCQYHSSPSWTFGQGTRLEIK	338
BCMA-27	VH	EVQLVETGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKLEWWSAISGSGGSTYYADSVKGRFTISRDN SKNTLYLQMNTLKAEDTAVYYCARATYKRELRYYYGMDVWGQGTMTVSS	339
	VL	EIVLTQSPSTLSLSPGESATLSCRASQSVSTTFLAWYQQKPGQAPRLIYGSSNRATGIPDRFSGSGSGTDFTLTIRRLEPEDFAVYYCQQYHSSPSWTFGQGTKVEIK	340
	scFv	EVQLVETGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKLEWWSAISGSGGSTYYADSVKGRFTISRDN SKNTLYLQMNTLKAEDTAVYYCARATYKRELRYYYGMDVWGQGTMTVSSGGGGSGGGGSGGGGSEIVLTQSPSTLSLSPGESATLSCRASQSVSTTFLAWYQQKPGQAPRLIYGSSNRATGIPDRFSGSGSGTDFTLTIRRLEPED	341

TABLE 12A BCMA Binders – Variable domain and scFv sequences			
Antibody	Domain	Sequence	SEQ ID NO.
		FAVYYCQQYHSSPSWTFGQGTKVEIK	
BCMA-28	VH	EVQLVETGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGK GLEWWSGISWNSGSGISYADSVKGRFTISRDNKNSLYLQMNSLRD EDTAVYYCARVGKAVPDVWGQGTITVTVSS	342
	VL	DIVMTQTPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKL LIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQSY STPYSFGQGTRLEIK	343
	scFv	EVQLVETGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGK GLEWWSGISWNSGSGISYADSVKGRFTISRDNKNSLYLQMNSLRD EDTAVYYCARVGKAVPDVWGQGTITVTVSSGGGGSGGGSGGG GSDIVMTQTPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKA PKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQ QSYSTPYSFGQGTRLEIK	344
BCMA-29	VH	EVQLVESGGGLVQPGRSLRLSCTASGFTFDDYAMHWVRQRP GK GLEWWSINWKGNSLAYGDSVKGRFAISRDNKNTVFLQMNSLR EDTAVYYCASHQGVAYYNYAMDVWGRGTLTVTVSS	345
	VL	EIVLTQSPGTLTSLSPGERATLSCRATQSIGSSFLAWYQQRPGQAP RLLIYGASQRATGIPDRFSGRSGSGTDFTLTISRVEPEDSAVYYCQH YESSPSWTFGQGTKVEIK	346
	scFv	EVQLVESGGGLVQPGRSLRLSCTASGFTFDDYAMHWVRQRP GK GLEWWSINWKGNSLAYGDSVKGRFAISRDNKNTVFLQMNSLR EDTAVYYCASHQGVAYYNYAMDVWGRGTLTVTVSSGGGGSGGG GSGGGGSEIVLTQSPGTLTSLSPGERATLSCRATQSIGSSFLAWYQ QRPGQAPRLLIYGASQRATGIPDRFSGRSGSGTDFTLTISRVEPEDS AVYYCQHYESSPSWTFGQGTKVEIK	347
BCMA-30	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGK GLEWWSAISGSGGSTYYADSVKGRFTISRDNKNTLYLQMNSLRA EDTAVYYCAKVVRDGMVWGQGTITVTVSS	348
	VL	EIVLTQSPATLSTSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAP RLLIYGASSRATGIPDRFSGNGSGTDFTLTISRLEPEDFAVYYCQQ YGSPPRFTFGPGTKVDIK	349
	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGK GLEWWSAISGSGGSTYYADSVKGRFTISRDNKNTLYLQMNSLRA EDTAVYYCAKVVRDGMVWGQGTITVTVSSGGGGSGGGSGGG GSEIVLTQSPATLSTSLSPGERATLSCRASQSVSSSYLAWYQQKPGQ APRLLIYGASSRATGIPDRFSGNGSGTDFTLTISRLEPEDFAVYYC QQYGSPPRFTFGPGTKVDIK	350
BCMA-31	VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKG LEWWSAISGSGGSTYYADSVKGRFTISRDNKNTLYLQMNSLRAE DTAVYYCAKIPQTGTFDYWGQGTITVTVSS	351
	VL	EIVLTQSPGTLTSLSPGERATLSCRASQSVSSSYLAWYQQRPGQAP RLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQH YGSSPSWTFGQGTTRLEIK	352
	scFv	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKG LEWWSAISGSGGSTYYADSVKGRFTISRDNKNTLYLQMNSLRAE DTAVYYCAKIPQTGTFDYWGQGTITVTVSSGGGGSGGGSGGGG SEIVLTQSPGTLTSLSPGERATLSCRASQSVSSSYLAWYQQRPGQA PRLLIYGASSRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQ HYGSSPSWTFGQGTTRLEIK	353
BCMA-32	VH	EVQLVETGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGK GLEWWSAISGSGGSTYYADSVKGRFTMSRENDKNSVFLQMNSLR VEDTGVIYCARANYKRELRYYYGMDVWGQGTMTVTVSS	354
	VL	EIVMTQSPGTLTSLSPGESATLSCRASQSVASNYLAWYQHKPGQA PSLLISGASSRATGVPDRFSGSGSGTDFTLAISRLEPEDSAVYYCQ HYDSSPSWTFGQGTKVEIK	355

TABLE 12A			
BCMA Binders – Variable domain and scFv sequences			
Antibody	Domain	Sequence	SEQ ID NO.
	scFv	EVQLVETGGGLVQPGGSLRLSCAASGFTFSSYAMSWWRQAPGK GLEWWSAISGSGGSTYYADSVKGRFTMSRENDKNSVFLQMNSLR VEDTGVYYCARANYKRELRYYYGMDVWGQGTMTVSSGGGGS GGGSGGGGSEIVMTQSPGTLSPGESATLSCRASQRVASNYL AWYQHKPGQAPSLISGASSRATGVPDRFSGSGSGTDFTLAISRL EPEDSAVYYCQHYDSSPSWTFGQGTKVEIK	356
BCMA-33	VH	EVQLLETGGGLVQPGGSLRLSCAASGFSFSSYAMSWWRQAPGKG LEWWSAISGSGGSTYYADSVKGRFTISRDNKNTLYLQMNSLRAE DTAVYYCAKALVGATGAFDIWGQGTTLTVSS	357
	VL	EIVLTQSPGTLSPGERATLSCRASQSLSSNFLAWYQQKPGQAP GLLIYGASNWATGTPDRFSGSGSGTDFTLTITRLEPEDFAVYYCQY YGTSPMYTFGQGTKVEIK	358
	scFv	EVQLLETGGGLVQPGGSLRLSCAASGFSFSSYAMSWWRQAPGKG LEWWSAISGSGGSTYYADSVKGRFTISRDNKNTLYLQMNSLRAE DTAVYYCAKALVGATGAFDIWGQGTTLTVSSGGGSGGGGSGG GGSEIVLTQSPGTLSPGERATLSCRASQSLSSNFLAWYQQKPG QAPGLLIYGASNWATGTPDRFSGSGSGTDFTLTITRLEPEDFAVYY CQYYGTSPMYTFGQGTKVEIK	359
BCMA-34	VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWWRQAPGKG LEWWSAISGSGGSTYYADSVKGRFTISRDNKNTLYLQMNSLRAE DTAVYYCVLWFGEGFDPWGQGTTLTVSS	360
	VL	DIVLTQSPLSLPVTGPGEPAISCRSSQSLHNSNGYNYLDWYLQKPG QSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVY YCMQALQTPLTFGGGTKVDIK	361
	scFv	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWWRQAPGKG LEWWSAISGSGGSTYYADSVKGRFTISRDNKNTLYLQMNSLRAE DTAVYYCVLWFGEGFDPWGQGTTLTVSSGGGSGGGGSGGGG SDIVLTQSPLSLPVTGPGEPAISCRSSQSLHNSNGYNYLDWYLQKPG QSPQLLIYLGSNRASGVPDRFSGSGSGTDFTLKISRVEAEDVGVY YCMQALQTPLTFGGGTKVDIK	362
BCMA-35	VH	QVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWWRQAPGK GLEWWSAISGSGGSTYYADSVKGRFTISRDNKNTLYLQMNSLRA EDTAVYYCAKVGVDSSGYRDYYGMDVWGQGTTVTVSS	363
	VL	EIVLTQSPGTLSPGERATLSCRASQSVSSSYLAWYQQKPGQAP RLLIYGTSSRATGISDRFSGSGSGTDFTLTISRLEPEDFAVYYCQHY GNSPPKFTFGPGTKLEIK	364
	scFv	QVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWWRQAPGK GLEWWSAISGSGGSTYYADSVKGRFTISRDNKNTLYLQMNSLRA EDTAVYYCAKVGVDSSGYRDYYGMDVWGQGTTVTVSSGGGGS GGGSGGGGSEIVLTQSPGTLSPGERATLSCRASQSVSSSYLA WYQQKPGQAPRLLIYGTSSRATGISDRFSGSGSGTDFTLTISRLEP EDFAVYYCQHYGNSPPKFTFGPGTKLEIK	365
BCMA-36	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWWRQAPGK GLEWWSAISGSGGSTYYADSVKGRFTISRDNKNTLYLQMNSLRA EDTAVYYCAKMGWSSGYLGAFDIWGQGTTVTVSS	366
	VL	EIVLTQSPGTLSPGERATLSCRASQSVASSFLAWYQQKPGQAP RLLIYGASGRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQH YGGSPRLTFGGGTKVDIK	367
	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWWRQAPGK GLEWWSAISGSGGSTYYADSVKGRFTISRDNKNTLYLQMNSLRA EDTAVYYCAKMGWSSGYLGAFDIWGQGTTVTVSSGGGSGGGG SGGGGSEIVLTQSPGTLSPGERATLSCRASQSVASSFLAWYQQ KPGQAPRLLIYASGRATGIPDRFSGSGSGTDFTLTISRLEPEDFA VYYCQHYGGSPRLTFGGGTKVDIK	368
BCMA-37	VH	QIQLVQSGPDLKKPGETVKLSCKASGYTFTNFGMNWVKQAPGKG	369

TABLE 12A BCMA Binders – Variable domain and scFv sequences			
Antibody	Domain	Sequence	SEQ ID NO.
		FKWMAWINTYTGESYFADDFKGRFAFSVETSATTAYLQINNLTKE DTATYFCARGEIYYGYDGGFAYWGQGLTVSA	
	VL	DVVMQTQSHRFMSTSVGDRVSITCRASQDVNTAVSWYQQKPGQS PKLLIFSASYRYTGVPDRFTGSGSGADFTLTISVQAEDLAVYYCQ QHYSTPWTFGGGTKLDIK	370
	scFv	QIQLVQSGPDLKKPGETVKLSCKASGYTFTNFGMNWVKQAPGKG FKWMAWINTYTGESYFADDFKGRFAFSVETSATTAYLQINNLTKE DTATYFCARGEIYYGYDGGFAYWGQGLTVSAGGGGSGGGGS GGGSDVVMQTQSHRFMSTSVGDRVSITCRASQDVNTAVSWYQQ KPGQSPKLLIFSASYRYTGVPDRFTGSGSGADFTLTISVQAEDLA VYYCQQHYSTPWTFGGGTKLDIK	371
BCMA-38	VH	QIQLVQSGPELKKPGETVKISCKASGYTFTDYSINWVKRAPGKGLK WMGWINTETREPAYAYDFRGRFAFSLETSASTAYLQINNLTKE ATYFCALDYSYAMDYWGQGTSTVSS	372
	VL	DIVLTQSPASLMSLGKRATISCRASESVSVIGAHLIHWYQQKPGQ PPKLLIYLASNLETGVPARFSGSGSGTDFTLTIDPVEEDDVAIYSL QSRIFPRTFGGGTKLEIK	373
	scFv	QIQLVQSGPELKKPGETVKISCKASGYTFTDYSINWVKRAPGKGLK WMGWINTETREPAYAYDFRGRFAFSLETSASTAYLQINNLTKE ATYFCALDYSYAMDYWGQGTSTVSSGGGGSGGGGSGGGGSQI QLVQSGPELKKPGETVKISCKASGYTFTDYSINWVKRAPGKGLKW MGWINTETREPAYAYDFRGRFAFSLETSASTAYLQINNLTKE ATYFCALDYSYAMDYWGQGTSTVSS	374
BCMA-39	VH	QIQLVQSGPELKKPGETVKISCKASGYTFRHYSMNWVKQAPGKGL KWMGRINTESGVPIYADDFKGRFAFSVETSASTAYLVINNLTKE ASYFCSNDYLYSLDFWGQGTALTSS	375
	VL	DIVLTQSPPSLMSLGKRATISCRASESVTILGSHLIYWYQQKPGQ PPTLLIQLASNVQTGVPARFSGSGSRTDFTLTIDPVEEDDVAIYSL LQSRITPRTFGGKLEIK	376
	scFv	QIQLVQSGPELKKPGETVKISCKASGYTFRHYSMNWVKQAPGKGL KWMGRINTESGVPIYADDFKGRFAFSVETSASTAYLVINNLTKE ASYFCSNDYLYSLDFWGQGTALTSSGGGGSGGGGSGGGGSDI VLTQSPPSLMSLGKRATISCRASESVTILGSHLIYWYQQKPGQPP TLLIQLASNVQTGVPARFSGSGSRTDFTLTIDPVEEDDVAIYSL LQSRITPRTFGGKLEIK	377
BCMA-40	VH	QIQLVQSGPELKKPGETVKISCKASGYTFTHYSMNWVKQAPGKGL KWMGRINTETGEPLYADDFKGRFAFSLETSASTAYLVINNLTKE ATFFCSNDYLYSCDYWGQGTTLTSS	378
	VL	DIVLTQSPPSLMSLGKRATISCRASESVTILGSHLIYWYQQKPGQ PPTLLIQLASNVQTGVPARFSGSGSRTDFTLTIDPVEEDDVAIYSL LQSRITPRTFGGKLEIK	376

TABLE 12A			
BCMA Binders – Variable domain and scFv sequences			
Antibody	Domain	Sequence	SEQ ID NO.
	scFv	QIQLVQSGPELKKPGETVKISCKASGYTFTHYSMNWVKQAPGKGL KWMGRINTETGEPLYADDFKGRFAFSLETSASTAYLVINNLKNEDT ATFFCSNDYLYSCDYWGQGTTLTVSSGGGGSGGGGSGGGGSDI VLTQSPPSLAMSLGKRATISCRASESVTILGSHLIYWYQQKPGQPP TLLIQLASNVQTGVPARFSGSGSRTDFTLTIDPVEEDDVAVYYCLQ SRTIPRTFGGGTKLEIK	379

TABLE 12B						
BCMA Binders – Light chain CDR sequences according to Kabat numbering scheme						
Antibody	CDR-L1	SEQ ID NO:	CDR-L2	SEQ ID NO:	CDR-L3	SEQ ID NO:
BCMA-1	RASQSISSYLN	380	AASSLQS	412	QQSYSTPYT	441
BCMA-2	RASQSISSSFLA	381	GASRRAT	413	QQYHSSPSWT	442
BCMA-3	RSSQSLLHSNGYNYLD	382	LGSNRAS	414	MQALQTPYT	443
BCMA-4	KSSQSLLRNDGKTPLY	383	EVSNRFS	415	MQNIQFPS	444
BCMA-5	RSSQSLLHSNGYNYLN	384	LGSKRAS	416	MQALQTPYT	443
BCMA-6	RASQSISSYLN	380	GASTLAS	417	QQSYKRAS	445
BCMA-7	RSSQSLLYSNGYNYVD	385	LGSNRAS	414	MQGRQFPYS	446
BCMA-8	RASQSVSSNLA	386	GASTRAS	418	QQYGSSLT	447
BCMA-9	RASQSVSSKLA	387	GASIRAT	419	QQYGSSSWT	448
BCMA-10	RASQSVGSTNLA	388	DASNRAT	158	QQYGSSPPWT	449
BCMA-11	RASQSISSYLN	380	AASSLQS	412	QQSYTLA	450
BCMA-12	KSSESLVHNSGKTYLN	389	EVSNRDS	420	MQGTHWPGT	451
BCMA-13	QASEDINKFLN	390	DASTLQT	421	QQYESLPLT	452
BCMA-14	RASQSVGSNLA	391	GASTRAT	422	QQYNDWLPVT	453
BCMA-15	RASQSIGSSSLA	392	GASSRAS	423	QQYAGSPFFT	454
BCMA-16	KASQDIDDAMN	393	SATSPVP	424	LQHDNFPLT	455
BCMA-17	RASQDIYNNLA	394	AANKSQS	425	QHYYRFPYS	456
BCMA-18	RSSQSLLHSNGYNYLD	382	LGSNRAS	414	MQALQTPYT	443
BCMA-19	GGNNIGTKSVH	395	DDSVRPS	426	QVWDSDSEHVV	457
BCMA-20	SGDGLSKKYVS	396	RDKERPS	427	QAWDDTTVV	458
BCMA-21	RASQGIRNWLA	397	AASNLQS	428	QKYNSAPFT	459
BCMA-22	GGNNIGSKSVH	398	GKNNRPS	429	SSRDSSGDHLRV	460
BCMA-23	QGDSLGNYYAT	399	GTNNRPS	430	NSRDSSGHLL	461
BCMA-24	RASQSVSSAYLA	400	GASTRAT	422	QHYGSSFNSSLFT	462
BCMA-25	RASQSVSNSLA	401	DASSRAT	431	QQFGTSSGLT	463
BCMA-26	RASQSVSSSFLA	402	GASSRAT	432	QQYHSSPSWT	442
BCMA-27	RASQSVSTTFLA	403	GSSNRAT	433	QQYHSSPSWT	442
BCMA-28	RASQSISSYLN	380	AASSLQS	412	QQSYSTPYS	464

TABLE 12B						
BCMA Binders – Light chain CDR sequences according to Kabat numbering scheme						
BCMA-29	RATQSIGSSFLA	404	GASQRAT	434	QHYESSPSWT	465
BCMA-30	RASQSVSSSYLA	405	GASSRAT	432	QQYGSPPRFT	466
BCMA-31	RASQSVSSSYLA	405	GASSRAT	432	QHYGSSPSWT	467
BCMA-32	RASQRVASNYLA	406	GASSRAT	432	QHYDSSPSWT	468
BCMA-33	RASQSLSSNFLA	407	GASNWAT	435	QYYGTSPMYT	469
BCMA-34	RSSQSLLSHNGYNYLD	382	LGSNRAS	414	MQALQTPLT	470
BCMA-35	RASQSVSSSYLA	405	GTSSRAT	436	QHYGNSPPKFT	471
BCMA-36	RASQSVASSFLA	408	GASGRAT	437	QHYGGSPRLT	472
BCMA-37	RASQDVNTAVS	409	SASYRYT	438	QQHYSTPWT	473
BCMA-38	RASESVSVIGAHLIH	410	LASNLET	439	LQSRIFPRT	474
BCMA-39	RASESVTILGSHLIY	411	LASNVQT	440	LQSRTIPRT	475
BCMA-40	RASESVTILGSHLIY	411	LASNVQT	440	LQSRTIPRT	475

TABLE 12C						
BCMA Binders – Light chain CDR sequences according to Chothia numbering scheme						
Antibody	CDR-L1	SEQ ID NO:	CDR-L2	SEQ ID NO:	CDR-L3	SEQ ID NO:
BCMA-1	SQSISSY	476	AAS	507	SYSTPY	520
BCMA-2	SQSISSSF	477	GAS	508	YHSSPSW	521
BCMA-3	SQSLLSHNGYNY	478	LGS	509	ALQTPY	522
BCMA-4	SQSLLRNDGKTP	479	EVS	510	NIQFP	523
BCMA-5	SQSLLSHNGYNY	478	LGS	509	ALQTPY	522
BCMA-6	SQSISSY	476	GAS	508	SYKRA	524
BCMA-7	SQSLLYSNGYNY	480	LGS	509	GRQFPY	525
BCMA-8	SQSVSSN	481	GAS	508	YGSSL	526
BCMA-9	SQSVSSK	482	GAS	508	YGSSSW	527
BCMA-10	SQSVGSTN	483	DAS	217	YGSSPPW	528
BCMA-11	SQSISSY	476	AAS	507	SYTL	529
BCMA-12	SESLVHNSGKTY	484	EVS	510	GTHWPG	530
BCMA-13	SEDINKF	485	DAS	217	YESLPL	531
BCMA-14	SQSVGSN	486	GAS	508	YNDWLPV	532
BCMA-15	SQSIGSSS	487	GAS	508	YAGSPPF	533
BCMA-16	SQDIDDA	488	SAT	511	HDNFPL	534
BCMA-17	SQDIYNN	489	AAN	512	YYRFPY	535

TABLE 12C						
BCMA Binders – Light chain CDR sequences according to Chothia numbering scheme						
BCMA-18	SQSLLSNGYNY	478	LGS	509	ALQTPY	522
BCMA-19	NNIGTKS	490	DDS	513	WDSDSEHV	536
BCMA-20	DGLSKKY	491	RDK	514	WDDTTV	537
BCMA-21	SQGIRNW	492	AAS	507	YNSAPF	538
BCMA-22	NNIGSKS	493	GKN	515	RDSSGDHLR	539
BCMA-23	DSLGNYY	494	GTN	213	RDSSGHHL	540
BCMA-24	SQSVSSAY	495	GAS	508	YGSSFNGSSLF	541
BCMA-25	SQSVSNS	496	DAS	217	FGTSSGL	542
BCMA-26	SQSVSSSF	497	GAS	508	YHSSPSW	521
BCMA-27	SQSVSTTF	498	GSS	516	YHSSPSW	521
BCMA-28	SQSISSY	476	AAS	507	SYSTPY	520
BCMA-29	TQSIGSSF	499	GAS	508	YESSPSW	543
BCMA-30	SQSVSSSY	500	GAS	508	YGSPPRF	544
BCMA-31	SQSVSSSY	500	GAS	508	YGSSPSW	545
BCMA-32	SQRVASNY	501	GAS	508	YDSSPSW	546
BCMA-33	SQSLSSNF	502	GAS	508	YGTSPMY	547
BCMA-34	SQSLLSNGYNY	478	LGS	509	ALQTPL	548
BCMA-35	SQSVSSSY	500	GTS	517	YGNSPPKF	549
BCMA-36	SQSVASSF	503	GAS	508	YGGSPRL	550
BCMA-37	SQDVNTA	504	SAS	518	HYSTPW	551
BCMA-38	SESVVIG AHL	505	LAS	519	SRIFPR	552
BCMA-39	SESVTILGSHL	506	LAS	519	SRTIPR	553
BCMA-40	SESVTILGSHL	506	LAS	519	SRTIPR	553

TABLE 12D						
BCMA Binders – Light chain CDR sequences according to combination of Kabat and Chothia numbering schemes						
Antibody	CDR-L1	SEQ ID NO:	CDR-L2	SEQ ID NO:	CDR-L3	SEQ ID NO:
BCMA-1	RASQSISSYLN	380	AASSLQS	412	QQSYSTPYT	441
BCMA-2	RASQSISSFLA	381	GASRRAT	413	QQYHSSPSWT	442

TABLE 12D						
BCMA Binders – Light chain CDR sequences according to combination of Kabat and Chothia numbering schemes						
BCMA-3	RSSQSLLHSNGYN YLD	382	LGSNRAS	414	MQALQTPYT	443
BCMA-4	KSSQSLLRNDGKT PLY	383	EVSNRFS	415	MQNIQFPS	444
BCMA-5	RSSQSLLHSNGYN YLN	384	LGSKRAS	416	MQALQTPYT	443
BCMA-6	RASQSISSYLN	380	GASTLAS	417	QQSYKRAS	445
BCMA-7	RSSQSLLYSNGYN YVD	385	LGSNRAS	414	MQGRQFPYS	446
BCMA-8	RASQSVSSNLA	386	GASTRAS	418	QQYGSSLT	447
BCMA-9	RASQSVSSKLA	387	GASIRAT	419	QQYGSSSWT	448
BCMA-10	RASQSVGSTNLA	388	DASNRAT	158	QQYGSSPPWT	449
BCMA-11	RASQSISSYLN	380	AASSLQS	412	QQSYTLA	450
BCMA-12	KSSQSLVHNSGKT YLN	389	EVSNRDS	420	MQGTHWPGT	451
BCMA-13	QASEDINKFLN	390	DASTLQT	421	QQYESLPLT	452
BCMA-14	RASQSVGSNLA	391	GASTRAT	422	QQYNDWLPVT	453
BCMA-15	RASQSIGSSSLA	392	GASSRAS	423	QQYAGSPFPT	454
BCMA-16	KASQDIDDAMN	393	SATSPVP	424	LQHDNFPLT	455
BCMA-17	RASQDIYNNLA	394	AANKSQS	425	QHYYRFPYS	456
BCMA-18	RSSQSLLHSNGYN YLD	382	LGSNRAS	414	MQALQTPYT	443
BCMA-19	GGNNIGTKSVH	395	DDSVRPS	426	QVWDSSEHVV	457
BCMA-20	SGDGLSKKYVS	396	RDKERPS	427	QAWDDTTVV	458
BCMA-21	RASQGIRNWLA	397	AASNLSQS	428	QKYNAPFT	459
BCMA-22	GGNNIGSKSVH	398	GKNNRPS	429	SSRDSSGDHLRV	460
BCMA-23	QGDSLGNYYAT	399	GTNNRPS	430	NSRDSSGHLL	461
BCMA-24	RASQSVSSAYLA	400	GASTRAT	422	QHYGSSFNSSL FT	462
BCMA-25	RASQSVSNSLA	401	DASSRAT	431	QQFGTSSGLT	463
BCMA-26	RASQSVSSSFLA	402	GASSRAT	432	QQYHSSPSWT	442
BCMA-27	RASQSVSTTFLA	403	GSSNRAT	433	QQYHSSPSWT	442
BCMA-28	RASQSISSYLN	380	AASSLQS	412	QQSYSTPYS	464
BCMA-29	RATQSIGSSFLA	404	GASQRAT	434	QHYESSPSWT	465
BCMA-30	RASQSVSSSYLA	405	GASSRAT	432	QQYGSPPRFT	466
BCMA-31	RASQSVSSSYLA	405	GASSRAT	432	QHYGSSPSWT	467
BCMA-32	RASQSVASNYLA	406	GASSRAT	432	QHYDSSPSWT	468
BCMA-33	RASQSLSSNFLA	407	GASNWAT	435	QYYGTSPMYT	469
BCMA-34	RSSQSLLHSNGYN YLD	382	LGSNRAS	414	MQALQTPLT	470
BCMA-35	RASQSVSSSYLA	405	GTSSRAT	436	QHYGNPPKFT	471
BCMA-36	RASQSVASSFLA	408	GASGRAT	437	QHYGGSPRLT	472
BCMA-37	RASQDVNTAVS	409	SASYRYT	438	QQHYSTPWT	473
BCMA-38	RASESVSVIGAHLI H	410	LASNLET	439	LQSRIFPRT	474
BCMA-39	RASESVTILGSHLI	411	LASNVQT	440	LQSRTIPRT	475

TABLE 12D						
BCMA Binders – Light chain CDR sequences according to combination of Kabat and Chothia numbering schemes						
	Y					
BCMA-40	RASESVTILGSHLI Y	411	LASNVQT	440	LQSRTIPRT	475

TABLE 12E						
BCMA Binders – Heavy chain CDR sequences according to Kabat numbering scheme						
Antibody	CDR-H1	SEQ ID NO:	CDR-H2	SEQ ID NO:	CDR-H3	SEQ ID NO:
BCMA-1	NHGMS	554	GIVYSGSTYYAASVK G	573	HGGESDV	595
BCMA-2	NYAMS	555	GISRSGENTYYADSV KG	574	SPAHHYYGGMDV	596
BCMA-3	DYAMH	556	GISWNSGSIGYADSV KG	575	HSFLAY	597
BCMA-4	NHGMS	554	GIVYSGSTYYAASVK G	573	HGGESDV	595
BCMA-5	NFGIN	557	WINPKNNNTNYAQKF QG	576	GPYYYQSYMDV	598
BCMA-6	SDAMT	558	VISGSGGTTYADSV KG	577	LDSSGYYYARGPR Y	599
BCMA-7	NYGIT	559	WISAYNGNTNYAQKF QG	578	GPYYYYMDV	600
BCMA-8	NHGMS	554	GIVYSGSTYYAASVK G	573	HGGESDV	595
BCMA-9	NHGMS	554	GIVYSGSTYYAASVK G	573	HGGESDV	595
BCMA-10	NHGMS	554	GIVYSGSTYYAASVK G	573	HGGESDV	595
BCMA-11	DYYMS	560	YISSSGSTIYYADSVK G	579	ESGDGMDV	601
BCMA-12	DYYMS	560	YISSSGNTIYYADSVK G	580	STMVREDY	602
BCMA-13	NHGMS	554	GIVYSGSTYYAASVK G	573	HGGESDV	595
BCMA-14	NHGMS	554	GIVYSGSTYYAASVK G	573	HGGESDV	595
BCMA-15	NHGMS	554	GIVYSGSTYYAASVK G	573	HGGESDV	595
BCMA-16	SSYYYW G	561	SIYYSGSAYYNPSLKS	581	HWQEWPAFDI	603
BCMA-17	TSGMCV S	562	RIDWDEDKFYSTSLK T	582	SGAGGTSATAFDI	604
BCMA-18	SYSMN	563	SISSSSYIYYADSVK G	583	TIAAVYAFDI	605
BCMA-19	DYYMS	560	YISSSGSTIYYADSVK G	579	DLRGAFDI	606
BCMA-20	SHYIH	564	MINPSGGVTAYSQTL QG	584	EGSGSGWYFDF	607
BCMA-21	SGGYW	565	YIYYSGSTYYNPSLKS	585	AGIAARLRGAFDI	608

TABLE 12E						
BCMA Binders – Heavy chain CDR sequences according to Kabat numbering scheme						
	S					
BCMA-22	SYAIS	566	GIIPFGTANYAQKFQ G	586	RGGYQLLRWDVG LLRSAFDI	609
BCMA-23	SNSAAW N	567	RTYYRSKWYSFYAISL KS	587	SSPEGLFLYWFDV	610
BCMA-24	SYAMS	568	AISGSGGSTYYADSV KG	588	VEGSGSLDY	611
BCMA-25	RYPMS	569	GISDSGVSTYYADSA KG	589	RAGSEASDI	612
BCMA-26	SYAMS	568	AISGSGGSTYYADSV KG	588	ATYKRELRYYYGM DV	613
BCMA-27	SYAMS	568	AISGSGGSTYYADSV KG	588	ATYKRELRYYYGM DV	613
BCMA-28	DYAMH	556	GISWNSGSIGYADSV KG	575	VGKAVPDV	614
BCMA-29	DYAMH	556	SINWKGNSLAYGDSV KG	590	HQGVAYYNYAMD V	615
BCMA-30	SYAMS	568	AISGSGGSTYYADSV KG	588	VVRDGMDV	616
BCMA-31	SYAMS	568	AISGSGGSTYYADSV KG	588	IPQTGTFDY	617
BCMA-32	SYAMS	568	AISGSGGSTYYADSV KG	588	ANYKRELRYYYGM DV	618
BCMA-33	SYAMS	568	AISGSGGSTYYADSV KG	588	ALVGATGAFDI	619
BCMA-34	SYAMS	568	AISGSGGSTYYADSV KG	588	WFGEGFDP	620
BCMA-35	SYAMS	568	AISGSGGSTYYADSV KG	588	VGVDSSGYRDY GMDV	621
BCMA-36	SYAMS	568	AISGSGGSTYYADSV KG	588	MGWSSGYLGAFDI	622
BCMA-37	NFGMN	570	WINTYTGESYFADDF KG	591	GEIYYGYDGGFAY	623
BCMA-38	DYSIN	571	WINTETREPAYAYDF RG	592	DYSYAMDY	624
BCMA-39	HYSMN	572	RINTESGVPIYADDFK G	593	DYLYSLDF	625
BCMA-40	HYSMN	572	RINTETGEPLYADDFK G	594	DYLYSCDY	626

TABLE 12F						
BCMA Binders – Heavy chain CDR sequences according to Chothia numbering scheme						
Antibody	CDR-H1	SEQ ID NO:	CDR-H2	SEQ ID NO:	CDR-H3	SEQ ID NO:
BCMA-1	GFALSNH	627	VYSGS	647	HGGESDV	595
BCMA-2	GFTFSNY	628	SRSGEN	648	SPAHYYGGMDV	596
BCMA-3	GFTFDDY	629	SWNSGS	649	HSFLAY	597

TABLE 12F						
BCMA Binders – Heavy chain CDR sequences according to Chothia numbering scheme						
Antibody	CDR-H1	SEQ ID NO:	CDR-H2	SEQ ID NO:	CDR-H3	SEQ ID NO:
BCMA-4	GFALSNH	627	VYSGS	647	HGGESDV	595
BCMA-5	GYIFDNF	630	NPKNNN	650	GPYYYQSYMDV	598
BCMA-6	GFTFSSD	631	SGSGGT	651	LDSSGYYYARGPRY	599
BCMA-7	GYTFSNY	632	SAYNGN	652	GPYYYMDV	600
BCMA-8	GFALSNH	627	VYSGS	647	HGGESDV	595
BCMA-9	GFALSNH	627	VYSGS	647	HGGESDV	595
BCMA-10	GFALSNH	627	VYSGS	647	HGGESDV	595
BCMA-11	GFTFSDY	633	SSSGST	653	ESGDGMDV	601
BCMA-12	GFTFSDY	633	SSSGNT	654	STMVREDY	602
BCMA-13	GFALSNH	627	VYSGS	647	HGGESDV	595
BCMA-14	GFALSNH	627	VYSGS	647	HGGESDV	595
BCMA-15	GFALSNH	627	VYSGS	647	HGGESDV	595
BCMA-16	GGSISSS YY	634	YYSGS	655	HWQEWPAFDI	603
BCMA-17	GFSLRTS GM	635	DWDED	656	SGAGGTSATAFDI	604
BCMA-18	GFTFSSY	636	SSSSSY	657	TIAAVYAFDI	605
BCMA-19	GFTFSDY	633	SSSGST	653	DLRGAFDI	606
BCMA-20	GYTVTSH	637	NPSGGV	658	EGSGSGWYFDF	607
BCMA-21	GGSISSG GY	638	YYSGS	655	AGIAARLRGAFDI	608
BCMA-22	GGTFSSY	639	IPIFGT	659	RGGYQLLRWDVGLLR AFDI	609
BCMA-23	GDSVSSN SA	640	YYRSKWY	660	SSPEGLFLYWFDV	610
BCMA-24	GFTFSSY	636	SGSGGS	661	VEGSGSLDY	611
BCMA-25	GITFSRY	641	SDSGVS	662	RAGSEASDI	612
BCMA-26	GFTFSSY	636	SGSGGS	661	ATYKRELRYYYGMDV	613
BCMA-27	GFTFSSY	636	SGSGGS	661	ATYKRELRYYYGMDV	613
BCMA-28	GFTFDDY	629	SWNSGS	649	VGKAVPDV	614

TABLE 12F						
BCMA Binders – Heavy chain CDR sequences according to Chothia numbering scheme						
Antibody	CDR-H1	SEQ ID NO:	CDR-H2	SEQ ID NO:	CDR-H3	SEQ ID NO:
BCMA-29	GFTFDDY	629	NWKGNS	663	HQGVAYYNYAMDV	615
BCMA-30	GFTFSSY	636	SGSGGS	661	VVRDGMMDV	616
BCMA-31	GFTFSSY	636	SGSGGS	661	IPQTGTFDY	617
BCMA-32	GFTFSSY	636	SGSGGS	661	ANYKRELRYYYGMDV	618
BCMA-33	GFSFSSY	642	SGSGGS	661	ALVGATGAFDI	619
BCMA-34	GFTFSSY	636	SGSGGS	661	WFGEGFDP	620
BCMA-35	GFTFSSY	636	SGSGGS	661	VGYDSSGYRDIYGM V	621
BCMA-36	GFTFSSY	636	SGSGGS	661	MGWSSGYLGAFDI	622
BCMA-37	GYTFTNF	643	NTYTGE	664	GEIYYGYDGGFAY	623
BCMA-38	GYTFTDY	644	NTETRE	665	DYSYAMDY	624
BCMA-39	GYTFRHY	645	NTESGV	666	DYLYSLDF	625
BCMA-40	GYTFTHY	646	NTETGE	667	DYLYSCDY	626

TABLE 12G						
BCMA Binders – Heavy chain CDR sequences according to combination of Kabat and Chothia numbering schemes						
Antibody	CDR-H1	SEQ ID NO:	CDR-H2	SEQ ID NO:	CDR-H3	SEQ ID NO:
BCMA-1	GFALSNHG MS	668	GIVYSGSTYYAAS VKG	573	HGGESDV	595
BCMA-2	GFTFSNYA MS	669	GISRSGENTYYAD SVKG	574	SPAHYYGGMDV	596
BCMA-3	GFTFDDYA MH	670	GISWNSGSIGYAD SVKG	575	HSFLAY	597
BCMA-4	GFALSNHG MS	668	GIVYSGSTYYAAS VKG	573	HGGESDV	595
BCMA-5	GYIFDNFGI N	671	WINPKNNNTNYA QKFQG	576	GPYYYQSYMDV	598
BCMA-6	GFTFSSDA MT	672	VISGSGGTTYAD SVKG	577	LDSSGYYYARGPR Y	599
BCMA-7	GYTFSNYG	673	WISAYNGNTNYA	578	GPYYYYMDV	600

TABLE 12G						
BCMA Binders – Heavy chain CDR sequences according to combination of Kabat and Chothia numbering schemes						
Antibody	CDR-H1	SEQ ID NO:	CDR-H2	SEQ ID NO:	CDR-H3	SEQ ID NO:
	IT		QKFQG			
BCMA-8	GFALSNHG MS	668	GIVYSGSTYYAAS VKG	573	HGGESDV	595
BCMA-9	GFALSNHG MS	668	GIVYSGSTYYAAS VKG	573	HGGESDV	595
BCMA-10	GFALSNHG MS	668	GIVYSGSTYYAAS VKG	573	HGGESDV	595
BCMA-11	GFTFSDYY MS	674	YISSSGSTIYYADS VKG	579	ESGDGMDV	601
BCMA-12	GFTFSDYY MS	674	YISSSGNTIYYAD SVKG	580	STMVREDY	602
BCMA-13	GFALSNHG MS	668	GIVYSGSTYYAAS VKG	573	HGGESDV	595
BCMA-14	GFALSNHG MS	668	GIVYSGSTYYAAS VKG	573	HGGESDV	595
BCMA-15	GFALSNHG MS	668	GIVYSGSTYYAAS VKG	573	HGGESDV	595
BCMA-16	GGSISSSY YYWG	675	SIYYSGSAYYNPS LKS	581	HWQEWPAFDI	603
BCMA-17	GFSLRTSG MCVS	676	RIDWDEDKFYSTS LKT	582	SGAGGTSATAFDI	604
BCMA-18	GFTFSSYS MN	677	SISSSSSYIYYADS VKG	583	TIAAVYAFDI	605
BCMA-19	GFTFSDYY MS	674	YISSSGSTIYYADS VKG	579	DLRGAFDI	606
BCMA-20	GYTVTSHYI H	678	MINPSGGVTAYS QTLQG	584	EGSGSGWYFDF	607
BCMA-21	GGSISSGG YYWS	679	YIYYSGSTYYNPS LKS	585	AGIAARLRGAFDI	608
BCMA-22	GGTFSSYAI S	680	GIPIFGTANYAQK FQG	586	RGGYQLLRWDVGL LRSAFDI	609
BCMA-23	GDSVSSNS AAWN	681	RTYYRSKWYSFY AISLKS	587	SSPEGLFLYWFD P	610

TABLE 12G						
BCMA Binders – Heavy chain CDR sequences according to combination of Kabat and Chothia numbering schemes						
Antibody	CDR-H1	SEQ ID NO:	CDR-H2	SEQ ID NO:	CDR-H3	SEQ ID NO:
BCMA-24	GFTFSSYA MS	682	AISGSGGSTYYAD SVKG	588	VEGSGSLDY	611
BCMA-25	GITFSRYP MS	683	GISDSGVSTYYAD SAKG	589	RAGSEASDI	612
BCMA-26	GFTFSSYA MS	682	AISGSGGSTYYAD SVKG	588	ATYKRELRYYYGM DV	613
BCMA-27	GFTFSSYA MS	682	AISGSGGSTYYAD SVKG	588	ATYKRELRYYYGM DV	613
BCMA-28	GFTFDDYA MH	670	GISWNSGSIGYAD SVKG	575	VGKAVPDV	614
BCMA-29	GFTFDDYA MH	670	SINWKGNLAYG DSVKG	590	HQGVAYYNYAMDV	615
BCMA-30	GFTFSSYA MS	682	AISGSGGSTYYAD SVKG	588	VVRDGM DV	616
BCMA-31	GFTFSSYA MS	682	AISGSGGSTYYAD SVKG	588	IPQTGTFDY	617
BCMA-32	GFTFSSYA MS	682	AISGSGGSTYYAD SVKG	588	ANYKRELRYYYGM DV	618
BCMA-33	GFSFSSYA MS	684	AISGSGGSTYYAD SVKG	588	ALVGATGAFDI	619
BCMA-34	GFTFSSYA MS	682	AISGSGGSTYYAD SVKG	588	WFGEGFDP	620
BCMA-35	GFTFSSYA MS	682	AISGSGGSTYYAD SVKG	588	VGYDSSGYRDYY GMDV	621
BCMA-36	GFTFSSYA MS	682	AISGSGGSTYYAD SVKG	588	MGWSSGYLGAFDI	622
BCMA-37	GYTFTNFG MN	685	WINTYTGESYFAD DFKG	591	GEIYYGYDGGFAY	623
BCMA-38	GYTFTDYSI N	686	WINTETREPAYAY DFRG	592	DYSYAMDY	624
BCMA-39	GYTFRHYS MN	687	RINTESGVPIYAD DFKG	593	DYLYSLDF	625
BCMA-40	GYTFTHYS MN	688	RINTETGEPLYAD DFKG	594	DYLYSCDY	626

[illegible]

[0370] In some embodiments, the CDRs are defined by Kabat numbering, as set forth in Table 12B and 10E. In other embodiments, the CDRs are defined by Chothia numbering, as set forth in Table 12C and 10F. In yet other embodiments, the CDRs are defined by a combination of Kabat and Chothia numbering, as set forth in Table 12D and 10G.

[0371] In some embodiments, the TBMs comprising a ABM that binds to BCMA can comprise the heavy and light chain variable sequences of any of BCMA-1 to BCMA-40.

[0372] In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-1, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-2, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-3, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-4, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-5, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-6, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-7, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-8, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-9, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-10, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-11, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-12, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-13, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-14, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-15, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-16, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-17, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-18, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-19, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-20, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-21, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-22, as set forth in Table 12A.

In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-23, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-24, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-25, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-26, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-27, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-28, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-29, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-30, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-31, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-32, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-33, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-34, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-35, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-36, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-37, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-38, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-39, as set forth in Table 12A. In some embodiments, the ABM comprises the heavy and light chain variable sequences of BCMA-40, as set forth in Table 12A.

6.7.2. CD19

[0373] B cells express cell surface proteins which can be utilized as markers for differentiation and identification. One such human B-cell marker is a CD19 antigen and is found on mature B cells but not on plasma cells. CD19 is expressed during early pre-B cell development and remains until plasma cell differentiation. CD19 is expressed on both normal B cells and malignant B cells whose abnormal growth can lead to B-cell lymphomas. For example, CD19 is expressed on B-cell lineage malignancies, including, but not limited to non-Hodgkin's lymphoma (B-NHL), chronic lymphocytic leukemia, and acute lymphoblastic leukemia.

[0374] In certain aspects, a TBM of the disclosure comprises an ABM3 that specifically binds to CD19. Exemplary CDR and variable domain sequences that can be incorporated into an ABM3 that specifically binds to CD19 are set forth in Table 13 below

TABLE 13 CD19 Binders			
Name	Domain	Sequence	SEQ ID NO:
CD19-H1	CDR-H1	DYGVS	689
CD19-H2A	CDR-H2	VIWGSETTYNSALKS	690
CD19-H2B	CDR-H2	VIWGSETTYSSSLKS	691
CD19-H2C	CDR-H2	VIWGSETTYQSSLKS	692
CD19-H2D	CDR-H2	VIWGSETTYNSSLKS	693
CD19-H3	CDR-H3	HYYYGGSYAMDY	694
CD19-L1	CDR-L1	RASQDISKYLN	695
CD19-L2	CDR-L2	HTSRLHS	696
CD19-L3	CDR-L3	QQGNTLPYT	697
CD19-VHA	VH	EVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPRKGLEWLGVIWGSETTYNSALKSRLTIKDNSK SQVFLKMNSLQTD DTAIYYCAKHYYYGGSYAMDYWG QGTSVTVSS	698
CD19-VHB	VH	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYSSSLKSRVTISKDNSKN QVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQ GTLVTVSS	699
CD19-VHC	VH	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYQSSLKSRVTISKDNSKN QVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQ GTLVTVSS	700
CD19-VHD	VH	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYNSSLKSRVTISKDNSKN QVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQ GTLVTVSS	701
CD19-VLA	VL	DIQMTQTTSLSASLGDRVTISCRASQDISKYLNWYQQ KPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISN LEQEDIATYFCQQGNTLPYTFGGGGTKLEIT	702
CD19-VLB	VL	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQ KPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISS LQPEDFAVYFCQQGNTLPYTFGQGTKLEIK	703
CD19-scFv1	scFv	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQ KPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISS LQPEDFAVYFCQQGNTLPYTFGQGTKLEIKGGGGSGG GSGGGGSQVQLQESGPGLVKPSETLSLTCTVSGVSL PDYGVSWIRQPPGKGLEWIGVIWGSETTYSSSLKSR VTISKDNSKNQVSLKLSSVTAADTAVYYCAKHYYYGGS	704

TABLE 13 CD19 Binders			
Name	Domain	Sequence	SEQ ID NO:
		YAMDYWGQGTLVTVSS	
CD19-scFv2	scFv	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQ KPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISS LQPEDFAVYFCQQGNTLPYTFGQGTKLEIKGGGGSGG GGSGGGGSQVQLQESGPGLVKPSSETLSLTCTVSGVSL PDYGVSWIRQPPGKGLEWIGVIWGSETTYQSSLSR VTISKDNSKNQVSLKLSSVTAADTAVYYCAKHYYYGGS YAMDYWGQGTLVTVSS	705
CD19-scFv3	scFv	QVQLQESGPGLVKPSSETLSLTCTVSGVSLPDYGVSWIR QPPGKGLEWIGVIWGSETTYSSSLKSRVTISKDNSKN QVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQ GTLVTVSSGGGGSGGGSGGGGSEIVMTQSPATLSLS PGERATLSCRASQDISKYLNWYQQKPGQAPRLLIYHTS RLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQ GNTLPYTFGQGTKLEIK	706
CD19-scFv4	scFv	QVQLQESGPGLVKPSSETLSLTCTVSGVSLPDYGVSWIR QPPGKGLEWIGVIWGSETTYQSSLSKSRVTISKDNSKN QVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQ GTLVTVSSGGGGSGGGSGGGGSEIVMTQSPATLSLS PGERATLSCRASQDISKYLNWYQQKPGQAPRLLIYHTS RLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQ GNTLPYTFGQGTKLEIK	707
CD19-scFv5	scFv	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQ KPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISS LQPEDFAVYFCQQGNTLPYTFGQGTKLEIKGGGGSGG GGSGGGGSQVQLQESGPGLVKPSSETLSLTCT VSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYYS SSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCAKH YYYGGSYAMDYWGQGTLVTVSS	708
CD19-scFv6	scFv	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQ KPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISS LQPEDFAVYFCQQGNTLPYTFGQGTKLEIKGGGGSGG GGSGGGGSQVQLQESGPGLVKPSSETLSLTCT VSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYQ SSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCAKH YYYGGSYAMDYWGQGTLVTVSS	709
CD19-scFv7	scFv	QVQLQESGPGLVKPSSETLSLTCTVSGVSLPDYGVSWIR QPPGKGLEWIGVIWGSETTYSSSLKSRVTISKDNSKN QVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQ GTLVTVSSGGGGSGGGSGGGGSGGGGSEIVMTQS PATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAP RLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDF AVYFCQQGNTLPYTFGQGTKLEIK	710

TABLE 13 CD19 Binders			
Name	Domain	Sequence	SEQ ID NO:
CD19-scFv8	scFv	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIR QPPGKGLEWIGVIWGSETTYQSSLSKSRVTISKDNSKN QVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQ GTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVMTQS PATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAP RLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDF AVYFCQQGNTLPYTFGQGGTKLEIK	711
CD19-scFv9	scFv	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQ KPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISS LQPEDFAVYFCQQGNTLPYTFGQGGTKLEIKGGGGSGG GGSGGGGSGGGGSGVQLQESGPGLVKPSETLSLTCT VSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYN SSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCAKH YYYGGSYAMDYWGQGTLVTVSS	712
CD19-scFv10	scFv	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIR QPPGKGLEWIGVIWGSETTYNSSLKSRVTISKDNSKN QVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQ GTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVMTQS PATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAP RLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDF AVYFCQQGNTLPYTFGQGGTKLEIK	713
CD19-scFv11	scFv	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQ KPGQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISS LQPEDFAVYFCQQGNTLPYTFGQGGTKLEIKGGGGSGG GGSGGGGSGVQLQESGPGLVKPSETLSLTCTVSGVSL PDYGVSWIRQPPGKGLEWIGVIWGSETTYNSSLKSR VTISKDNSKNQVSLKLSSVTAADTAVYYCAKHYYYGG SYAMDYWGQGTLVTVSS	714
CD19-scFv12	scFv	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIR QPPGKGLEWIGVIWGSETTYNSSLKSRVTISKDNSKN QVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQ GTLVTVSSGGGGSGGGGSGGGGSEIVMTQSPATLSL SPGERATLSCRASQDISKYLNWYQQKPGQAPRLLIYHTS RLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQQ GNTLPYTFGQGGTKLEIK	715

[0375] In certain aspects, the ABM3 comprises heavy chain CDRs having the amino acid sequences of CD19-H1, CD19-H2A, and CD19-H3 as set forth in Table 13 and light chain CDRs having the amino acid sequences of CD19-L1, CD19-L2, and CD19-L3 as set forth in

Table 13. In a specific embodiment, the ABM3 comprises a heavy chain variable region having the amino acid sequences of VHA as set forth in Table 13 and a light chain variable region having the amino acid sequences of VLA as set forth in Table 13.

[0376] In other aspects, the ABM3 comprises heavy chain CDRs having the amino acid sequences of CD19-H1, CD19-H2B, and CD19-H3 as set forth in Table 13 and light chain CDRs having the amino acid sequences of CD19-L1, CD19-L2, and CD19-L3 as set forth in Table 13. In a specific embodiment, the ABM3 comprises a heavy chain variable region having the amino acid sequences of VHB as set forth in Table 13 and a light chain variable region having the amino acid sequences of VLB as set forth in Table 13.

[0377] In further aspects, the ABM3 comprises heavy chain CDRs having the amino acid sequences of CD19-H1, CD19-H2C, and CD19-H3 as set forth in Table 13 and light chain CDRs having the amino acid sequences of CD19-L1, CD19-L2, and CD19-L3 as set forth in Table 13. In a specific embodiment, ABM3 comprises a heavy chain variable region having the amino acid sequences of VHC as set forth in Table 13 and a light chain variable region having the amino acid sequences of VLB as set forth in Table 13.

[0378] In further aspects, the ABM3 comprises heavy chain CDRs having the amino acid sequences of CD19-H1, CD19-H2D, and CD19-H3 as set forth in Table 13 and light chain CDRs having the amino acid sequences of CD19-L1, CD19-L2, and CD19-L3 as set forth in Table 13. In a specific embodiment, the ABM3 comprises a heavy chain variable region having the amino acid sequences of VHD as set forth in Table 13 and a light chain variable region having the amino acid sequences of VLB as set forth in Table 13.

[0379] In yet further aspects, the ABM3 is in the form of an scFV. Exemplary anti-CD19 scFvs comprise the amino acid sequence of any one of CD19-scFv1 through CD19-scFv12 as set forth in Table 13.

6.8. Nucleic Acids and Host Cells

[0380] In another aspect, the disclosure provides nucleic acids encoding the TBMs of the disclosure. In some embodiments, the TBMs are encoded by a single nucleic acid. In other embodiments, the TBMs are encoded by a plurality (e.g., two, three, four or more) nucleic acids.

[0381] A single nucleic acid can encode a TBM that comprises a single polypeptide chain, a TBM that comprises two or more polypeptide chains, or a portion of a TBM that comprises more than two polypeptide chains (for example, a single nucleic acid can encode two polypeptide chains of a TBM comprising three, four or more polypeptide chains, or three polypeptide chains of a TBM comprising four or more polypeptide chains). For separate control of expression, the open reading frames encoding two or more polypeptide chains can be under the control of

separate transcriptional regulatory elements (*e.g.*, promoters and/or enhancers). The open reading frames encoding two or more polypeptides can also be controlled by the same transcriptional regulatory elements, and separated by internal ribosome entry site (IRES) sequences allowing for translation into separate polypeptides.

[0382] In some embodiments, a TBM comprising two or more polypeptide chains is encoded by two or more nucleic acids. The number of nucleic acids encoding a TBM can be equal to or less than the number of polypeptide chains in the TBM (for example, when more than one polypeptide chains are encoded by a single nucleic acid).

[0383] The nucleic acids of the disclosure can be DNA or RNA (*e.g.*, mRNA).

[0384] In another aspect, the disclosure provides host cells and vectors containing the nucleic acids of the disclosure. The nucleic acids may be present in a single vector or separate vectors present in the same host cell or separate host cell, as described in more detail herein below.

6.8.1. Vectors

[0385] The disclosure provides vectors comprising nucleotide sequences encoding a TBM or a TBM component described herein. In one embodiment, the vectors comprise nucleotides encoding an immunoglobulin-based ABM described herein. In one embodiment, the vectors comprise nucleotides encoding an Fc domain described herein. In one embodiment, the vectors comprise nucleotides encoding a recombinant non-immunoglobulin based ABM described herein. A vector of the disclosure can encode one or more ABMs, one or more Fc domains, one or more non-immunoglobulin based ABM, or a combination thereof (*e.g.*, when multiple components or sub-components are encoded as a single polypeptide chain). In one embodiment, the vectors comprise the nucleotide sequences described herein. The vectors include, but are not limited to, a virus, plasmid, cosmid, lambda phage or a yeast artificial chromosome (YAC).

[0386] Numerous vector systems can be employed. For example, one class of vectors utilizes DNA elements which are derived from animal viruses such as, for example, bovine papilloma virus, polyoma virus, adenovirus, vaccinia virus, baculovirus, retroviruses (Rous Sarcoma Virus, MMTV or MOMLV) or SV40 virus. Another class of vectors utilizes RNA elements derived from RNA viruses such as Semliki Forest virus, Eastern Equine Encephalitis virus and Flaviviruses.

[0387] Additionally, cells which have stably integrated the DNA into their chromosomes may be selected by introducing one or more markers which allow for the selection of transfected host cells. The marker may provide, for example, prototrophy to an auxotrophic host, biocide resistance (*e.g.*, antibiotics), or resistance to heavy metals such as copper, or the like. The selectable marker gene can be either directly linked to the DNA sequences to be expressed, or introduced into the same cell by cotransformation. Additional elements may also be needed for

optimal synthesis of mRNA. These elements may include splice signals, as well as transcriptional promoters, enhancers, and termination signals.

[0388] Once the expression vector or DNA sequence containing the constructs has been prepared for expression, the expression vectors may be transfected or introduced into an appropriate host cell. Various techniques may be employed to achieve this, such as, for example, protoplast fusion, calcium phosphate precipitation, electroporation, retroviral transduction, viral transfection, gene gun, lipid based transfection or other conventional techniques. Methods and conditions for culturing the resulting transfected cells and for recovering the expressed polypeptides are known to those skilled in the art, and may be varied or optimized depending upon the specific expression vector and mammalian host cell employed, based upon the present description.

6.8.2. Cells

[0389] The disclosure also provides host cells comprising a nucleic acid of the disclosure.

[0390] In one embodiment, the host cells are genetically engineered to comprise one or more nucleic acids described herein.

[0391] In one embodiment, the host cells are genetically engineered by using an expression cassette. The phrase "expression cassette," refers to nucleotide sequences, which are capable of affecting expression of a gene in hosts compatible with such sequences. Such cassettes may include a promoter, an open reading frame with or without introns, and a termination signal. Additional factors necessary or helpful in effecting expression may also be used, such as, for example, an inducible promoter.

[0392] The disclosure also provides host cells comprising the vectors described herein.

[0393] The cell can be, but is not limited to, a eukaryotic cell, a bacterial cell, an insect cell, or a human cell. Suitable eukaryotic cells include, but are not limited to, Vero cells, HeLa cells, COS cells, CHO cells, HEK293 cells, BHK cells and MDCKII cells. Suitable insect cells include, but are not limited to, Sf9 cells.

6.9. Antibody-Drug Conjugates

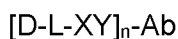
[0394] The TBMs of the disclosure can be conjugated, *e.g.*, via a linker, to a drug moiety. Such conjugates are referred to herein as antibody-drug conjugates (or "ADCs") for convenience, notwithstanding the fact that one or more (or all) of the ABMs might be based on non-immunoglobulin scaffolds.

[0395] In certain aspects, the drug moiety exerts a cytotoxic or cytostatic activity. In one embodiment, the drug moiety is chosen from a maytansinoid, a kinesin-like protein KIF11 inhibitor, a V-ATPase (vacuolar-type H⁺-ATPase) inhibitor, a pro-apoptotic agent, a Bcl2 (B-cell lymphoma 2) inhibitor, an MCL1 (myeloid cell leukemia 1) inhibitor, a HSP90 (heat shock

protein 90) inhibitor, an IAP (inhibitor of apoptosis) inhibitor, an mTOR (mechanistic target of rapamycin) inhibitor, a microtubule stabilizer, a microtubule destabilizer, an auristatin, a dolastatin, a MetAP (methionine aminopeptidase), a CRM1 (chromosomal maintenance 1) inhibitor, a DPPIV (dipeptidyl peptidase IV) inhibitor, a proteasome inhibitor, an inhibitor of a phosphoryl transfer reaction in mitochondria, a protein synthesis inhibitor, a kinase inhibitor, a CDK2 (cyclin-dependent kinase 2) inhibitor, a CDK9 (cyclin-dependent kinase 9) inhibitor, a kinesin inhibitor, an HDAC (histone deacetylase) inhibitor, a DNA damaging agent, a DNA alkylating agent, a DNA intercalator, a DNA minor groove binder, a RNA polymerase inhibitor, a topoisomerase inhibitor, or a DHFR (dihydrofolate reductase) inhibitor.

[0396] In one embodiment, the linker is chosen from a cleavable linker, a non-cleavable linker, a hydrophilic linker, a procharged linker, or a dicarboxylic acid based linker.

[0397] In specific embodiments, the ADCs are compounds according to structural formula (I):



or salts thereof, where each “D” represents, independently of the others, a cytotoxic and/or cytostatic agent (“drug”); each “L” represents, independently of the others, a linker; “Ab” represents a TBM described herein; each “XY” represents a linkage formed between a functional group R^x on the linker and a “complementary” functional group R^y on the antibody, and n represents the number of drugs linked to, or drug-to-antibody ratio (DAR), of the ADC.

[0398] Specific embodiments of the various antibodies (Ab) that can comprise the ADCs include the various embodiments of TBMs described above.

[0399] In some specific embodiments of the ADCs and/or salts of structural formula (I), each D is the same and/or each L is the same.

[0400] Specific embodiments of cytotoxic and/or cytostatic agents (D) and linkers (L) that can comprise the ADCs of the disclosure, as well as the number of cytotoxic and/or cytostatic agents linked to the ADCs, are described in more detail below.

6.9.1. Cytotoxic and/or Cytostatic Agents

[0401] The cytotoxic and/or cytostatic agents may be any agents known to inhibit the growth and/or replication of and/or kill cells, and in particular cancer and/or tumor cells. Numerous agents having cytotoxic and/or cytostatic properties are known in the literature. Non-limiting examples of classes of cytotoxic and/or cytostatic agents include, by way of example and not limitation, radionuclides, alkylating agents, topoisomerase I inhibitors, topoisomerase II inhibitors, DNA intercalating agents (e.g., groove binding agents such as minor groove binders), RNA/DNA antimetabolites, cell cycle modulators, kinase inhibitors, protein synthesis inhibitors, histone deacetylase inhibitors, mitochondria inhibitors, and antimitotic agents.

[0402] Specific non-limiting examples of agents within certain of these various classes are provided below.

[0403] Alkylating Agents: asaley ((L-Leucine, N-[N-acetyl-4-[bis-(2-chloroethyl)amino]-DL-phenylalanyl]-, ethylester; NSC 167780; CAS Registry No. 3577897)); AZQ ((1,4-cyclohexadiene-1,4-dicarbamic acid, 2,5-bis(1-aziridinyl)-3,6-dioxo-, diethyl ester; NSC 182986; CAS Registry No. 57998682)); BCNU ((N,N'-Bis(2-chloroethyl)-N-nitrosourea; NSC 409962; CAS Registry No. 154938)); busulfan (1,4-butanediol dimethanesulfonate; NSC 750; CAS Registry No. 55981); (carboxyphthalato)platinum (NSC 27164; CAS Registry No. 65296813); CBDCA ((cis-(1,1-cyclobutanedicarboxylato)diammineplatinum(II)); NSC 241240; CAS Registry No. 41575944)); CCNU ((N-(2-chloroethyl)-N'-cyclohexyl-N-nitrosourea; NSC 79037; CAS Registry No. 13010474)); CHIP (ipropatin; NSC 256927); chlorambucil (NSC 3088; CAS Registry No. 305033); chlorozotocin ((2-[[[(2-chloroethyl) nitrosoamino]carbonyl]amino]-2-deoxy-D-glucopyranose; NSC 178248; CAS Registry No. 54749905)); cis-platinum (cisplatin; NSC 119875; CAS Registry No. 15663271); clomesone (NSC 338947; CAS Registry No. 88343720); cyanomorpholinodoxorubicin (NCS 357704; CAS Registry No. 88254073); cyclodisone (NSC 348948; CAS Registry No. 99591738); dianhydrogalactitol (5,6-diepoxydulcitol; NSC 132313; CAS Registry No. 23261203); fluorodopan ((5-[(2-chloroethyl)-(2-fluoroethyl)amino]-6-methyl-uracil; NSC 73754; CAS Registry No. 834913); hepsulfam (NSC 329680; CAS Registry No. 96892578); hycanthone (NSC 142982; CAS Registry No. 23255938); melphalan (NSC 8806; CAS Registry No. 3223072); methyl CCNU ((1-(2-chloroethyl)-3-(trans-4-methylcyclohexane)-1-nitrosourea; NSC 95441; 13909096); mitomycin C (NSC 26980; CAS Registry No. 50077); mitozolamide (NSC 353451; CAS Registry No. 85622953); nitrogen mustard ((bis(2-chloroethyl)methylamine hydrochloride; NSC 762; CAS Registry No. 55867); PCNU ((1-(2-chloroethyl)-3-(2,6-dioxo-3-piperidyl)-1-nitrosourea; NSC 95466; CAS Registry No. 13909029)); piperazine alkylator ((1-(2-chloroethyl)-4-(3-chloropropyl)-piperazine dihydrochloride; NSC 344007)); piperazinedione (NSC 135758; CAS Registry No. 41109802); pipobroman ((N,N-bis(3-bromopropionyl) piperazine; NSC 25154; CAS Registry No. 54911)); porfiromycin (N-methylmitomycin C; NSC 56410; CAS Registry No. 801525); spirohydantoin mustard (NSC 172112; CAS Registry No. 56605164); teroxirone (triglycidylisocyanurate; NSC 296934; CAS Registry No. 2451629); tetraplatin (NSC 363812; CAS Registry No. 62816982); thio-tepa (N,N',N''-tri-1,2-ethanediylthio phosphoramidate; NSC 6396; CAS Registry No. 52244); triethylenemelamine (NSC 9706; CAS Registry No. 51183); uracil nitrogen mustard (desmethylidopan; NSC 34462; CAS Registry No. 66751); Yoshi-864 ((bis(3-mesyloxy propyl)amine hydrochloride; NSC 102627; CAS Registry No. 3458228).

[0404] Topoisomerase I Inhibitors: camptothecin (NSC 94600; CAS Registry No. 7689-03-4); various camptothecin derivatives and analogs (for example, NSC 100880, NSC 603071, NSC 107124, NSC 643833, NSC 629971, NSC 295500, NSC 249910, NSC 606985, NSC 74028,

NSC 176323, NSC 295501, NSC 606172, NSC 606173, NSC 610458, NSC 618939, NSC 610457, NSC 610459, NSC 606499, NSC 610456, NSC 364830, and NSC 606497); morpholinisoxorubicin (NSC 354646; CAS Registry No. 89196043); SN-38 (NSC 673596; CAS Registry No. 86639-52-3).

[0405] Topoisomerase II Inhibitors: doxorubicin (NSC 123127; CAS Registry No. 25316409); amonafide (benzisoquinolinedione; NSC 308847; CAS Registry No. 69408817); m-AMSA ((4'-(9-acridinylamino)-3'-methoxymethanesulfonanilide; NSC 249992; CAS Registry No. 51264143)); anthrapyrazole derivative ((NSC 355644); etoposide (VP-16; NSC 141540; CAS Registry No. 33419420); pyrazoloacridine ((pyrazolo[3,4,5-kl]acridine-2(6H)-propanamine, 9-methoxy-N, N-dimethyl-5-nitro-, monomethanesulfonate; NSC 366140; CAS Registry No. 99009219); bisantrene hydrochloride (NSC 337766; CAS Registry No. 71439684); daunorubicin (NSC 821151; CAS Registry No. 23541506); deoxydoxorubicin (NSC 267469; CAS Registry No. 63950061); mitoxantrone (NSC 301739; CAS Registry No. 70476823); menogaril (NSC 269148; CAS Registry No. 71628961); N,N-dibenzyl daunomycin (NSC 268242; CAS Registry No. 70878512); oxanthrazole (NSC 349174; CAS Registry No. 105118125); rubidazole (NSC 164011; CAS Registry No. 36508711); teniposide (VM-26; NSC 122819; CAS Registry No. 29767202).

[0406] DNA Intercalating Agents: anthramycin (CAS Registry No. 4803274); chicamycin A (CAS Registry No. 89675376); tomaymycin (CAS Registry No. 35050556); DC-81 (CAS Registry No. 81307246); sibiromycin (CAS Registry No. 12684332); pyrrolobenzodiazepine derivative (CAS Registry No. 945490095); SGD-1882 ((S)-2-(4-aminophenyl)-7-methoxy-8-(3-(4(S)-7-methoxy-2-(4-methoxyphenyl)-- 5-oxo-5,11a-dihydro-1H-benzo[e]pyrrolo[1,2-a][1,4]diazepin-8-yl)oxy)propox- y)-1H-benzo[e]pyrrolo[1,2-a][1,4]diazepin-5(11aH)-one); SG2000 (SJG-136; (11aS,11a'S)-8,8'-(propane-1,3-diylbis(oxy))bis(7-methoxy-2-methylene-2,3--dihydro-1H-benzo[e]pyrrolo[1,2-a][1,4]diazepin-5(11aH)-one); NSC 694501; CAS Registry No. 232931576).

[0407] RNA/DNA Antimetabolites: L-alanosine (NSC 153353; CAS Registry No. 59163416); 5-azacytidine (NSC 102816; CAS Registry No. 320672); 5-fluorouracil (NSC 19893; CAS Registry No. 51218); acivicin (NSC 163501; CAS Registry No. 42228922); aminopterin derivative N-[2-chloro-5-[[[(2,4-diamino-5-methyl-6-quinazoliny)methyl]amino]benzoyl-]L-aspartic acid (NSC 132483); aminopterin derivative N-[4-[[[(2,4-diamino-5-ethyl-6-quinazoliny)methyl]amino]benzoyl]L-aspartic acid (NSC 184692); aminopterin derivative N-[2-chloro-4-[[[(2,4-diamino-6-pteridiny)methyl]amino]benzoyl]L-aspartic acid monohydrate (NSC 134033); an antifo ((N^α-(4-amino-4-deoxypteroyl)-N⁷-hemiphthaloyl-L-ornithin- e; NSC 623017)); Baker's soluble antifol (NSC 139105; CAS Registry No. 41191042); dichlorallyl lawsone ((2-(3,3-dichloroallyl)-3-hydroxy-1,4-naphthoquinone; NSC 126771; CAS Registry No.

36417160); brequinar (NSC 368390; CAS Registry No. 96201886); ftorafur ((pro-drug; 5-fluoro-1-(tetrahydro-2-furyl)-uracil; NSC 148958; CAS Registry No. 37076689); 5,6-dihydro-5-azacytidine (NSC 264880; CAS Registry No. 62402317); methotrexate (NSC 740; CAS Registry No. 59052); methotrexate derivative (N-[[4-[[[(2,4-diamino-6-pteridiny]methyl]methylamino]-1-naphthalenyl]carbonyl]L-glutamic acid; NSC 174121); PALA ((N-(phosphonoacetyl)-L-aspartate; NSC 224131; CAS Registry No. 603425565); pyrazofurin (NSC 143095; CAS Registry No. 30868305); trimetrexate (NSC 352122; CAS Registry No. 82952645).

[0408] DNA Antimetabolites: 3-HP (NSC 95678; CAS Registry No. 3814797); 2'-deoxy-5-fluorouridine (NSC 27640; CAS Registry No. 50919); 5-HP (NSC 107392; CAS Registry No. 19494894); α -TGDR (α -2'-deoxy-6-thioguanosine; NSC 71851 CAS Registry No. 2133815); aphidicolin glycinate (NSC 303812; CAS Registry No. 92802822); ara C (cytosine arabinoside; NSC 63878; CAS Registry No. 69749); 5-aza-2'-deoxycytidine (NSC 127716; CAS Registry No. 2353335); β -TGDR (β -2'-deoxy-6-thioguanosine; NSC 71261; CAS Registry No. 789617); cyclocytidine (NSC 145668; CAS Registry No. 10212256); guanazole (NSC 1895; CAS Registry No. 1455772); hydroxyurea (NSC 32065; CAS Registry No. 127071); inosine glycodialdehyde (NSC 118994; CAS Registry No. 23590990); macbecin II (NSC 330500; CAS Registry No. 73341738); pyrazoloimidazole (NSC 51143; CAS Registry No. 6714290); thioguanine (NSC 752; CAS Registry No. 154427); thiopurine (NSC 755; CAS Registry No. 50442).

[0409] Cell Cycle Modulators: silibinin (CAS Registry No. 22888-70-6); epigallocatechin gallate (EGCG; CAS Registry No. 989515); procyanidin derivatives (e.g., procyanidin A1 [CAS Registry No. 103883030], procyanidin B1 [CAS Registry No. 20315257], procyanidin B4 [CAS Registry No. 29106512], arecatannin B1 [CAS Registry No. 79763283]); isoflavones (e.g., genistein [4',5,7-trihydroxyisoflavone; CAS Registry No. 446720], daidzein [4',7-dihydroxyisoflavone, CAS Registry No. 486668]; indole-3-carbinol (CAS Registry No. 700061); quercetin (NSC 9219; CAS Registry No. 117395); estramustine (NSC 89201; CAS Registry No. 2998574); nocodazole (CAS Registry No. 31430189); podophyllotoxin (CAS Registry No. 518285); vinorelbine tartrate (NSC 608210; CAS Registry No. 125317397); cryptophycin (NSC 667642; CAS Registry No. 124689652).

[0410] Kinase Inhibitors: afatinib (CAS Registry No. 850140726); axitinib (CAS Registry No. 319460850); ARRY-438162 (binimetinib) (CAS Registry No. 606143899); bosutinib (CAS Registry No. 380843754); cabozantinib (CAS Registry No. 1140909483); ceritinib (CAS Registry No. 1032900256); crizotinib (CAS Registry No. 877399525); dabrafenib (CAS Registry No. 1195765457); dasatinib (NSC 732517; CAS Registry No. 302962498); erlotinib (NSC 718781; CAS Registry No. 183319699); everolimus (NSC 733504; CAS Registry No.

159351696); fostamatinib (NSC 745942; CAS Registry No. 901119355); gefitinib (NSC 715055; CAS Registry No. 184475352); ibrutinib (CAS Registry No. 936563961); imatinib (NSC 716051; CAS Registry No. 220127571); lapatinib (CAS Registry No. 388082788); lenvatinib (CAS Registry No. 857890392); mubritinib (CAS 366017096); nilotinib (CAS Registry No. 923288953); nintedanib (CAS Registry No. 656247175); palbociclib (CAS Registry No. 571190302); pazopanib (NSC 737754; CAS Registry No. 635702646); pegaptanib (CAS Registry No. 222716861); ponatinib (CAS Registry No. 1114544318); rapamycin (NSC 226080; CAS Registry No. 53123889); regorafenib (CAS Registry No. 755037037); AP 23573 (ridaforolimus) (CAS Registry No. 572924540); INCB018424 (ruxolitinib) (CAS Registry No. 1092939177); ARRY-142886 (selumetinib) (NSC 741078; CAS Registry No. 606143-52-6); sirolimus (NSC 226080; CAS Registry No. 53123889); sorafenib (NSC 724772; CAS Registry No. 475207591); sunitinib (NSC 736511; CAS Registry No. 341031547); tofacitinib (CAS Registry No. 477600752); temsirolimus (NSC 683864; CAS Registry No. 163635043); trametinib (CAS Registry No. 871700173); vandetanib (CAS Registry No. 443913733); vemurafenib (CAS Registry No. 918504651); SU6656 (CAS Registry No. 330161870); CEP-701 (lesaurtinib) (CAS Registry No. 111358884); XL019 (CAS Registry No. 945755566); PD-325901 (CAS Registry No. 391210109); PD-98059 (CAS Registry No. 167869218); ATP-competitive TORC1/TORC2 inhibitors including PI-103 (CAS Registry No. 371935749), PP242 (CAS Registry No. 1092351671), PP30 (CAS Registry No. 1092788094), Torin 1 (CAS Registry No. 1222998368), LY294002 (CAS Registry No. 154447366), XL-147 (CAS Registry No. 934526893), CAL-120 (CAS Registry No. 870281348), ETP-45658 (CAS Registry No. 1198357797), PX 866 (CAS Registry No. 502632668), GDC-0941 (CAS Registry No. 957054307), BGT226 (CAS Registry No. 1245537681), BEZ235 (CAS Registry No. 915019657), XL-765 (CAS Registry No. 934493762).

[0411] Protein Synthesis Inhibitors: acriflavine (CAS Registry No. 65589700); amikacin (NSC 177001; CAS Registry No. 39831555); arbekacin (CAS Registry No. 51025855); astromicin (CAS Registry No. 55779061); azithromycin (NSC 643732; CAS Registry No. 83905015); bekanamycin (CAS Registry No. 4696768); chlortetracycline (NSC 13252; CAS Registry No. 64722); clarithromycin (NSC 643733; CAS Registry No. 81103119); clindamycin (CAS Registry No. 18323449); clomocycline (CAS Registry No. 1181540); cycloheximide (CAS Registry No. 66819); dactinomycin (NSC 3053; CAS Registry No. 50760); dalfopristin (CAS Registry No. 112362502); demeclocycline (CAS Registry No. 127333); dibekacin (CAS Registry No. 34493986); dihydrostreptomycin (CAS Registry No. 128461); dirithromycin (CAS Registry No. 62013041); doxycycline (CAS Registry No. 17086281); emetine (NSC 33669; CAS Registry No. 483181); erythromycin (NSC 55929; CAS Registry No. 114078); flurithromycin (CAS Registry No. 83664208); framycetin (neomycin B; CAS Registry No. 119040); gentamycin (NSC 82261; CAS Registry No. 1403663); glycylicyclines, such as tigecycline (CAS Registry No. 220620097);

hygromycin B (CAS Registry No. 31282049); isepamicin (CAS Registry No. 67814760); josamycin (NSC 122223; CAS Registry No. 16846245); kanamycin (CAS Registry No. 8063078); ketolides such as telithromycin (CAS Registry No. 191114484), cethromycin (CAS Registry No. 205110481), and solithromycin (CAS Registry No. 760981837); lincomycin (CAS Registry No. 154212); lymecycline (CAS Registry No. 992212); meclocycline (NSC 78502; CAS Registry No. 2013583); metacycline (rondomycin; NSC 356463; CAS Registry No. 914001); midecamycin (CAS Registry No. 35457808); minocycline (NSC 141993; CAS Registry No. 10118908); miocamycin (CAS Registry No. 55881077); neomycin (CAS Registry No. 119040); netilmicin (CAS Registry No. 56391561); oleandomycin (CAS Registry No. 3922905); oxazolidinones, such as eperezolid (CAS Registry No. 165800044), linezolid (CAS Registry No. 165800033), posizolid (CAS Registry No. 252260029), radezolid (CAS Registry No. 869884786), ranbezolid (CAS Registry No. 392659380), sutezolid (CAS Registry No. 168828588), tedizolid (CAS Registry No. 856867555); oxytetracycline (NSC 9169; CAS Registry No. 2058460); paromomycin (CAS Registry No. 7542372); penimepicycline (CAS Registry No. 4599604); peptidyl transferase inhibitors, e.g., chloramphenicol (NSC 3069; CAS Registry No. 56757) and derivatives such as azidamfenicol (CAS Registry No. 13838089), florfenicol (CAS Registry No. 73231342), and thiamphenicol (CAS Registry No. 15318453), and pleuromutilins such as retapamulin (CAS Registry No. 224452668), tiamulin (CAS Registry No. 55297955), valnemulin (CAS Registry No. 101312929); pirlimycin (CAS Registry No. 79548735); puromycin (NSC 3055; CAS Registry No. 53792); quinupristin (CAS Registry No. 120138503); ribostamycin (CAS Registry No. 53797356); rokitamycin (CAS Registry No. 74014510); rolitetracycline (CAS Registry No. 751973); roxithromycin (CAS Registry No. 80214831); sisomicin (CAS Registry No. 32385118); spectinomycin (CAS Registry No. 1695778); spiramycin (CAS Registry No. 8025818); streptogramins such as pristinamycin (CAS Registry No. 270076603), quinupristin/dalfopristin (CAS Registry No. 126602899), and virginiamycin (CAS Registry No. 11006761); streptomycin (CAS Registry No. 57921); tetracycline (NSC 108579; CAS Registry No. 60548); tobramycin (CAS Registry No. 32986564); troleandomycin (CAS Registry No. 2751099); tylosin (CAS Registry No. 1401690); verdamicin (CAS Registry No. 49863481).

[0412] Histone Deacetylase Inhibitors: abexinostat (CAS Registry No. 783355602); belinostat (NSC 726630; CAS Registry No. 414864009); chidamide (CAS Registry No. 743420022); entinostat (CAS Registry No. 209783802); givinostat (CAS Registry No. 732302997); mocetinostat (CAS Registry No. 726169739); panobinostat (CAS Registry No. 404950807); quisinostat (CAS Registry No. 875320299); resminostat (CAS Registry No. 864814880); romidepsin (CAS Registry No. 128517077); sulforaphane (CAS Registry No. 4478937); thioureidobutyronitrile (Kevetrin™; CAS Registry No. 6659890); valproic acid (NSC 93819; CAS Registry No. 99661); vorinostat (NSC 701852; CAS Registry No. 149647789); ACY-1215

(rocilinostat; CAS Registry No. 1316214524); CUDC-101 (CAS Registry No. 1012054599); CHR-2845 (tefinostat; CAS Registry No. 914382608); CHR-3996 (CAS Registry No. 1235859138); 4SC-202 (CAS Registry No. 910462430); CG200745 (CAS Registry No. 936221339); SB939 (pracinostat; CAS Registry No. 929016966).

[0413] Mitochondria Inhibitors: pancratistatin (NSC 349156; CAS Registry No. 96281311); rhodamine-123 (CAS Registry No. 63669709); edelfosine (NSC 324368; CAS Registry No. 70641519); d-alpha-tocopherol succinate (NSC 173849; CAS Registry No. 4345033); compound 11 β (CAS Registry No. 865070377); aspirin (NSC 406186; CAS Registry No. 50782); ellipticine (CAS Registry No. 519233); berberine (CAS Registry No. 633658); cerulenin (CAS Registry No. 17397896); GX015-070 (Obatoclox®; 1H-Indole, 2-(2-((3,5-dimethyl-1H-pyrrol-2-yl)methylene)-3-methoxy-2H-pyrrol-5-yl)-; NSC 729280; CAS Registry No. 803712676); celastrol (tripterine; CAS Registry No. 34157830); metformin (NSC 91485; CAS Registry No. 1115704); Brilliant green (NSC 5011; CAS Registry No. 633034); ME-344 (CAS Registry No. 1374524556).

[0414] Antimitotic Agents: allocolchicine (NSC 406042); auristatins, such as MMAE (monomethyl auristatin E; CAS Registry No. 474645-27-7) and MMAF (monomethyl auristatin F; CAS Registry No. 745017-94-1; halichondrin B (NSC 609395); colchicine (NSC 757; CAS Registry No. 64868); colchicine derivative (N-benzoyl-deacetyl benzamide; NSC 33410; CAS Registry No. 63989753); dolastatin 10 (NSC 376128; CAS Registry No. 110417-88-4); maytansine (NSC 153858; CAS Registry No. 35846-53-8); rhoxoxin (NSC 332598; CAS Registry No. 90996546); taxol (NSC 125973; CAS Registry No. 33069624); taxol derivative ((2'-N-[3-(dimethylamino)propyl]glutaramate taxol; NSC 608832); thiocolchicine (3-demethylthiocolchicine; NSC 361792); trityl cysteine (NSC 49842; CAS Registry No. 2799077); vinblastine sulfate (NSC 49842; CAS Registry No. 143679); vincristine sulfate (NSC 67574; CAS Registry No. 2068782).

[0415] Any of these agents that include or that may be modified to include a site of attachment to a TBM may be included in the ADCs disclosed herein.

[0416] In a specific embodiment, the cytotoxic and/or cytostatic agent is an antimitotic agent.

[0417] In another specific embodiment, the cytotoxic and/or cytostatic agent is an auristatin, for example, monomethyl auristatin E ("MMAE") or monomethyl auristatin F ("MMAF").

6.9.2. ADC Linkers

[0418] In the ADCs of the disclosure, the cytotoxic and/or cytostatic agents are linked to the TBM by way of ADC linkers. The ADC linker linking a cytotoxic and/or cytostatic agent to the TBM of an ADC may be short, long, hydrophobic, hydrophilic, flexible or rigid, or may be composed of segments that each independently have one or more of the above-mentioned

properties such that the linker may include segments having different properties. The linkers may be polyvalent such that they covalently link more than one agent to a single site on the TBM, or monovalent such that covalently they link a single agent to a single site on the TBM.

[0419] As will be appreciated by skilled artisans, the ADC linkers link cytotoxic and/or cytostatic agents to the TBM by forming a covalent linkage to the cytotoxic and/or cytostatic agent at one location and a covalent linkage to the TBM at another. The covalent linkages are formed by reaction between functional groups on the ADC linker and functional groups on the agents and TBM. As used herein, the expression “ADC linker” is intended to include (i) unconjugated forms of the ADC linker that include a functional group capable of covalently linking the ADC linker to a cytotoxic and/or cytostatic agent and a functional group capable of covalently linking the ADC linker to a TBM; (ii) partially conjugated forms of the ADC linker that include a functional group capable of covalently linking the ADC linker to a TBM and that is covalently linked to a cytotoxic and/or cytostatic agent, or vice versa; and (iii) fully conjugated forms of the ADC linker that are covalently linked to both a cytotoxic and/or cytostatic agent and a TBM. In some specific embodiments of ADC linkers and ADCs of the disclosure, as well as synthons used to conjugate linker-agents to TBMs, moieties comprising the functional groups on the ADC linker and covalent linkages formed between the ADC linker and TBM are specifically illustrated as R_x and XY, respectively.

[0420] The ADC linkers are preferably, but need not be, chemically stable to conditions outside the cell, and may be designed to cleave, immolate and/or otherwise specifically degrade inside the cell. Alternatively, ADC linkers that are not designed to specifically cleave or degrade inside the cell may be used. Choice of stable versus unstable ADC linker may depend upon the toxicity of the cytotoxic and/or cytostatic agent. For agents that are toxic to normal cells, stable linkers are preferred. Agents that are selective or targeted and have lower toxicity to normal cells may utilize, chemical stability of the ADC linker to the extracellular milieu is less important. A wide variety of ADC linkers useful for linking drugs to TBMs in the context of ADCs are known in the art. Any of these ADC linkers, as well as other ADC linkers, may be used to link the cytotoxic and/or cytostatic agents to the TBM of the ADCs of the disclosure.

[0421] Exemplary polyvalent ADC linkers that may be used to link many cytotoxic and/or cytostatic agents to a single TBM molecule are described, for example, in WO 2009/073445; WO 2010/068795; WO 2010/138719; WO 2011/120053; WO 2011/171020; WO 2013/096901; WO 2014/008375; WO 2014/093379; WO 2014/093394; WO 2014/093640, the content of which are incorporated herein by reference in their entireties. For example, the Fleximer linker technology developed by Mersana *et al.* has the potential to enable high-DAR ADCs with good physicochemical properties. As shown below, the Mersana technology is based on incorporating drug molecules into a solubilizing poly-acetal backbone via a sequence of ester

bonds. The methodology renders highly-loaded ADCs (DAR up to 20) while maintaining good physicochemical properties.

[0422] Additional examples of dendritic type linkers can be found in US 2006/116422; US 2005/271615; de Groot *et al.*, 2003, *Angew. Chem. Int. Ed.* 42:4490-4494; Amir *et al.*, 2003, *Angew. Chem. Int. Ed.* 42:4494-4499; Shamis *et al.*, 2004, *J. Am. Chem. Soc.* 126:1726-1731; Sun *et al.*, 2002, *Bioorganic & Medicinal Chemistry Letters* 12:2213-2215; Sun *et al.*, 2003, *Bioorganic & Medicinal Chemistry* 11:1761-1768; King *et al.*, 2002, *Tetrahedron Letters* 43:1987-1990, each of which is incorporated herein by reference.

[0423] Exemplary monovalent ADC linkers that may be used are described, for example, in Nolting, 2013, *Antibody-Drug Conjugates*, *Methods in Molecular Biology* 1045:71-100; Kitson *et al.*, 2013, *CROs—MOs—Chemical—Engineering—Chemistry Today* 31(4):30-38; Ducry *et al.*, 2010, *Bioconjugate Chem.* 21:5-13; Zhao *et al.*, 2011, *J. Med. Chem.* 54:3606-3623; U.S. Pat. No. 7,223,837; U.S. Pat. No. 8,568,728; U.S. Pat. No. 8,535,678; and WO2004010957, each of which is incorporated herein by reference.

[0424] By way of example and not limitation, some cleavable and noncleavable ADC linkers that may be included in the ADCs of the disclosure are described below.

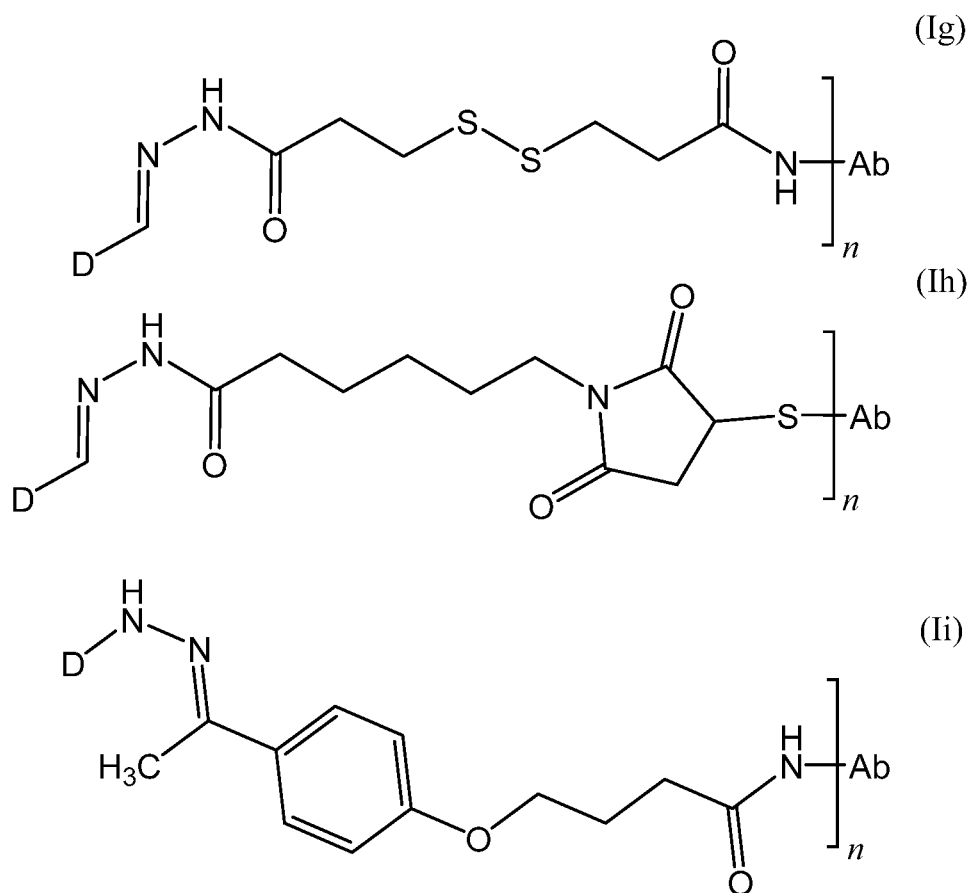
6.9.2.1. Cleavable ADC Linkers

[0425] In certain embodiments, the ADC linker selected is cleavable *in vivo*. Cleavable ADC linkers may include chemically or enzymatically unstable or degradable linkages. Cleavable ADC linkers generally rely on processes inside the cell to liberate the drug, such as reduction in the cytoplasm, exposure to acidic conditions in the lysosome, or cleavage by specific proteases or other enzymes within the cell. Cleavable ADC linkers generally incorporate one or more chemical bonds that are either chemically or enzymatically cleavable while the remainder of the ADC linker is noncleavable. In certain embodiments, an ADC linker comprises a chemically labile group such as hydrazone and/or disulfide groups. Linkers comprising chemically labile groups exploit differential properties between the plasma and some cytoplasmic compartments. The intracellular conditions to facilitate drug release for hydrazone containing ADC linkers are the acidic environment of endosomes and lysosomes, while the disulfide containing ADC linkers are reduced in the cytosol, which contains high thiol concentrations, e.g., glutathione. In certain embodiments, the plasma stability of an ADC linker comprising a chemically labile group may be increased by introducing steric hindrance using substituents near the chemically labile group.

[0426] Acid-labile groups, such as hydrazone, remain intact during systemic circulation in the blood's neutral pH environment (pH 7.3-7.5) and undergo hydrolysis and release the drug once the ADC is internalized into mildly acidic endosomal (pH 5.0-6.5) and lysosomal (pH 4.5-5.0) compartments of the cell. This pH dependent release mechanism has been associated with

nonspecific release of the drug. To increase the stability of the hydrazone group of the ADC linker, the ADC linker may be varied by chemical modification, *e.g.*, substitution, allowing tuning to achieve more efficient release in the lysosome with a minimized loss in circulation.

[0427] Hydrazone-containing ADC linkers may contain additional cleavage sites, such as additional acid-labile cleavage sites and/or enzymatically labile cleavage sites. ADCs including exemplary hydrazone-containing ADC linkers include the following structures:



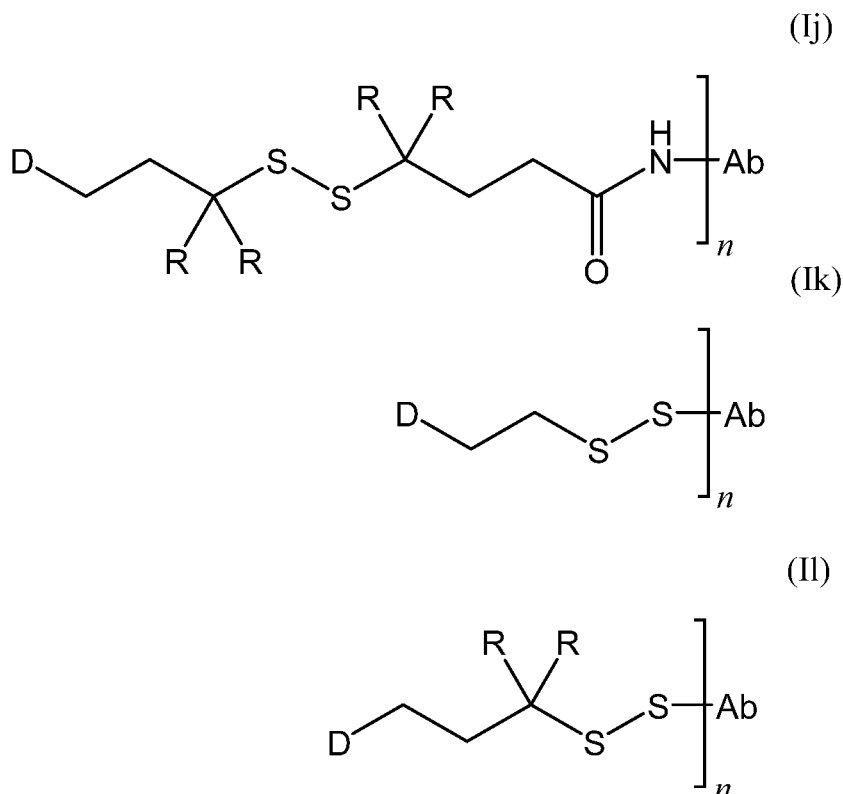
wherein D and Ab represent the cytotoxic and/or cytostatic agent (drug) and Ab, respectively, and n represents the number of drug-ADC linkers linked to the TBM. In certain ADC linkers such as linker (Ig), the ADC linker comprises two cleavable groups--a disulfide and a hydrazone moiety. For such ADC linkers, effective release of the unmodified free drug requires acidic pH or disulfide reduction and acidic pH. Linkers such as (Ih) and (Ii) have been shown to be effective with a single hydrazone cleavage site.

[0428] Additional ADC linkers which remain intact during systemic circulation and undergo hydrolysis and release the drug when the ADC is internalized into acidic cellular compartments include carbonates. Such ADC linkers can be useful in cases where the cytotoxic and/or cytostatic agent can be covalently attached through an oxygen.

[0429] Other acid-labile groups that may be included in ADC linkers include cis-aconityl-containing ADC linkers. cis-Aconityl chemistry uses a carboxylic acid juxtaposed to an amide bond to accelerate amide hydrolysis under acidic conditions.

[0430] Cleavable ADC linkers may also include a disulfide group. Disulfides are thermodynamically stable at physiological pH and are designed to release the drug upon internalization inside cells, wherein the cytosol provides a significantly more reducing environment compared to the extracellular environment. Scission of disulfide bonds generally requires the presence of a cytoplasmic thiol cofactor, such as (reduced) glutathione (GSH), such that disulfide-containing ADC linkers are reasonably stable in circulation, selectively releasing the drug in the cytosol. The intracellular enzyme protein disulfide isomerase, or similar enzymes capable of cleaving disulfide bonds, may also contribute to the preferential cleavage of disulfide bonds inside cells. GSH is reported to be present in cells in the concentration range of 0.5-10 mM compared with a significantly lower concentration of GSH or cysteine, the most abundant low-molecular weight thiol, in circulation at approximately 5 Tumor cells, where irregular blood flow leads to a hypoxic state, result in enhanced activity of reductive enzymes and therefore even higher glutathione concentrations. In certain embodiments, the *in vivo* stability of a disulfide-containing ADC linker may be enhanced by chemical modification of the ADC linker, e.g., use of steric hindrance adjacent to the disulfide bond.

[0431] ADCs including exemplary disulfide-containing ADC linkers include the following structures:



wherein D and Ab represent the drug and TBM, respectively, n represents the number of drug-ADC linkers linked to the TBM and R is independently selected at each occurrence from hydrogen or alkyl, for example. In certain embodiments, increasing steric hindrance adjacent to the disulfide bond increases the stability of the ADC linker. Structures such as (Ij) and (II) show increased *in vivo* stability when one or more R groups is selected from a lower alkyl such as methyl.

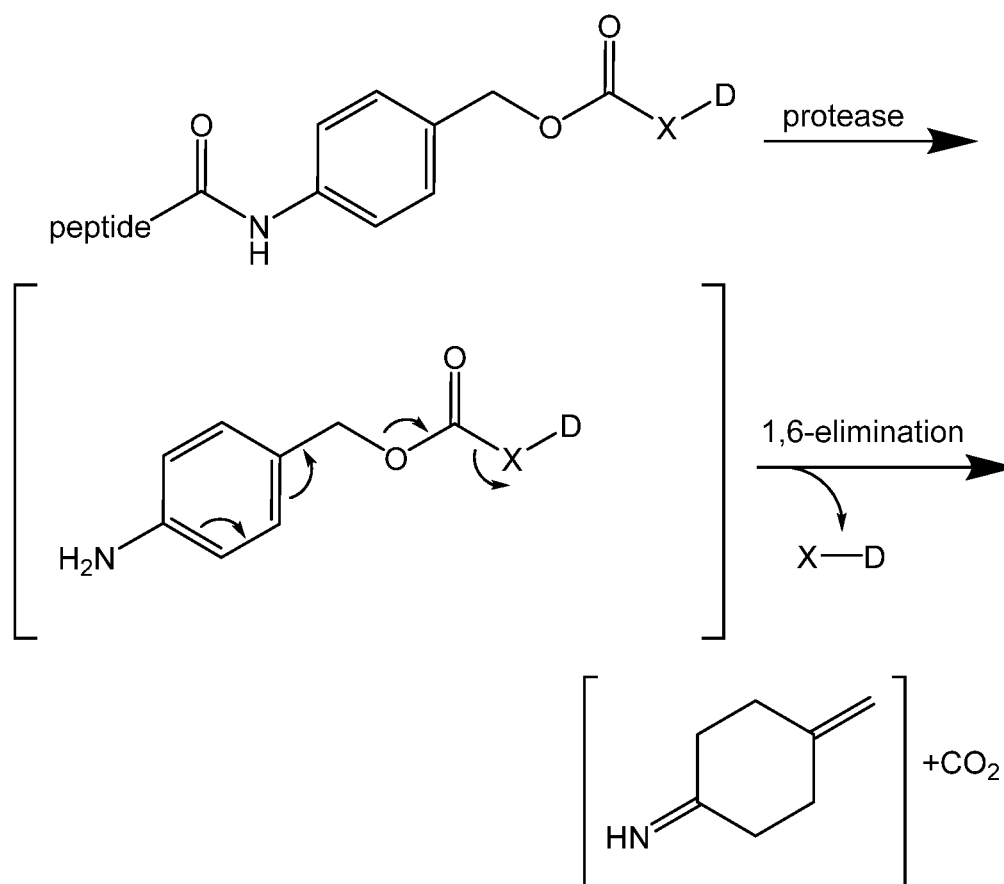
[0432] Another type of cleavable ADC linker that may be used is an ADC linker that is specifically cleaved by an enzyme. Such ADC linkers are typically peptide-based or include peptidic regions that act as substrates for enzymes. Peptide based ADC linkers tend to be more stable in plasma and extracellular milieu than chemically labile ADC linkers. Peptide bonds generally have good serum stability, as lysosomal proteolytic enzymes have very low activity in blood due to endogenous inhibitors and the unfavorably high pH value of blood compared to lysosomes. Release of a drug from a TBM occurs specifically due to the action of lysosomal proteases, *e.g.*, cathepsin and plasmin. These proteases may be present at elevated levels in certain tumor cells.

[0433] In exemplary embodiments, the cleavable peptide is selected from tetrapeptides such as Gly-Phe-Leu-Gly (SEQ ID NO: 716), Ala-Leu-Ala-Leu (SEQ ID NO: 717) or dipeptides such as Val-Cit, Val-Ala, Met-(D)Lys, Asn-(D)Lys, Val-(D)Asp, Phe-Lys, Ile-Val, Asp-Val, His-Val, NorVal-(D)Asp, Ala-(D)Asp 5, Met-Lys, Asn-Lys, Ile-Pro, Me3Lys-Pro, PhenylGly-(D)Lys, Met-(D)Lys, Asn-(D)Lys, Pro-(D)Lys, Met-(D)Lys, Asn-(D)Lys, AM Met-(D)Lys, Asn-(D)Lys, AW Met-(D)Lys, and Asn-(D)Lys. In certain embodiments, dipeptides are preferred over longer polypeptides due to hydrophobicity of the longer peptides.

[0434] A variety of dipeptide-based cleavable ADC linkers useful for linking drugs such as doxorubicin, mitomycin, camptothecin, pyrrolobenzodiazepine, tallysomycin and auristatin/auristatin family members to TBMs have been described (see, Dubowchik *et al.*, 1998, J. Org. Chem. 67:1866-1872; Dubowchik *et al.*, 1998, Bioorg. Med. Chem. Lett. 8(21):3341-3346; Walker *et al.*, 2002, Bioorg. Med. Chem. Lett. 12:217-219; Walker *et al.*, 2004, Bioorg. Med. Chem. Lett. 14:4323-4327; Sutherland *et al.*, 2013, Blood 122: 1455-1463; and Francisco *et al.*, 2003, Blood 102:1458-1465, of each of which is incorporated herein by reference). All of these dipeptide ADC linkers, or modified versions of these dipeptide ADC linkers, may be used in the ADCs of the disclosure. Other dipeptide ADC linkers that may be used include those found in ADCs such as Seattle Genetics' Brentuximab Vendotin SGN-35 (Adcetris™), Seattle Genetics SGN-75 (anti-CD-70, Val-Cit-monomethyl auristatin F(MMAF)), Seattle Genetics SGN-CD33A (anti-CD-33, Val-Ala-(SGD-1882)), Celldex Therapeutics glembatumumab (CDX-011) (anti-NMB, Val-Cit-monomethyl auristatin E (MMAE)), and Cytogen PSMA-ADC (PSMA-ADC-1301) (anti-PSMA, Val-Cit-MMAE).

[0435] Enzymatically cleavable ADC linkers may include a self-immolative spacer to spatially separate the drug from the site of enzymatic cleavage. The direct attachment of a drug to a peptide ADC linker can result in proteolytic release of an amino acid adduct of the drug, thereby impairing its activity. The use of a self-immolative spacer allows for the elimination of the fully active, chemically unmodified drug upon amide bond hydrolysis.

[0436] One self-immolative spacer is the bifunctional para-aminobenzyl alcohol group, which is linked to the peptide through the amino group, forming an amide bond, while amine containing drugs may be attached through carbamate functionalities to the benzylic hydroxyl group of the ADC linker (PABC). The resulting prodrugs are activated upon protease-mediated cleavage, leading to a 1,6-elimination reaction releasing the unmodified drug, carbon dioxide, and remnants of the ADC linker group. The following scheme depicts the fragmentation of p-amidobenzyl ether and release of the drug:

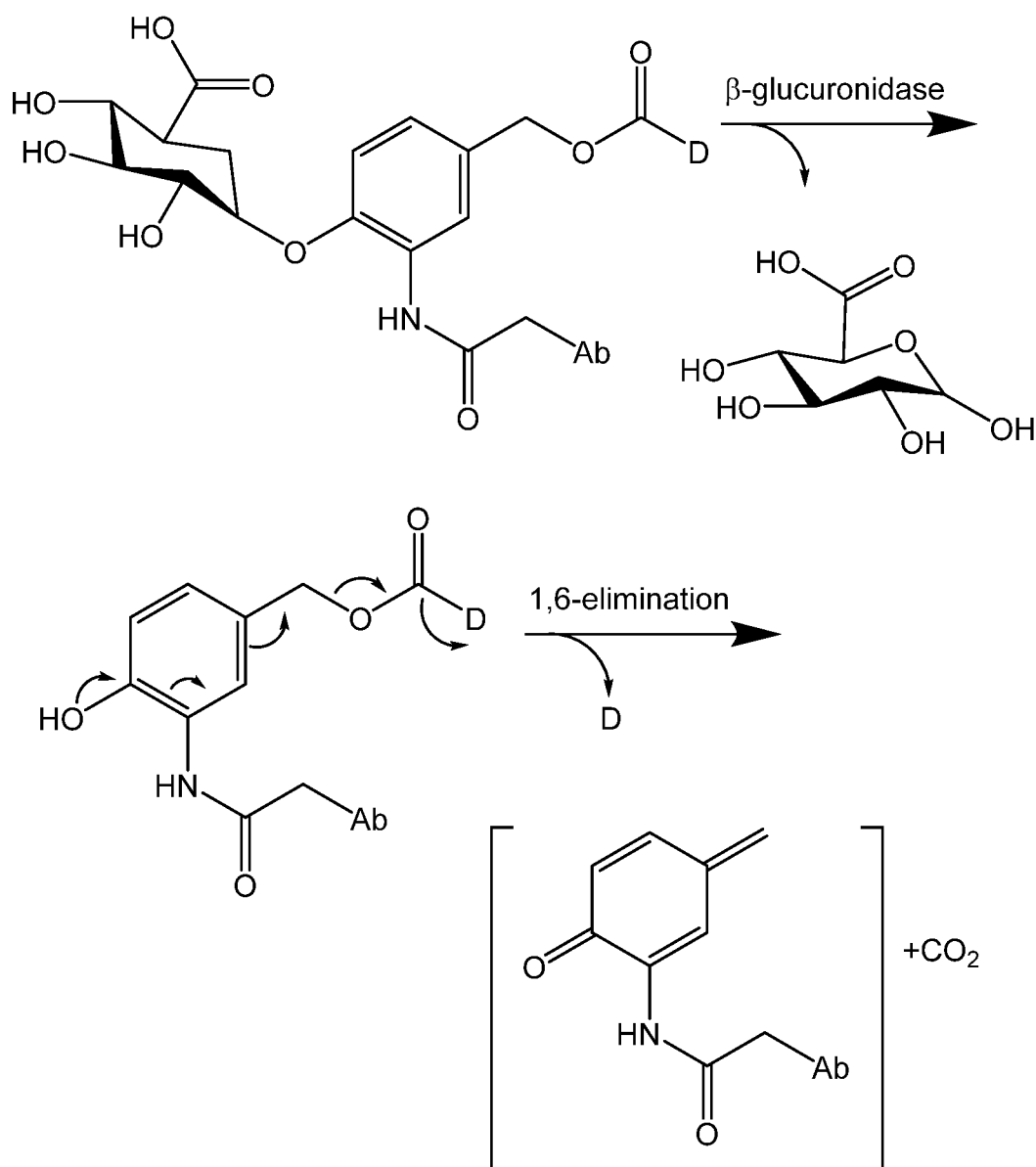


wherein X-D represents the unmodified drug.

[0437] Heterocyclic variants of this self-immolative group have also been described. See for example, U.S. Pat. No. 7,989,434, incorporated herein by reference.

[0438] In some embodiments, the enzymatically cleavable ADC linker is a β -glucuronic acid-based ADC linker. Facile release of the drug may be realized through cleavage of the β -

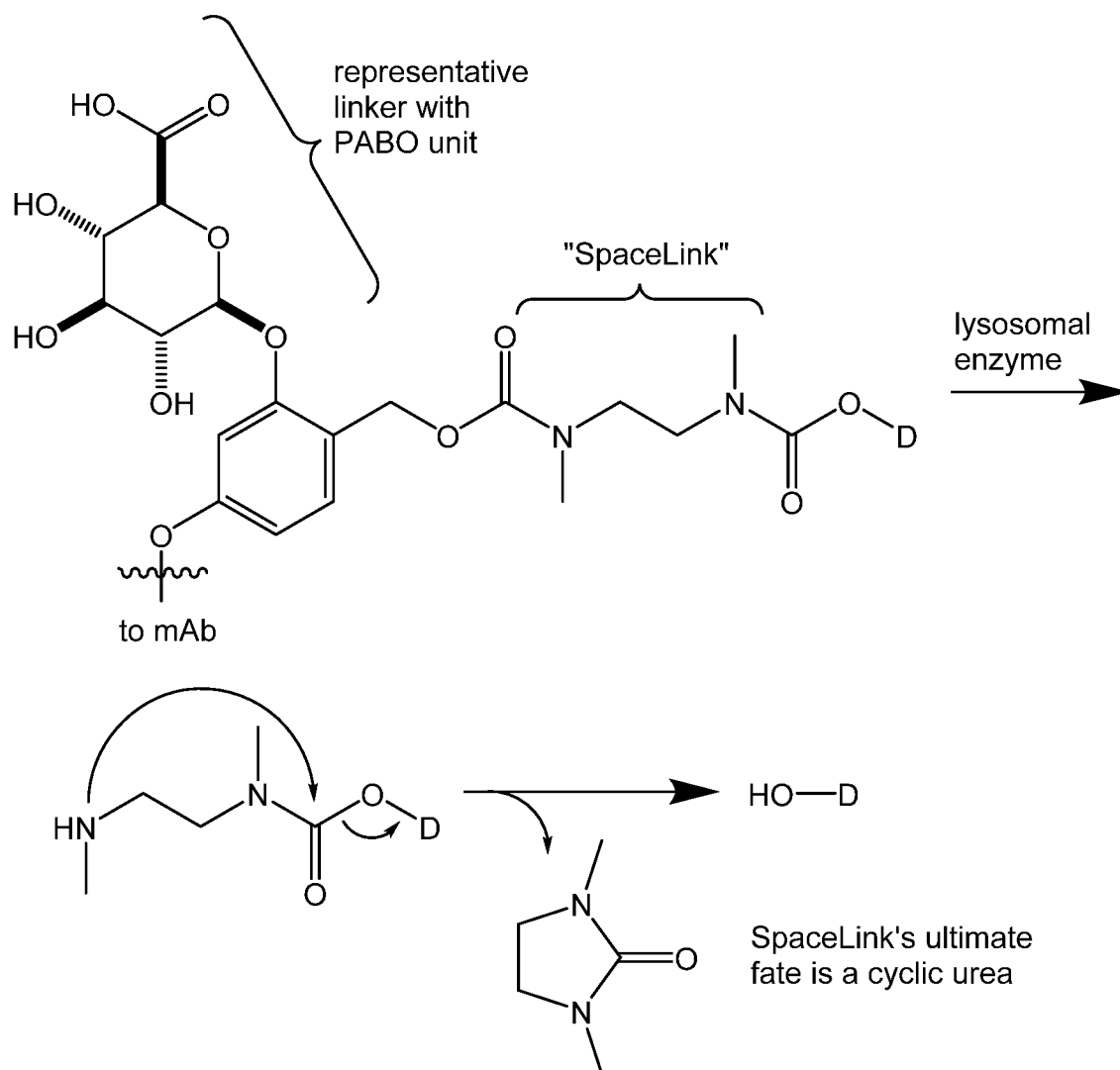
glucuronide glycosidic bond by the lysosomal enzyme β -glucuronidase. This enzyme is present abundantly within lysosomes and is overexpressed in some tumor types, while the enzyme activity outside cells is low. β -Glucuronic acid-based ADC linkers may be used to circumvent the tendency of an ADC to undergo aggregation due to the hydrophilic nature of β -glucuronides. In some embodiments, β -glucuronic acid-based ADC linkers are preferred as ADC linkers for ADCs linked to hydrophobic drugs. The following scheme depicts the release of the drug from an ADC containing a β -glucuronic acid-based ADC linker:



[0439] A variety of cleavable β -glucuronic acid-based ADC linkers useful for linking drugs such as auristatins, camptothecin and doxorubicin analogues, CBI minor-groove binders, and psymberin to TBMs have been described (see, see Nolting, Chapter 5 "Linker Technology in Antibody-Drug Conjugates," In: Antibody-Drug Conjugates: Methods in Molecular Biology, vol. 1045, pp. 71-100, Laurent Ducry (Ed.), Springer Science & Business Media, LLC, 2013;

Jeffrey *et al.*, 2006, *Bioconjug. Chem.* 17:831-840; Jeffrey *et al.*, 2007, *Bioorg. Med. Chem. Lett.* 17:2278-2280; and Jiang *et al.*, 2005, *J. Am. Chem. Soc.* 127:11254-11255, each of which is incorporated herein by reference). All of these β -glucuronic acid-based ADC linkers may be used in the ADCs of the disclosure.

[0440] Additionally, cytotoxic and/or cytostatic agents containing a phenol group can be covalently bonded to an ADC linker through the phenolic oxygen. One such ADC linker, described in WO 2007/089149, relies on a methodology in which a diamino-ethane "SpaceLink" is used in conjunction with traditional "PABO"-based self-immolative groups to deliver phenols. The cleavage of the ADC linker is depicted schematically below, where D represents a cytotoxic and/or cytostatic agent having a phenolic hydroxyl group.

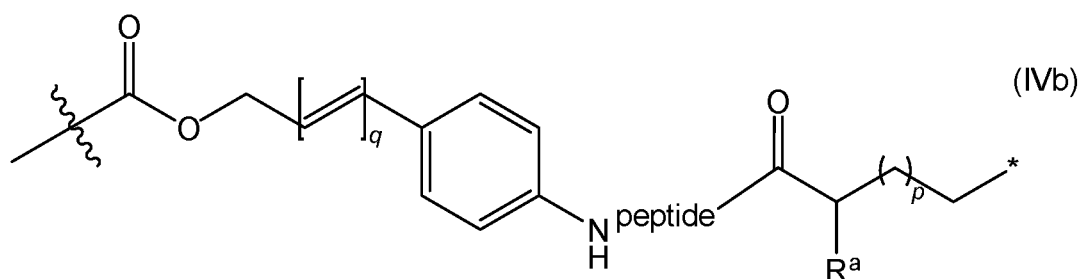
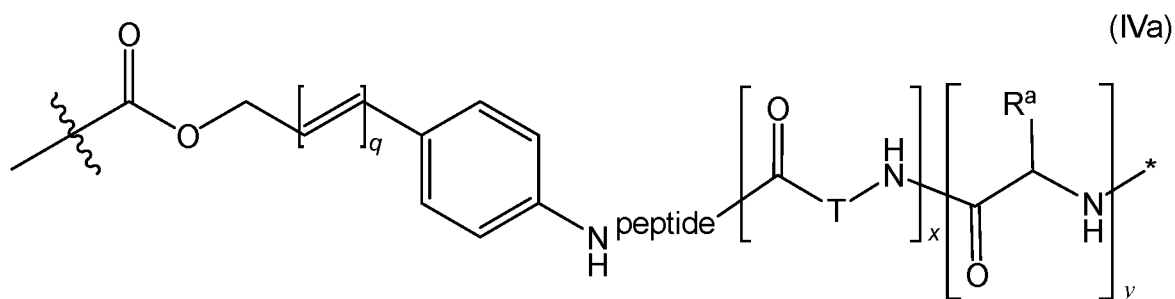


[0441] Cleavable ADC linkers may include noncleavable portions or segments, and/or cleavable segments or portions may be included in an otherwise non-cleavable ADC linker to render it cleavable. By way of example only, polyethylene glycol (PEG) and related polymers may include cleavable groups in the polymer backbone. For example, a polyethylene glycol or

polymer ADC linker may include one or more cleavable groups such as a disulfide, a hydrazone or a dipeptide.

[0442] Other degradable linkages that may be included in ADC linkers include ester linkages formed by the reaction of PEG carboxylic acids or activated PEG carboxylic acids with alcohol groups on a biologically active agent, wherein such ester groups generally hydrolyze under physiological conditions to release the biologically active agent. Hydrolytically degradable linkages include, but are not limited to, carbonate linkages; imine linkages resulting from reaction of an amine and an aldehyde; phosphate ester linkages formed by reacting an alcohol with a phosphate group; acetal linkages that are the reaction product of an aldehyde and an alcohol; orthoester linkages that are the reaction product of a formate and an alcohol; and oligonucleotide linkages formed by a phosphoramidite group, including but not limited to, at the end of a polymer, and a 5' hydroxyl group of an oligonucleotide.

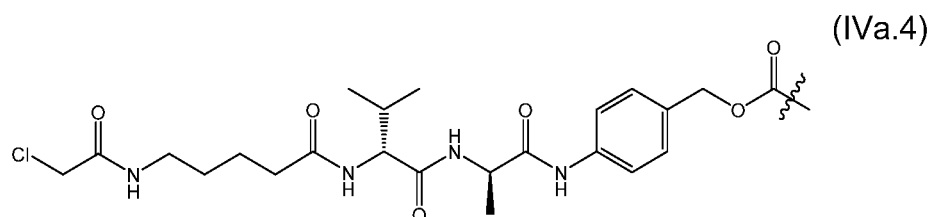
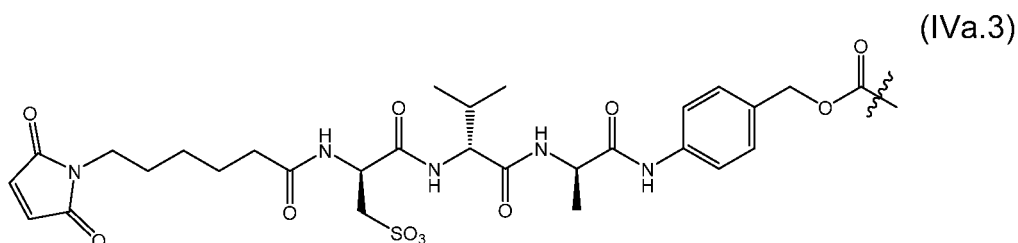
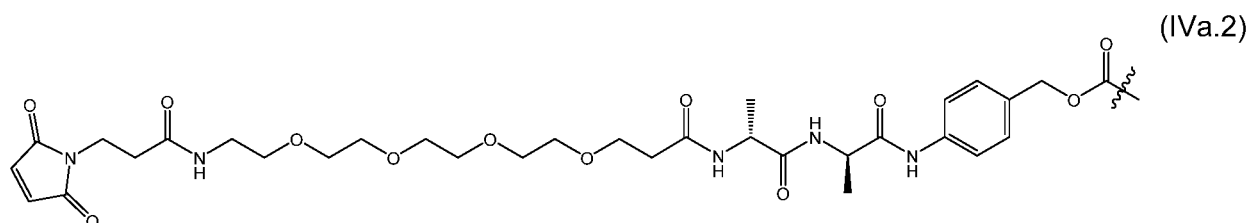
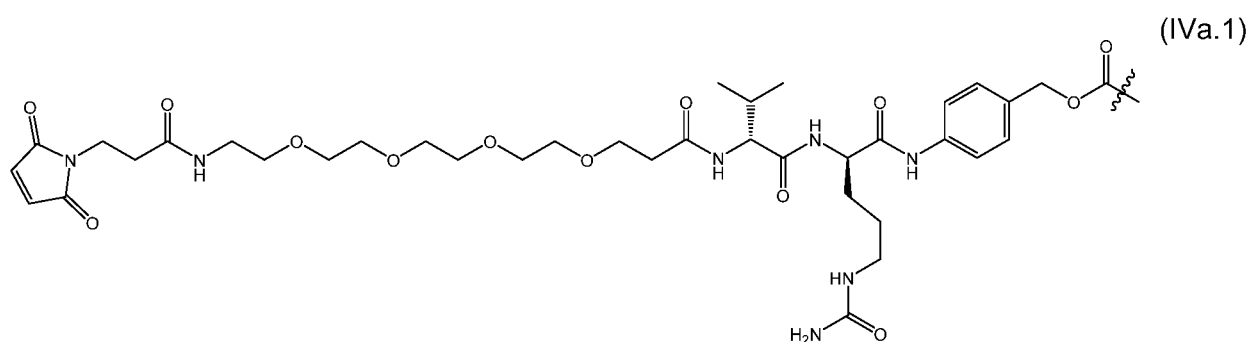
[0443] In certain embodiments, the ADC linker comprises an enzymatically cleavable peptide moiety, for example, an ADC linker comprising structural formula (IVa) or (IVb):

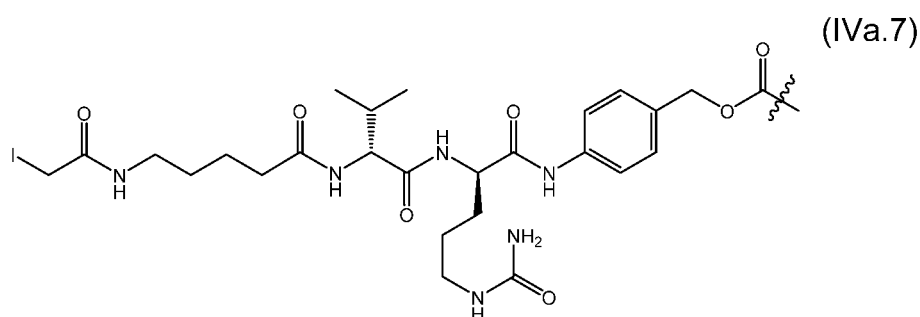
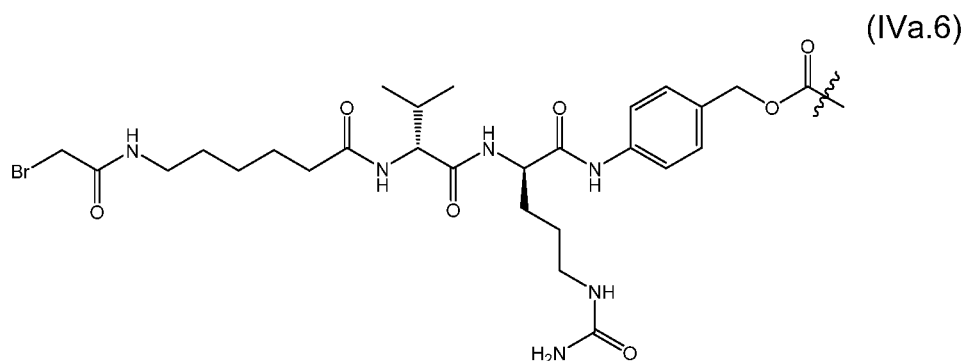
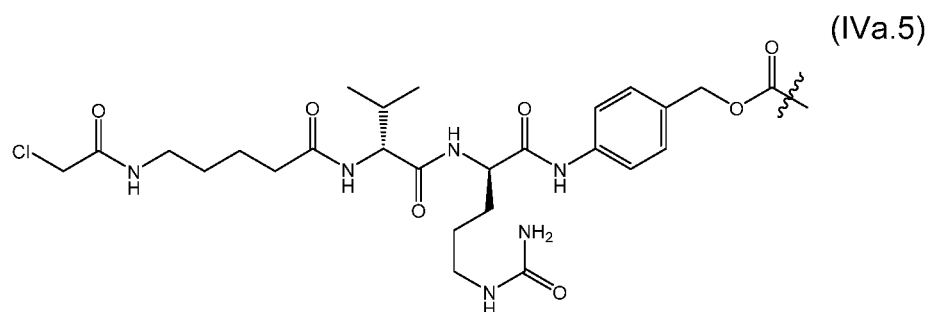


or a salt thereof, wherein: peptide represents a peptide (illustrated C→N and not showing the carboxy and amino “termini”) cleavable by a lysosomal enzyme; T represents a polymer comprising one or more ethylene glycol units or an alkylene chain, or combinations thereof; R^a is selected from hydrogen, alkyl, sulfonate and methyl sulfonate; p is an integer ranging from 0 to 5; q is 0 or 1; x is 0 or 1; y is 0 or 1; represents the point of attachment of the ADC linker to a cytotoxic and/or cytostatic agent; and * represents the point of attachment to the remainder of the ADC linker.

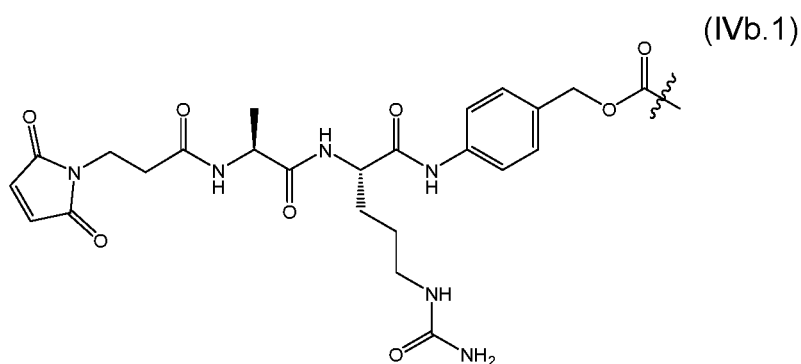
[0444] In certain embodiments, the peptide is selected from a tripeptide or a dipeptide. In particular embodiments, the dipeptide is selected from: Val-Cit; Cit-Val; Ala-Ala; Ala-Cit; Cit-Ala; Asn-Cit; Cit-Asn; Cit-Cit; Val-Glu; Glu-Val; Ser-Cit; Cit-Ser; Lys-Cit; Cit-Lys; Asp-Cit; Cit-Asp; Ala-Val; Val-Ala; Phe-Lys; Val-Lys; Ala-Lys; Phe-Cit; Leu-Cit; Ile-Cit; Phe-Arg; and Trp-Cit. In certain embodiments, the dipeptide is selected from: Cit-Val; and Ala-Val.

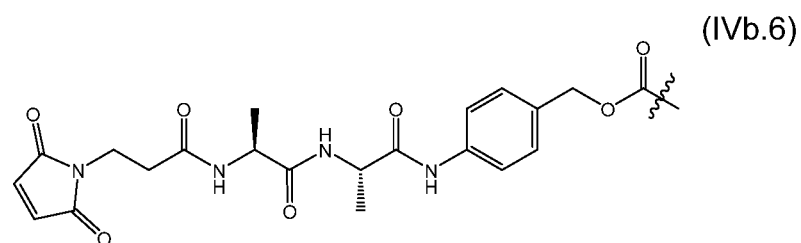
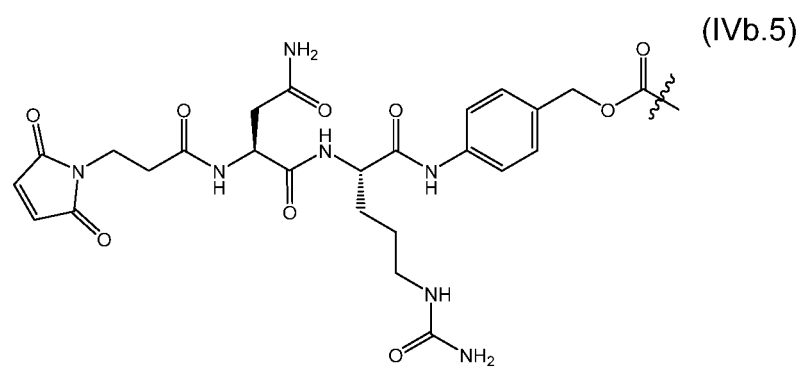
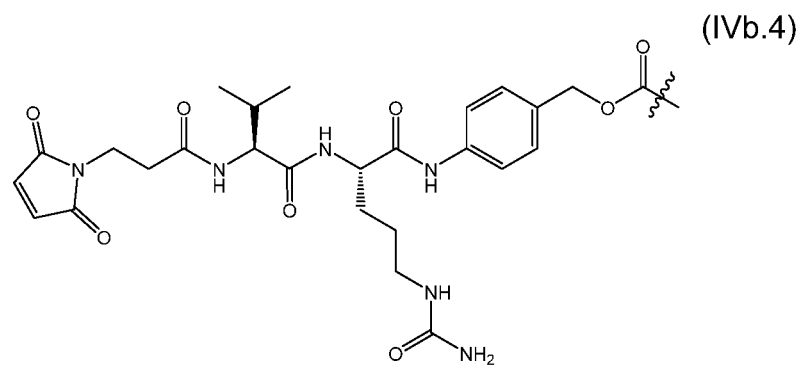
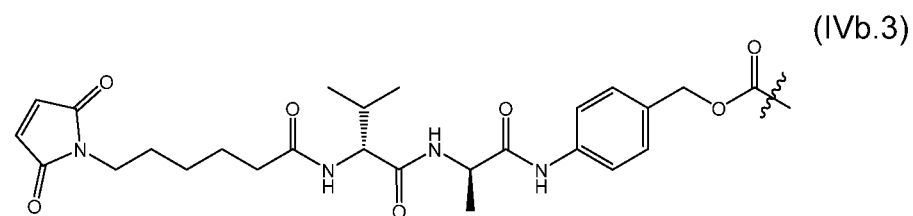
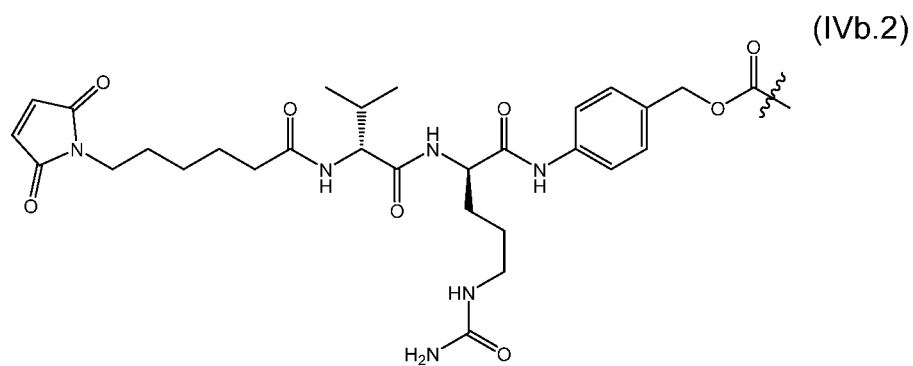
[0445] Specific exemplary embodiments of ADC linkers according to structural formula (IVa) that may be included in the ADCs of the disclosure include the ADC linkers illustrated below (as illustrated, the ADC linkers include a group suitable for covalently linking the ADC linker to a TBM):

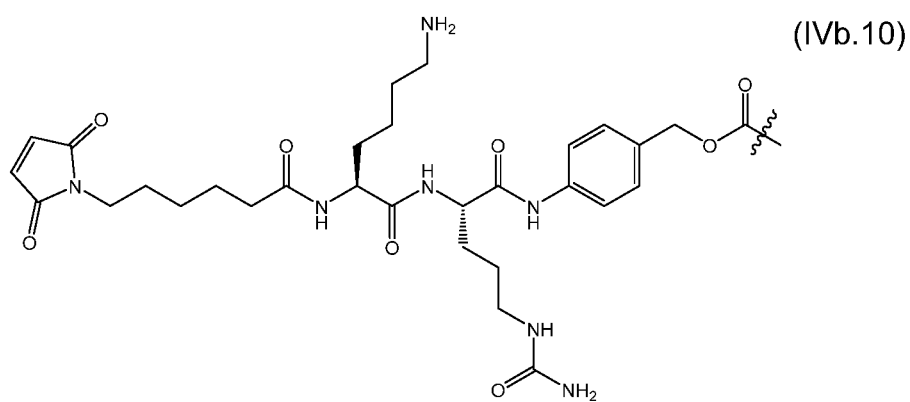
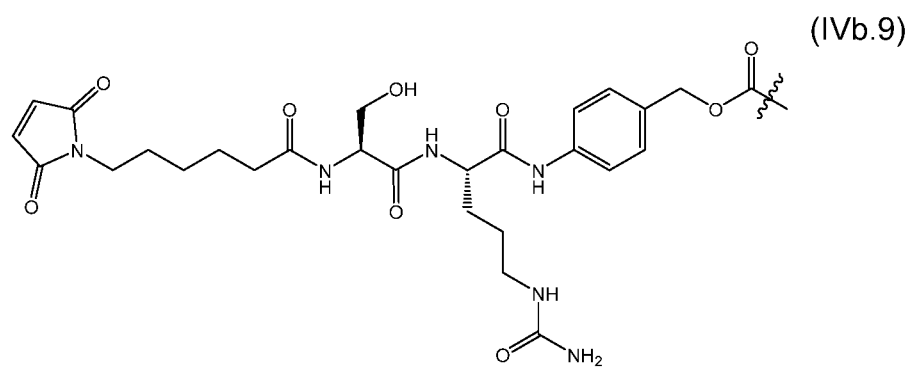
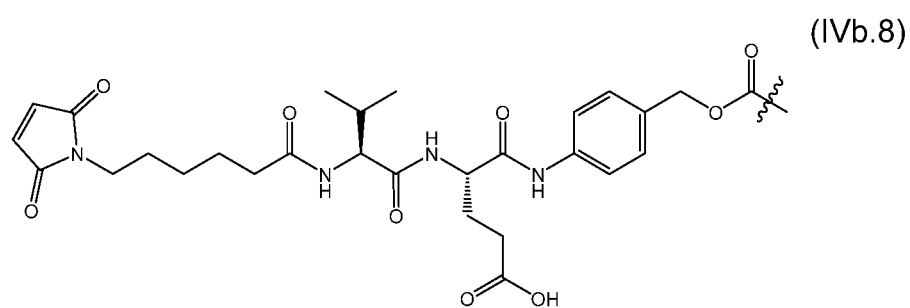
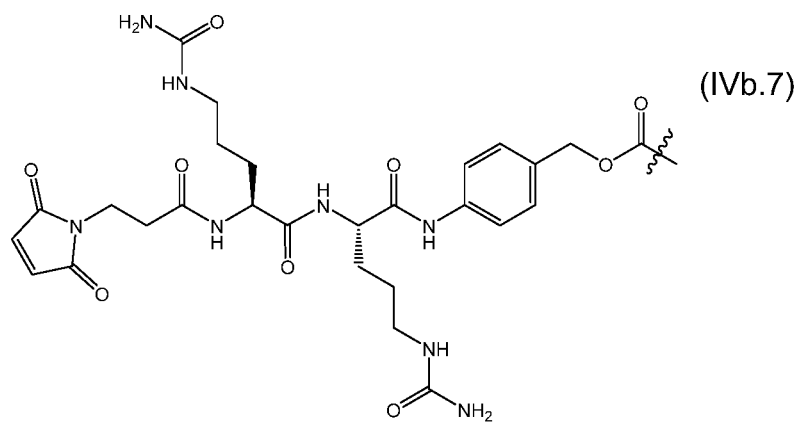




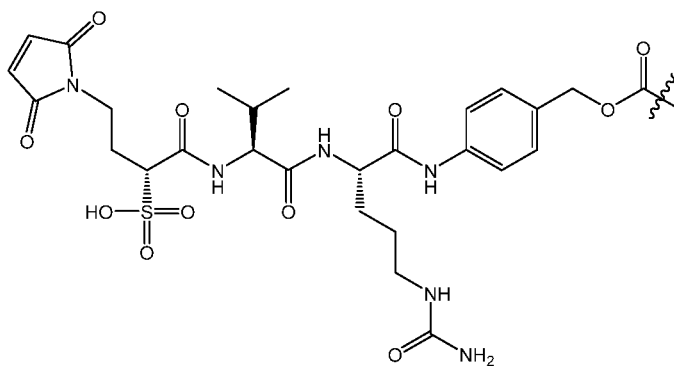
[0446] Specific exemplary embodiments of ADC linkers according to structural formula (IVb) that may be included in the ADCs of the disclosure include the ADC linkers illustrated below (as illustrated, the ADC linkers include a group suitable for covalently linking the ADC linker to a TBM):



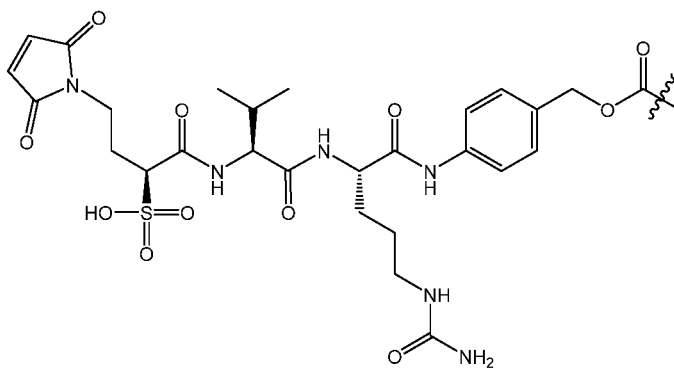




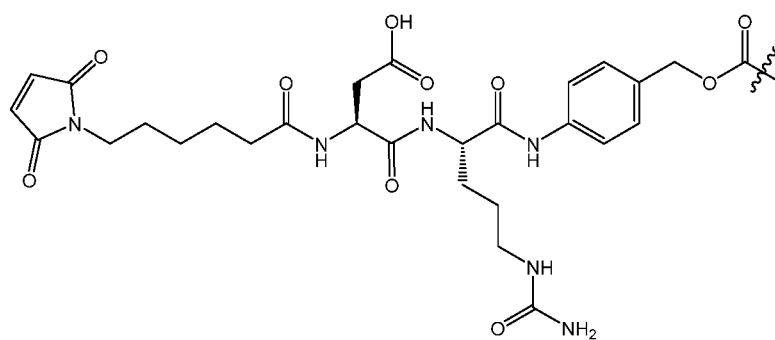
(IVb.11)



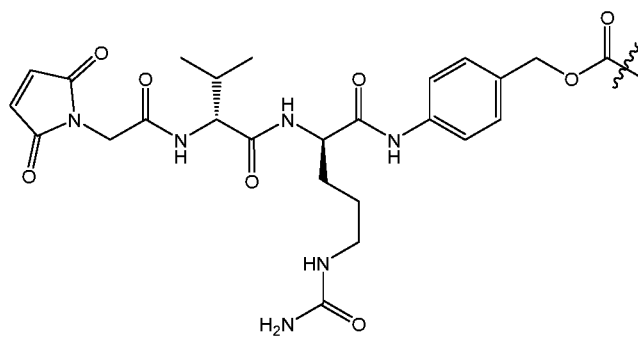
(IVb.12)



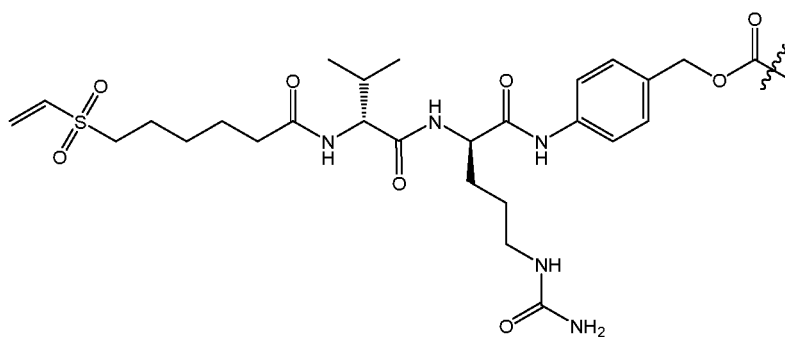
(IVb.13)



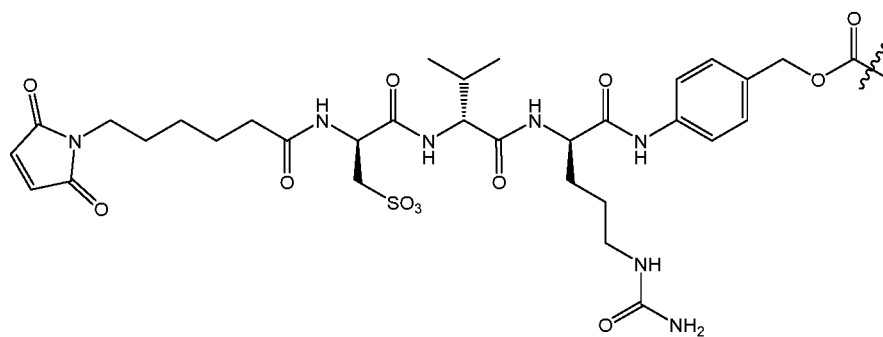
(IVb.14)



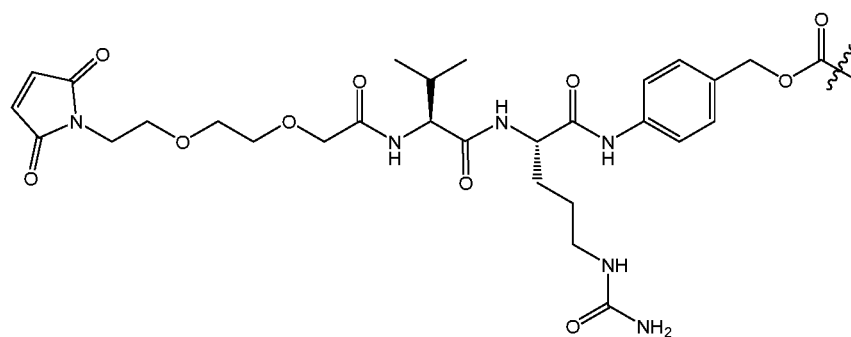
(IVb.15)



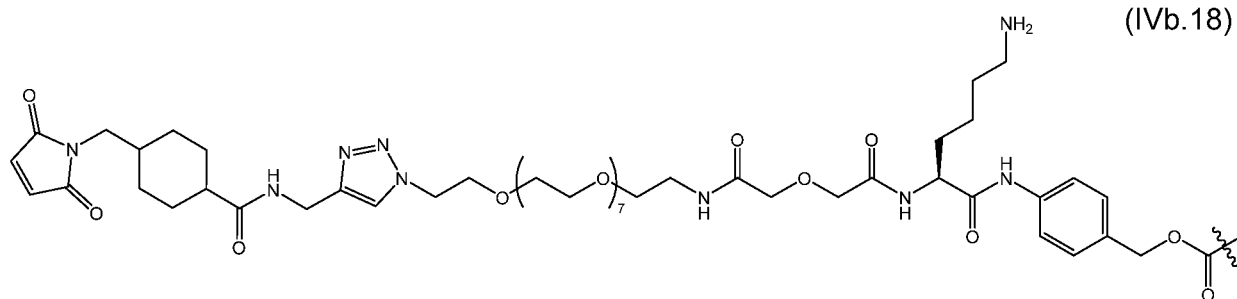
(IVb.16)



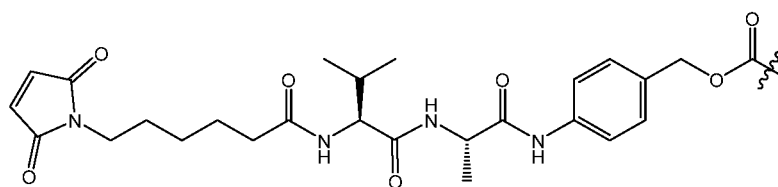
(IVb.17)



(IVb.18)

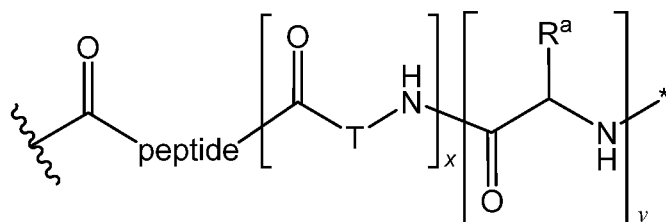


(IVb.19)

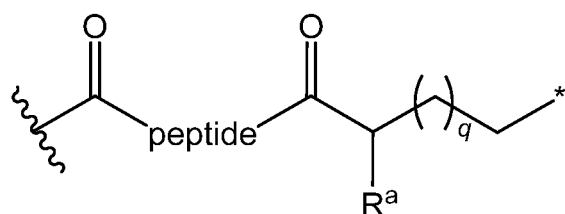


[0447] In certain embodiments, the ADC linker comprises an enzymatically cleavable peptide moiety, for example, an ADC linker comprising structural formula (IVc) or (IVd):

(IVc)

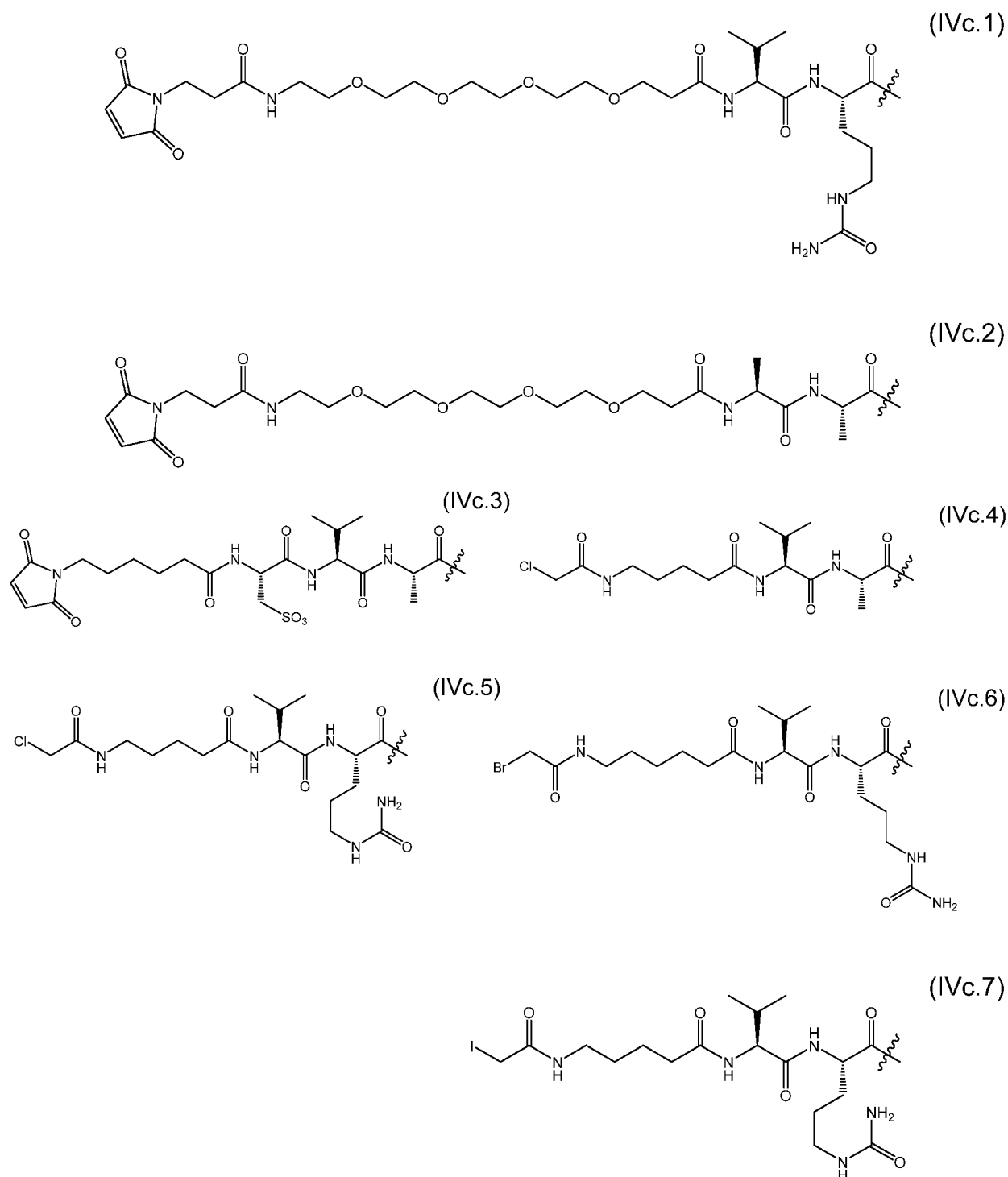


(IVd)

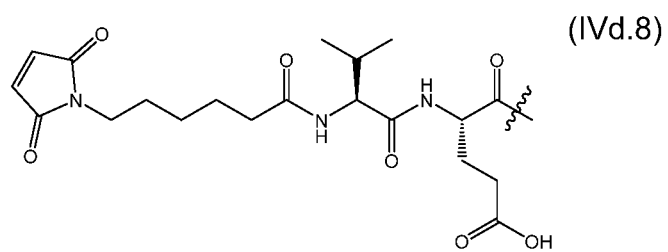
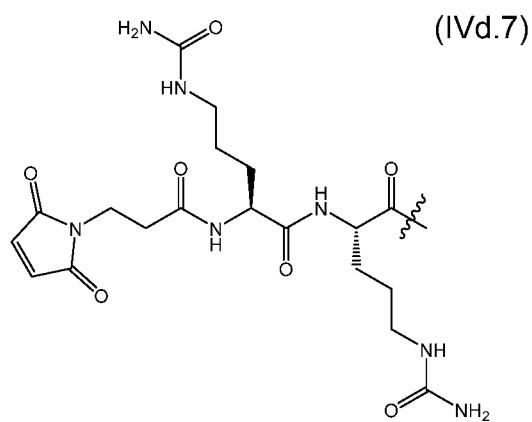
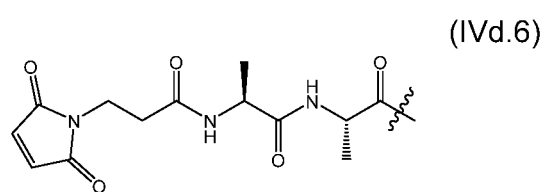
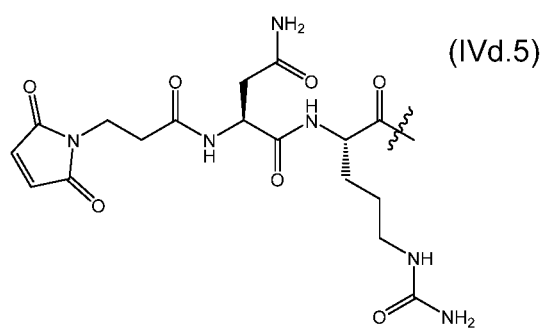
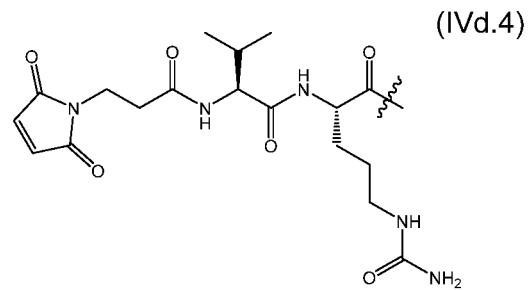
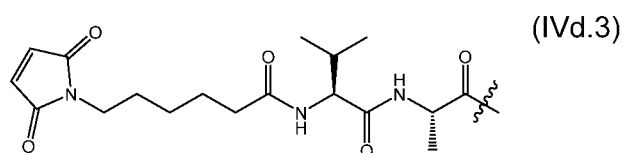
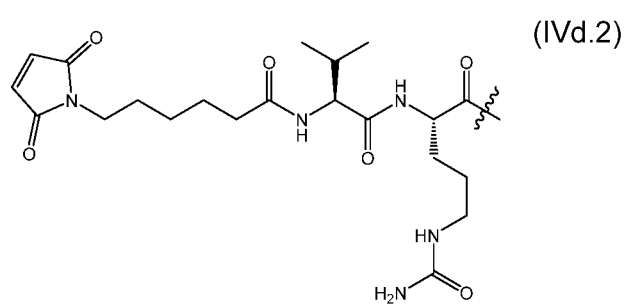
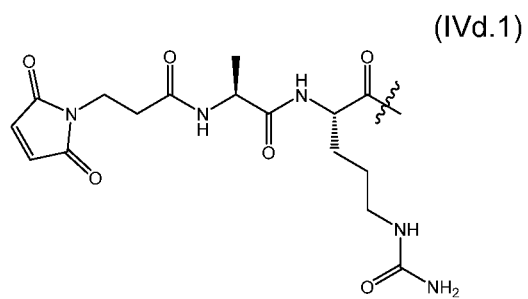


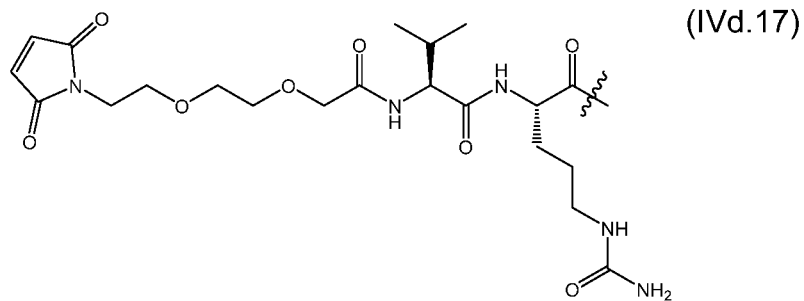
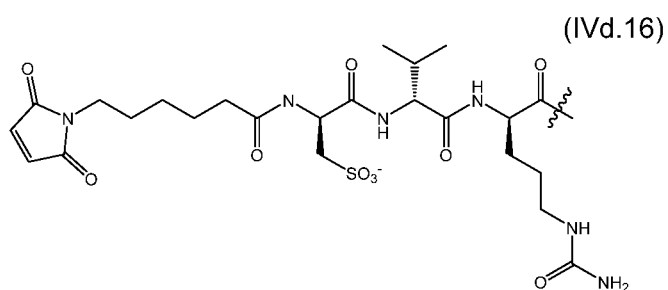
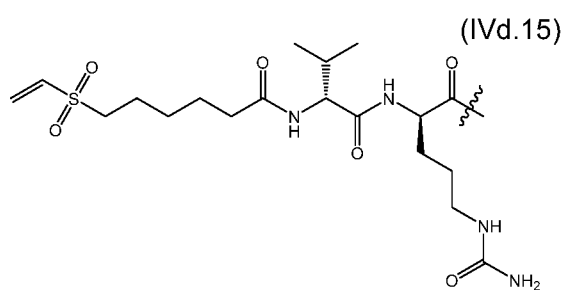
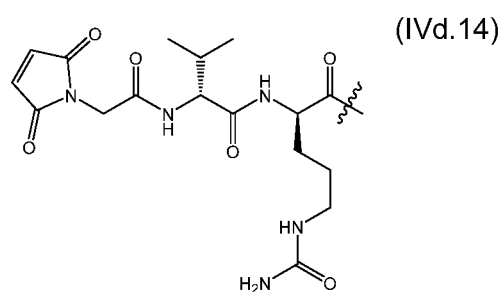
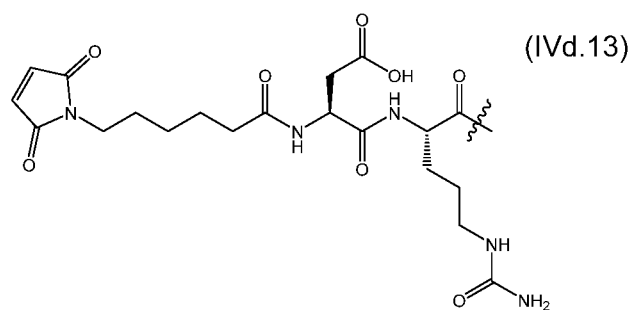
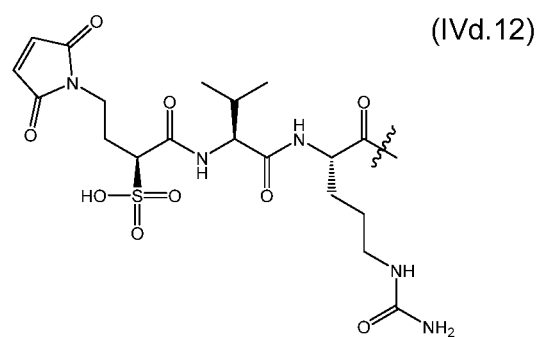
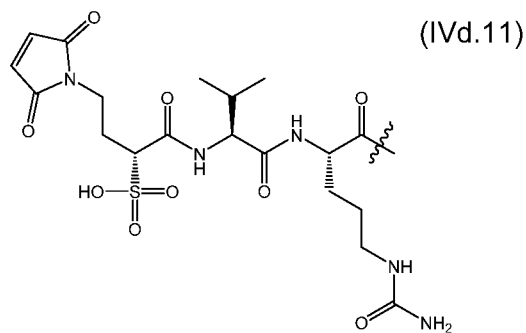
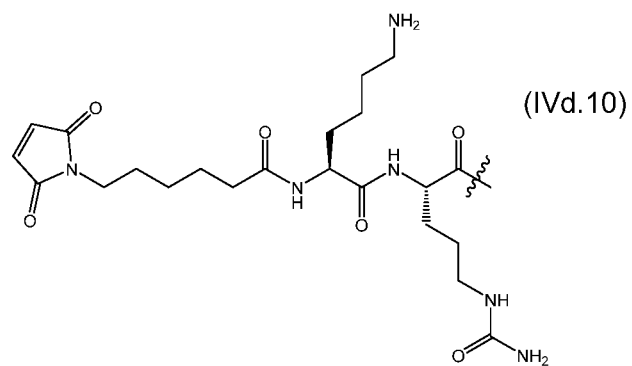
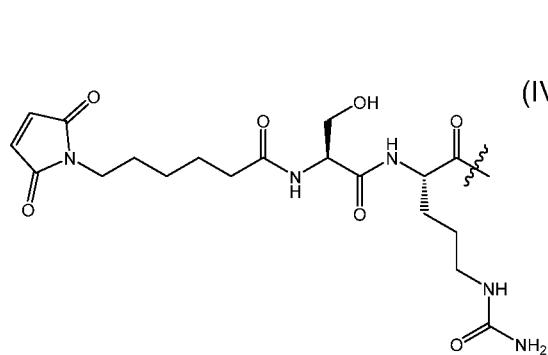
or a salt thereof, wherein: peptide represents a peptide (illustrated C→N and not showing the carboxy and amino “termini”) cleavable by a lysosomal enzyme; T represents a polymer comprising one or more ethylene glycol units or an alkylene chain, or combinations thereof; R^a is selected from hydrogen, alkyl, sulfonate and methyl sulfonate; p is an integer ranging from 0 to 5; q is 0 or 1; x is 0 or 1; y is 0 or 1; $\times$ represents the point of attachment of the ADC linker to a cytotoxic and/or cytostatic agent; and * represents the point of attachment to the remainder of the ADC linker.

[0448] Specific exemplary embodiments of ADC linkers according to structural formula (IVc) that may be included in the ADCs of the disclosure include the ADC linkers illustrated below (as illustrated, the ADC linkers include a group suitable for covalently linking the ADC linker to a TBM):



[0449] Specific exemplary embodiments of ADC linkers according to structural formula (IVd) that may be included in the ADCs of the disclosure include the ADC linkers illustrated below (as illustrated, the ADC linkers include a group suitable for covalently linking the ADC linker to a TBM):





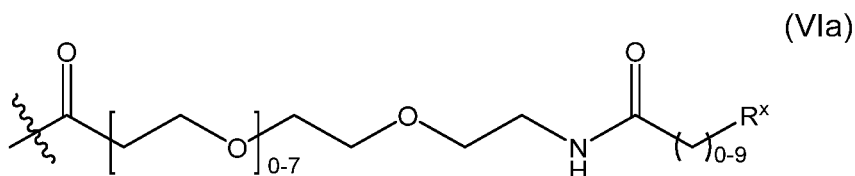
[0450] In certain embodiments, the ADC linker comprising structural formula (IVa), (IVb), (IVc), or (IVd) further comprises a carbonate moiety cleavable by exposure to an acidic medium. In particular embodiments, the ADC linker is attached through an oxygen to a cytotoxic and/or cytostatic agent.

6.9.2.2. Non-Cleavable Linkers

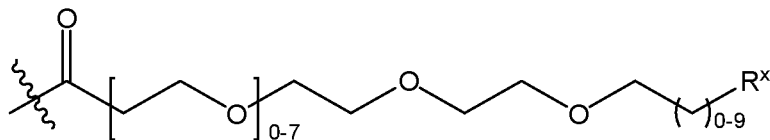
[0451] Although cleavable ADC linkers may provide certain advantages, the ADC linkers comprising the ADCs of the disclosure need not be cleavable. For noncleavable ADC linkers, the release of drug does not depend on the differential properties between the plasma and some cytoplasmic compartments. The release of the drug is postulated to occur after internalization of the ADC via antigen-mediated endocytosis and delivery to lysosomal compartment, where the TBM is degraded to the level of amino acids through intracellular proteolytic degradation. This process releases a drug derivative, which is formed by the drug, the ADC linker, and the amino acid residue to which the ADC linker was covalently attached. The amino acid drug metabolites from conjugates with noncleavable ADC linkers are more hydrophilic and generally less membrane permeable, which leads to less bystander effects and less nonspecific toxicities compared to conjugates with a cleavable ADC linker. In general, ADCs with noncleavable ADC linkers have greater stability in circulation than ADCs with cleavable ADC linkers. Non-cleavable ADC linkers may be alkylene chains, or maybe polymeric in natures, such as, for example, based upon polyalkylene glycol polymers, amide polymers, or may include segments of alkylene chains, polyalkylene glycols and/or amide polymers.

[0452] A variety of non-cleavable ADC linkers used to link drugs to TBMs have been described. See, Jeffrey *et al.*, 2006, Bioconjug. Chem. 17; 831-840; Jeffrey *et al.*, 2007, Bioorg. Med. Chem. Lett. 17:2278-2280; and Jiang *et al.*, 2005, J. Am. Chem. Soc. 127:11254-11255, each of which is incorporated herein by reference. All of these ADC linkers may be included in the ADCs of the disclosure.

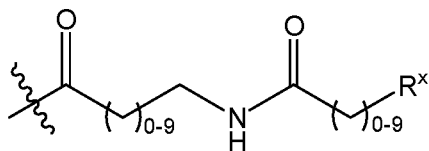
[0453] In certain embodiments, the ADC linker is non-cleavable *in vivo*, for example an ADC linker according to structural formula (VIa), (VIb), (VIc) or (VI d) (as illustrated, the ADC linkers include a group suitable for covalently linking the ADC linker to a TBM:



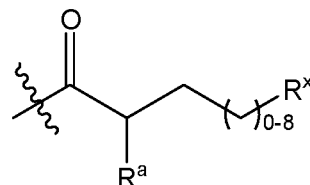
(Vlb)



(Vlc)



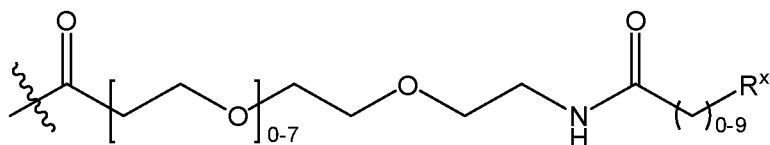
(Vld)



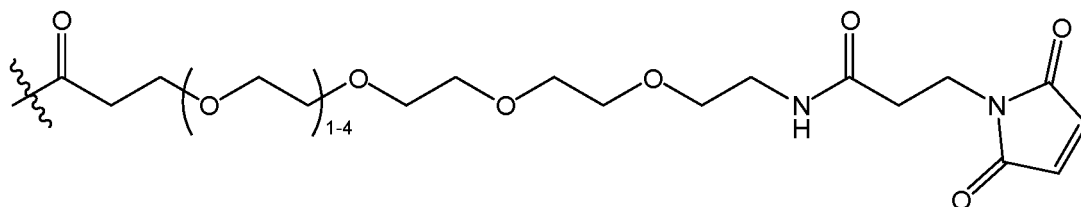
or salts thereof, wherein: R^a is selected from hydrogen, alkyl, sulfonate and methyl sulfonate; R^x is a moiety including a functional group capable of covalently linking the ADC linker to a TBM; and  represents the point of attachment of the ADC linker to a cytotoxic and/or cytostatic agent.

[0454] Specific exemplary embodiments of ADC linkers according to structural formula (Vla)-(Vld) that may be included in the ADCs of the disclosure include the ADC linkers illustrated below (as illustrated, the ADC linkers include a group suitable for covalently linking the ADC linker to a TBM, and  represents the point of attachment to a cytotoxic and/or cytostatic agent):

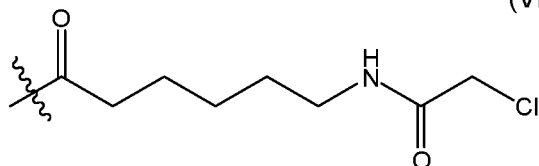
(Vla)



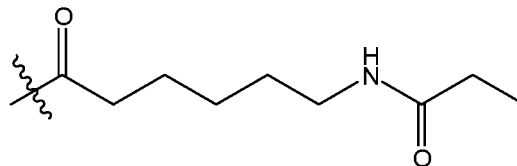
(Vla.1)

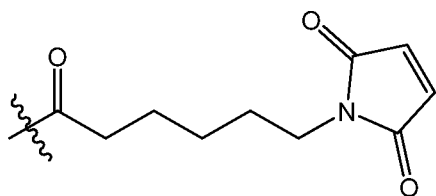


(Vlc.1)

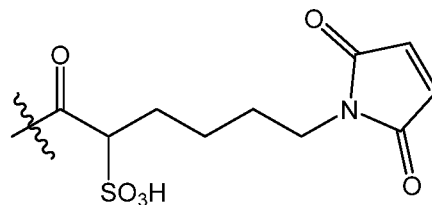


(Vlc.2)

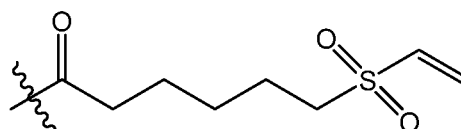




(Vld.1)



(Vld.2)



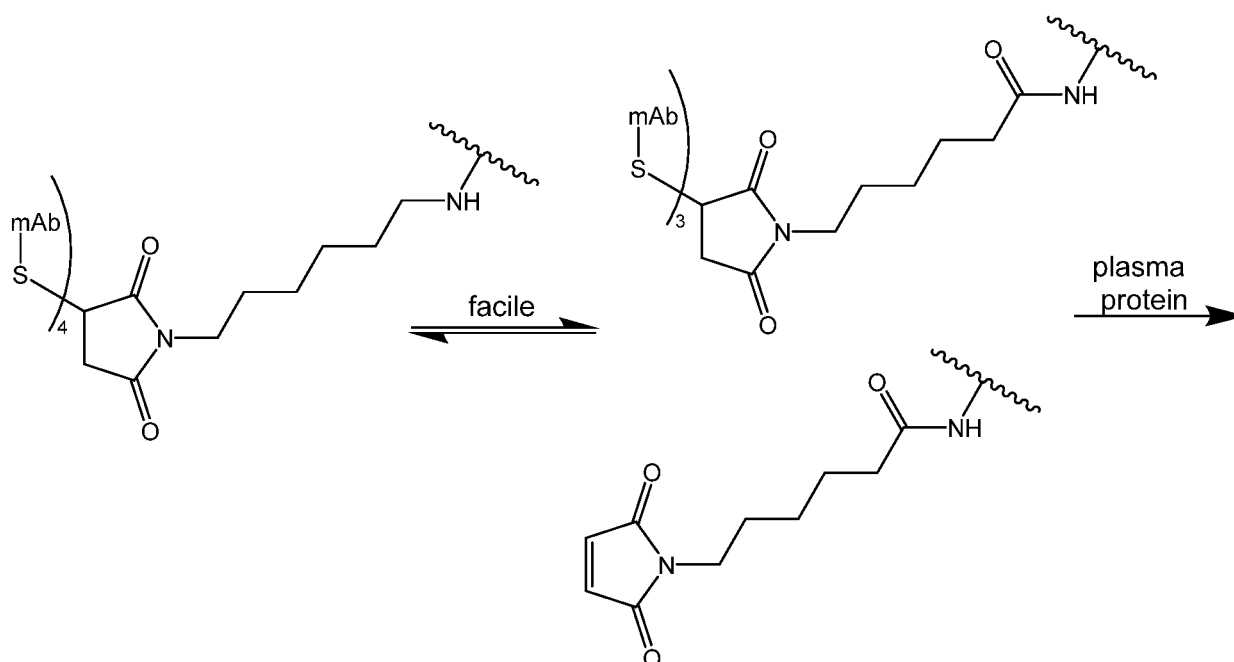
(Vld.3)

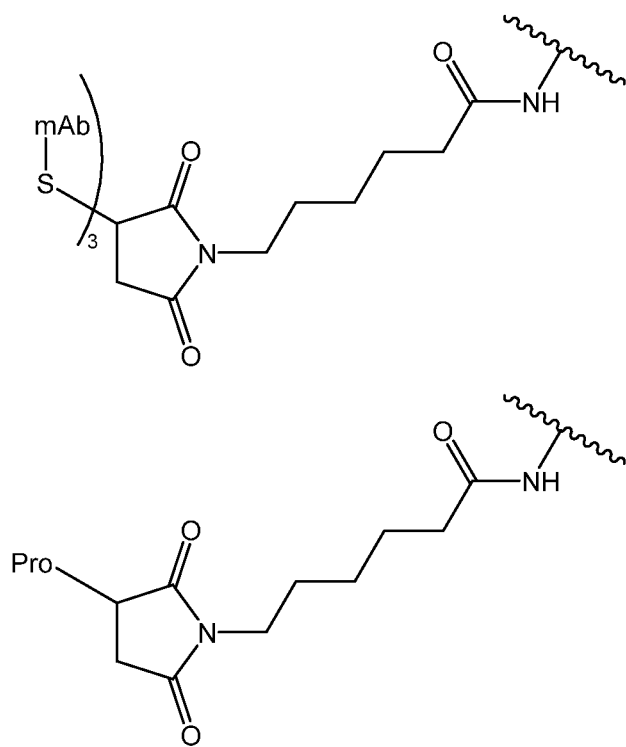
6.9.2.3. Groups Used to Attach Linkers to TBMs

[0455] A variety of groups may be used to attach ADC linker-drug synthons to TBMs to yield ADCs. Attachment groups can be electrophilic in nature and include: maleimide groups, activated disulfides, active esters such as NHS esters and HOBt esters, haloformates, acid halides, alkyl and benzyl halides such as haloacetamides. As discussed below, there are also emerging technologies related to “self-stabilizing” maleimides and “bridging disulfides” that can be used in accordance with the disclosure. The specific group used will depend, in part, on the site of attachment to the TBM.

[0456] One example of a “self-stabilizing” maleimide group that hydrolyzes spontaneously under TBM conjugation conditions to give an ADC species with improved stability is depicted in the schematic below. See US20130309256 A1; also Lyon *et al.*, Nature Biotech published online, doi:10.1038/nbt.2968.

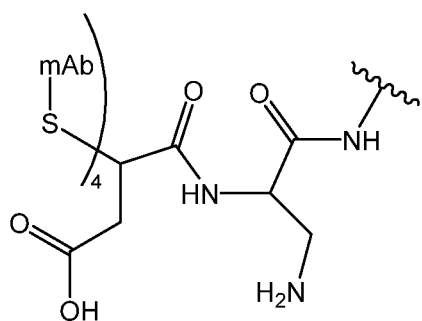
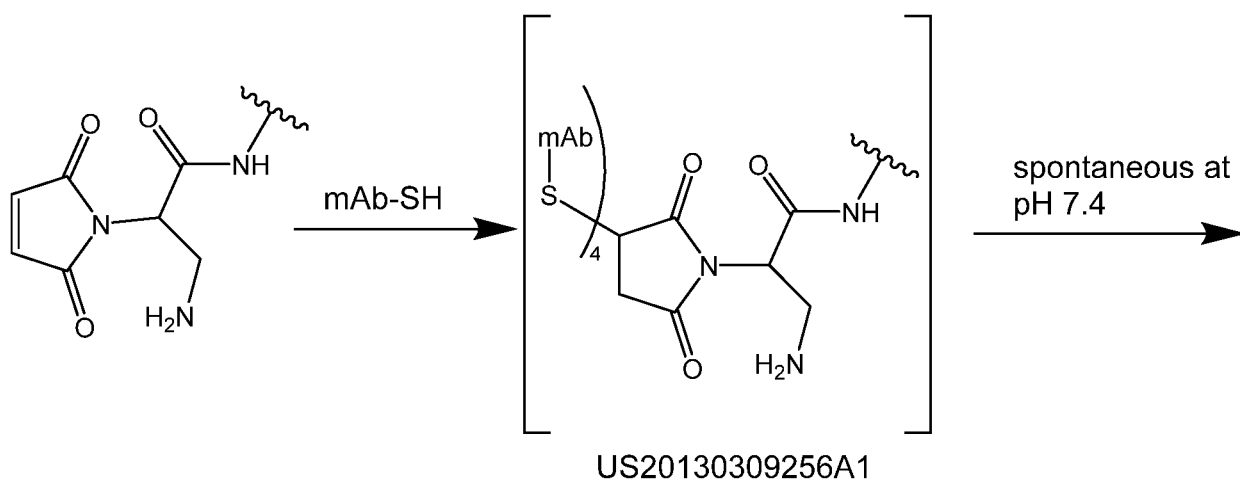
Normal system:





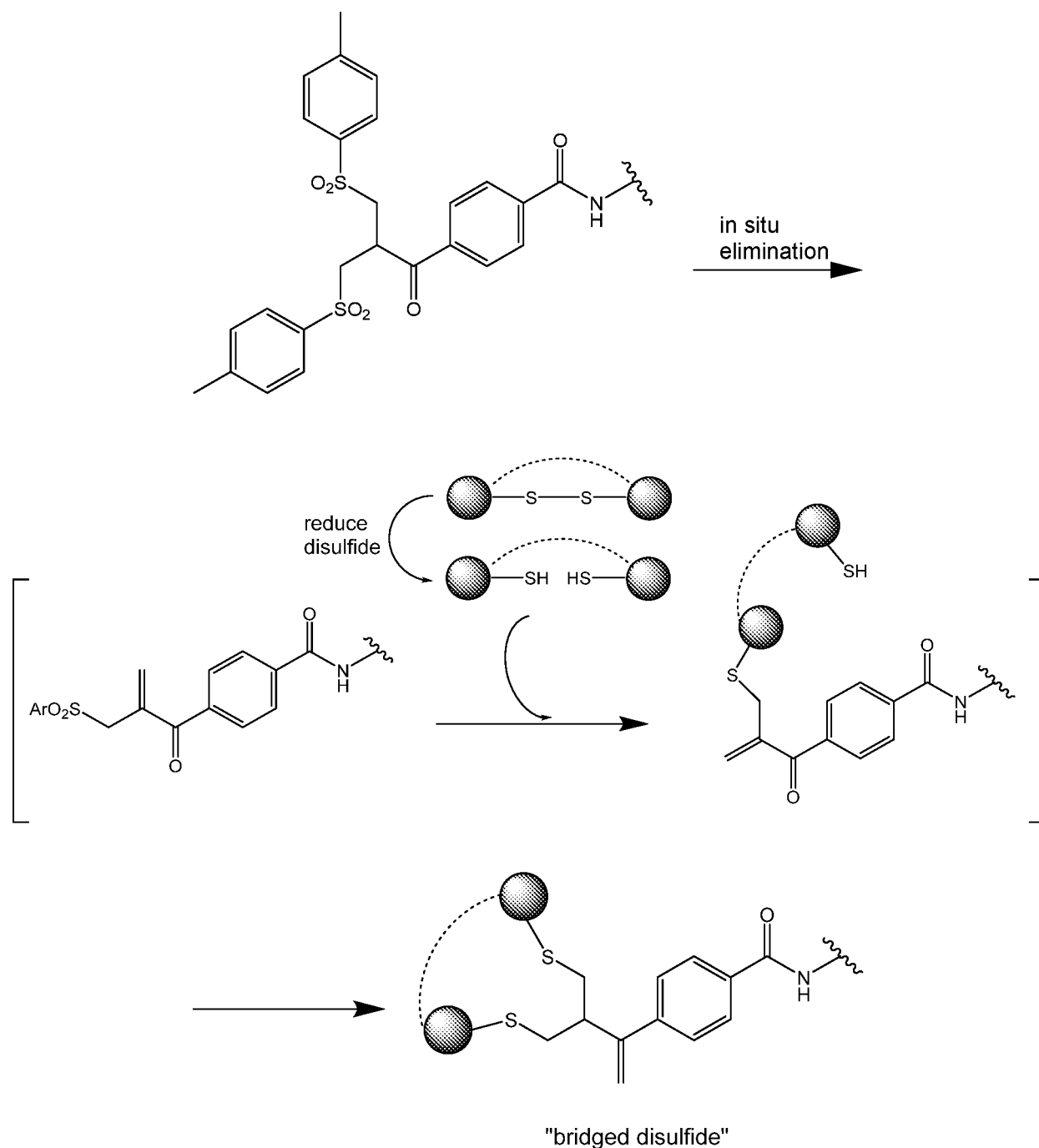
Leads to "DAR loss" over time

SGN MaIDPR (maleimido dipropylamino) system:

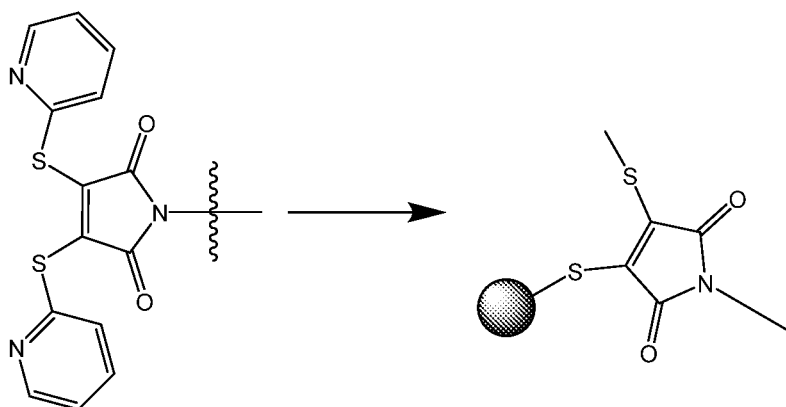


stable in plasma
(retro hetero-Michael
reaction shown above slow)

[0457] Polytherics has disclosed a method for bridging a pair of sulfhydryl groups derived from reduction of a native hinge disulfide bond. See, Badescu *et al.*, 2014, Bioconjugate Chem. 25:1124-1136. The reaction is depicted in the schematic below. An advantage of this methodology is the ability to synthesize enriched DAR4 ADCs by full reduction of IgGs (to give 4 pairs of sulfhydryls) followed by reaction with 4 equivalents of the alkylating agent. ADCs containing "bridged disulfides" are also said to have increased stability.



[0458] Similarly, as depicted below, a maleimide derivative (1, below) that is capable of bridging a pair of sulfhydryl groups has been developed. See WO2013/085925.



6.9.2.4. ADC Linker Selection Considerations

[0459] As is known by skilled artisans, the ADC linker selected for a particular ADC may be influenced by a variety of factors, including but not limited to, the site of attachment to the TBM (e.g., lys, cys or other amino acid residues), structural constraints of the drug pharmacophore and the lipophilicity of the drug. The specific ADC linker selected for an ADC should seek to balance these different factors for the specific TBM/drug combination. For a review of the factors that are influenced by choice of ADC linkers in ADCs, see Nolting, Chapter 5 “Linker Technology in Antibody-Drug Conjugates,” In: *Antibody-Drug Conjugates: Methods in Molecular Biology*, vol. 1045, pp. 71-100, Laurent Ducry (Ed.), Springer Science & Business Media, LLC, 2013.

[0460] For example, ADCs have been observed to effect killing of bystander antigen-negative cells present in the vicinity of the antigen-positive tumor cells. The mechanism of bystander cell killing by ADCs has indicated that metabolic products formed during intracellular processing of the ADCs may play a role. Neutral cytotoxic metabolites generated by metabolism of the ADCs in antigen-positive cells appear to play a role in bystander cell killing while charged metabolites may be prevented from diffusing across the membrane into the medium and therefore cannot affect bystander killing. In certain embodiments, the ADC linker is selected to attenuate the bystander killing effect caused by cellular metabolites of the ADC. In certain embodiments, the ADC linker is selected to increase the bystander killing effect.

[0461] The properties of the ADC linker may also impact aggregation of the ADC under conditions of use and/or storage. Typically, ADCs reported in the literature contain no more than 3-4 drug molecules per antibody molecule (see, e.g., Chari, 2008, *Acc Chem Res* 41:98-107). Attempts to obtain higher drug-to-antibody ratios (“DAR”) often failed, particularly if both the drug and the ADC linker were hydrophobic, due to aggregation of the ADC (King *et al.*, 2002, *J Med Chem* 45:4336-4343; Hollander *et al.*, 2008, *Bioconjugate Chem* 19:358-361; Burke *et al.*, 2009 *Bioconjugate Chem* 20:1242-1250). In many instances, DARs higher than 3-4 could be beneficial as a means of increasing potency. In instances where the cytotoxic and/or

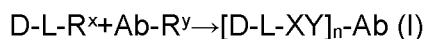
cytostatic agent is hydrophobic in nature, it may be desirable to select ADC linkers that are relatively hydrophilic as a means of reducing ADC aggregation, especially in instances where DARS greater than 3-4 are desired. Thus, in certain embodiments, the ADC linker incorporates chemical moieties that reduce aggregation of the ADCs during storage and/or use. An ADC linker may incorporate polar or hydrophilic groups such as charged groups or groups that become charged under physiological pH to reduce the aggregation of the ADCs. For example, an ADC linker may incorporate charged groups such as salts or groups that deprotonate, *e.g.*, carboxylates, or protonate, *e.g.*, amines, at physiological pH.

[0462] Exemplary polyvalent ADC linkers that have been reported to yield DARs as high as 20 that may be used to link numerous cytotoxic and/or cytostatic agents to a TBM are described in WO 2009/073445; WO 2010/068795; WO 2010/138719; WO 2011/120053; WO 2011/171020; WO 2013/096901; WO 2014/008375; WO 2014/093379; WO 2014/093394; WO 2014/093640, the content of which are incorporated herein by reference in their entireties.

[0463] In particular embodiments, the aggregation of the ADCs during storage or use is less than about 10% as determined by size-exclusion chromatography (SEC). In particular embodiments, the aggregation of the ADCs during storage or use is less than 10%, such as less than about 5%, less than about 4%, less than about 3%, less than about 2%, less than about 1%, less than about 0.5%, less than about 0.1%, or even lower, as determined by size-exclusion chromatography (SEC).

6.9.3. Methods of Making ADCs

[0464] The ADCs of the disclosure may be synthesized using chemistries that are well-known. The chemistries selected will depend upon, among other things, the identity of the cytotoxic and/or cytostatic agent(s), the ADC linker and the groups used to attach ADC linker to the TBM. Generally, ADCs according to formula (I) may be prepared according to the following scheme:



[0465] where D, L, Ab, XY and n are as previously defined, and R^x and R^y represent complementary groups capable of forming a covalent linkages with one another, as discussed above.

[0466] The identities of groups R^x and R^y will depend upon the chemistry used to link synthon D-L- R^x to the TBM. Generally, the chemistry used should not alter the integrity of the TBM, for example its ability to bind its target. Preferably, the binding properties of the conjugated antibody will closely resemble those of the unconjugated TBM. A variety of chemistries and techniques for conjugating molecules to biological molecules and in particular to immunoglobulins, whose components are typically building blocks of the TBMs of the disclosure, are well-known. See, *e.g.*, Amon *et al.*, "Monoclonal Antibodies For

Immunotargeting Of Drugs In Cancer Therapy,” in: Monoclonal Antibodies And Cancer Therapy, Reisfeld *et al.* Eds., Alan R. Liss, Inc., 1985; Hellstrom *et al.*, “Antibodies For Drug Delivery,” in: Controlled Drug Delivery, Robinson *et al.* Eds., Marcel Dekker, Inc., 2nd Ed. 1987; Thorpe, “Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review,” in: Monoclonal Antibodies '84: Biological And Clinical Applications, Pinchera *et al.*, Eds., 1985; “Analysis, Results, and Future Prospective of the Therapeutic Use of Radiolabeled Antibody In Cancer Therapy,” in: Monoclonal Antibodies For Cancer Detection And Therapy, Baldwin *et al.*, Eds., Academic Press, 1985; Thorpe *et al.*, 1982, Immunol. Rev. 62:119-58; PCT publication WO 89/12624. Any of these chemistries may be used to link the synthons to a TBM.

[0467] A number of functional groups R^x and chemistries useful for linking synthons to accessible lysine residues are known, and include by way of example and not limitation NHS-esters and isothiocyanates.

[0468] A number of functional groups R^x and chemistries useful for linking synthons to accessible free sulfhydryl groups of cysteine residues are known, and include by way of example and not limitation haloacetyls and maleimides.

[0469] However, conjugation chemistries are not limited to available side chain groups. Side chains such as amines may be converted to other useful groups, such as hydroxyls, by linking an appropriate small molecule to the amine. This strategy can be used to increase the number of available linking sites on the antibody by conjugating multifunctional small molecules to side chains of accessible amino acid residues of the TBM. Functional groups R^x suitable for covalently linking the synthons to these “converted” functional groups are then included in the synthons.

[0470] The TBM may also be engineered to include amino acid residues for conjugation. An approach for engineering TBMs to include non-genetically encoded amino acid residues useful for conjugating drugs in the context of ADCs is described by Axup *et al.*, 2012, Proc Natl Acad Sci USA. 109(40):16101-16106, as are chemistries and functional group useful for linking synthons to the non-encoded amino acids.

[0471] Typically, the synthons are linked to the side chains of amino acid residues of the TBM, including, for example, the primary amino group of accessible lysine residues or the sulfhydryl group of accessible cysteine residues. Free sulfhydryl groups may be obtained by reducing interchain disulfide bonds.

[0472] For linkages where R^y is a sulfhydryl group (for example, when R^x is a maleimide), the TBM is generally first fully or partially reduced to disrupt interchain disulfide bridges between cysteine residues.

[0473] Cysteine residues that do not participate in disulfide bridges may be engineered into a TBM by modification of one or more codons. Reducing these unpaired cysteines yields a sulfhydryl group suitable for conjugation. Preferred positions for incorporating engineered cysteines include, by way of example and not limitation, positions S112C, S113C, A114C, S115C, A176C, 5180C, S252C, V286C, V292C, S357C, A359C, S398C, S428C (Kabat numbering) on the human IgG₁ heavy chain and positions V110C, S114C, S121C, S127C, S168C, V205C (Kabat numbering) on the human Ig kappa light chain (see, e.g., U.S. Pat. No. 7,521,541, U.S. Pat. No. 7,855,275 and U.S. Pat. No. 8,455,622).

[0474] As will be appreciated by skilled artisans, the number of cytotoxic and/or cytostatic agents linked to a TBM molecule may vary, such that a collection of ADCs may be heterogeneous in nature, where some TBMs contain one linked agent, some two, some three, *etc.* (and some none). The degree of heterogeneity will depend upon, among other things, the chemistries used for linking the cytotoxic and/or cytostatic agents. For example, where the TBMs are reduced to yield sulfhydryl groups for attachment, heterogeneous mixtures of TBMs having zero, 2, 4, 6 or 8 linked agents per molecule are often produced. Furthermore, by limiting the molar ratio of attachment compound, TBMs having zero, 1, 2, 3, 4, 5, 6, 7 or 8 linked agents per molecule are often produced. Thus, it will be understood that depending upon context, stated drug TBM ratios (DTRs) may be averages for a collection of TBMs. For example, "DTR4" can refer to an ADC preparation that has not been subjected to purification to isolate specific DTR peaks and can comprise a heterogeneous mixture of ADC molecules having different numbers of cytostatic and/or cytotoxic agents attached per TBM (e.g., 0, 2, 4, 6, 8 agents per TBM), but has an average drug-to-TBM ratio of 4. Similarly, in some embodiments, "DTR2" refers to a heterogeneous ADC preparation in which the average drug-to-TBM ratio is 2.

[0475] When enriched preparations are desired, TBMs having defined numbers of linked cytotoxic and/or cytostatic agents may be obtained via purification of heterogeneous mixtures, for example, via column chromatography, e.g., hydrophobic interaction chromatography.

[0476] Purity may be assessed by a variety of methods, as is known in the art. As a specific example, an ADC preparation may be analyzed via HPLC or other chromatography and the purity assessed by analyzing areas under the curves of the resultant peaks.

6.10. Preparations

[0477] The disclosure provides preparations comprising a plurality of TBMs and/or a plurality of TBM conjugates, e.g., at least 100, at least 1,000, at least 10,000, or at least 100,000 TBMs and/or TBM conjugates. Preparations include, for example, cell culture supernatants comprising TBM molecules and compositions of enriched or purified TBM molecules (e.g., TBMs fractionated or purified from a cell culture supernatant).

[0478] Preparations can comprise, for example, a plurality of TBMs or conjugates wherein at least 50% (*e.g.*, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 97%, at least 98%, at least 99%) of the trispecific molecules in the preparation have the same primary amino acid sequence. In various embodiments, 50% to 99% of the trispecific molecules in a preparation have the same primary amino acid sequence (*e.g.*, 50% to 95%, 50% to 80%, 50% to 70%, 60% to 95%, 60% to 80%, 60% to 70%, 70% to 95%, 70% to 80%, 80% to 95%, 95% to 99%, or any range bounded by any two of the foregoing values).

[0479] In some embodiments, a majority of the the trispecific molecules in a preparation have the same interchain crosslinks (*e.g.*, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 97%, at least 98%, or at least 99%). As used herein, an “interchain crosslink” refers to a crosslink between two linear polypeptide chains, *e.g.*, crosslinks created by disulfide bridges. In various embodiments, 50% to 99% of the trispecific molecules in a preparation have the same interchain crosslinks (*e.g.*, 50% to 95%, 50% to 80%, 50% to 70%, 60% to 95%, 60% to 80%, 60% to 70%, 70% to 95%, 70% to 80%, 80% to 95%, 95% to 99%, or any range bounded by any two of the foregoing values).

[0480] In some embodiments, a majority of the the trispecific molecules in a preparation have the same ABM1:ABM2:ABM3 ratio (*e.g.*, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 97%, at least 98%, or at least 99%). In various embodiments, 50% to 99% of the trispecific molecules in a preparation have the same ABM1:ABM2:ABM3 ratio (*e.g.*, 50% to 95%, 50% to 80%, 50% to 70%, 60% to 95%, 60% to 80%, 60% to 70%, 70% to 95%, 70% to 80%, 80% to 95%, 95% to 99%, or any range bounded by any two of the foregoing values).

6.11. Pharmaceutical compositions

[0481] The TBMs of the disclosure (as well as their conjugates; references to TBMs in this disclosure also refers to conjugates comprising the TBMs, such as ADCs, unless the context dictates otherwise) can be formulated as pharmaceutical compositions comprising the TBMs, for example containing one or more pharmaceutically acceptable excipients or carriers. To prepare pharmaceutical or sterile compositions comprising the TBMs of the present disclosure a TBM preparation can be combined with one or more pharmaceutically acceptable excipient or carrier.

[0482] For example, formulations of TBMs can be prepared by mixing TBMs with physiologically acceptable carriers, excipients, or stabilizers in the form of, *e.g.*, lyophilized powders, slurries, aqueous solutions, lotions, or suspensions (see, *e.g.*, Hardman *et al.*, 2001, Goodman and Gilman's The Pharmacological Basis of Therapeutics, McGraw-Hill, New York, N.Y.; Gennaro, 2000, Remington: The Science and Practice of Pharmacy, Lippincott, Williams, and Wilkins, New York, N.Y.; Avis, *et al.* (eds.), 1993, Pharmaceutical Dosage Forms: General

Medications, Marcel Dekker, NY; Lieberman, *et al.* (eds.), 1990, Pharmaceutical Dosage Forms: Tablets, Marcel Dekker, NY; Lieberman, *et al.* (eds.), 1990, Pharmaceutical Dosage Forms: Disperse Systems, Marcel Dekker, NY; Weiner and Kotkoskie, 2000, Excipient Toxicity and Safety, Marcel Dekker, Inc., New York, N.Y.).

[0483] Selecting an administration regimen for a TBM depends on several factors, including the serum or tissue turnover rate of the TBM, the level of symptoms, the immunogenicity of the TBM, and the accessibility of the target cells. In certain embodiments, an administration regimen maximizes the amount of TBM delivered to the subject consistent with an acceptable level of side effects. Accordingly, the amount of TBM delivered depends in part on the particular TBM and the severity of the condition being treated. Guidance in selecting appropriate doses of antibodies and small molecules are available (see, e.g., Wawrzynczak, 1996, Antibody Therapy, Bios Scientific Pub. Ltd, Oxfordshire, UK; Kresina (ed.), 1991, Monoclonal Antibodies, Cytokines and Arthritis, Marcel Dekker, New York, N.Y.; Bach (ed.), 1993, Monoclonal Antibodies and Peptide Therapy in Autoimmune Diseases, Marcel Dekker, New York, N.Y.; Baert *et al.*, 2003, New Engl. J. Med. 348:601-608; Milgrom *et al.*, 1999, New Engl. J. Med. 341:1966-1973; Slamon *et al.*, 2001, New Engl. J. Med. 344:783-792; Beniaminovitz *et al.*, 2000, New Engl. J. Med. 342:613-619; Ghosh *et al.*, 2003, New Engl. J. Med. 348:24-32; Lipsky *et al.*, 2000, New Engl. J. Med. 343:1594-1602).

[0484] Determination of the appropriate dose is made by the clinician, e.g., using parameters or factors known or suspected in the art to affect treatment or predicted to affect treatment. Generally, the dose begins with an amount somewhat less than the optimum dose and it is increased by small increments thereafter until the desired or optimum effect is achieved relative to any negative side effects. Important diagnostic measures include those of symptoms of, e.g., the inflammation or level of inflammatory cytokines produced.

[0485] Actual dosage levels of the TBMs in the pharmaceutical compositions of the present disclosure may be varied so as to obtain an amount of the TBM which is effective to achieve the desired therapeutic response for a particular subject, composition, and mode of administration, without being toxic to the subject. The selected dosage level will depend upon a variety of pharmacokinetic factors including the activity of the particular TBM, the route of administration, the time of administration, the rate of excretion of the particular TBM being employed, the duration of the treatment, other agents (e.g., active agents such as therapeutic drugs or compounds and/or inert materials used as carriers) in combination with the particular TBM employed, the age, sex, weight, condition, general health and prior medical history of the subject being treated, and like factors known in the medical arts.

[0486] Compositions comprising the TBMs of the disclosure can be provided by continuous infusion, or by doses at intervals of, e.g., one day, one week, or 1-7 times per week. Doses can

be provided intravenously, subcutaneously, topically, orally, nasally, rectally, intramuscular, intracerebrally, or by inhalation. A specific dose protocol is one involving the maximal dose or dose frequency that avoids significant undesirable side effects.

[0487] An effective amount for a particular subject may vary depending on factors such as the condition being treated, the overall health of the subject, the method route and dose of administration and the severity of side effects (see, *e.g.*, Maynard, *et al.* (1996) A Handbook of SOPs for Good Clinical Practice, Interpharm Press, Boca Raton, Fla.; Dent (2001) Good Laboratory and Good Clinical Practice, Urch Publ., London, UK).

[0488] The route of administration may be by, *e.g.*, topical or cutaneous application, injection or infusion by intravenous, intraperitoneal, intracerebral, intramuscular, intraocular, intraarterial, intracerebrospinal, intralesional, or by sustained release systems or an implant (see, *e.g.*, Sidman *et al.*, 1983, Biopolymers 22:547-556; Langer *et al.*, 1981, J. Biomed. Mater. Res. 15:167-277; Langer, 1982, Chem. Tech. 12:98-105; Epstein *et al.*, 1985, Proc. Natl. Acad. Sci. USA 82:3688-3692; Hwang *et al.*, 1980, Proc. Natl. Acad. Sci. USA 77:4030-4034; U.S. Pat. Nos. 6,350,466 and 6,316,024). Where necessary, the composition may also include a solubilizing agent and a local anesthetic such as lidocaine to ease pain at the site of the injection. In addition, pulmonary administration can also be employed, *e.g.*, by use of an inhaler or nebulizer, and formulation with an aerosolizing agent. See, *e.g.*, U.S. Pat. Nos. 6,019,968, 5,985,320, 5,985,309, 5,934,272, 5,874,064, 5,855,913, 5,290,540, and 4,880,078; and PCT Publication Nos. WO 92/19244, WO 97/32572, WO 97/44013, WO 98/31346, and WO 99/66903, each of which is incorporated herein by reference their entirety.

[0489] A composition of the present disclosure may also be administered via one or more routes of administration using one or more of a variety of methods known in the art. As will be appreciated by the skilled artisan, the route and/or mode of administration will vary depending upon the desired results. Selected routes of administration for TBMs include intravenous, intramuscular, intradermal, intraperitoneal, subcutaneous, spinal or other general routes of administration, for example by injection or infusion. General administration may represent modes of administration other than enteral and topical administration, usually by injection, and includes, without limitation, intravenous, intramuscular, intraarterial, intrathecal, intracapsular, intraorbital, intracardiac, intradermal, intraperitoneal, transtracheal, subcutaneous, subcuticular, intraarticular, subcapsular, subarachnoid, intraspinal, epidural and intrasternal injection and infusion. Alternatively, a composition of the disclosure can be administered via a non-general route, such as a topical, epidermal or mucosal route of administration, for example, intranasally, orally, vaginally, rectally, sublingually or topically. In one embodiment, the TBMs is administered by infusion. In another embodiment, the multispecific epitope binding protein of the disclosure is administered subcutaneously.

[0490] If the TBMs are administered in a controlled release or sustained release system, a pump may be used to achieve controlled or sustained release (see Langer, *supra*; Sefton, 1987, CRC Crit. Ref Biomed. Eng. 14:20; Buchwald *et al.*, 1980, Surgery 88:507; Saudek *et al.*, 1989, N. Engl. J. Med. 321:574). Polymeric materials can be used to achieve controlled or sustained release of the therapies of the disclosure (see, e.g., Medical Applications of Controlled Release, Langer and Wise (eds.), CRC Pres., Boca Raton, Fla. (1974); Controlled Drug Bioavailability, Drug Product Design and Performance, Smolen and Ball (eds.), Wiley, New York (1984); Ranger and Peppas, 1983, J., Macromol. Sci. Rev. Macromol. Chem. 23:61; see also Levy *et al.*, 1985, Science 228:190; During *et al.*, 1989, Ann. Neurol. 25:351; Howard *et al.*, 1989, J. Neurosurg. 71:105); U.S. Pat. No. 5,679,377; U.S. Pat. No. 5,916,597; U.S. Pat. No. 5,912,015; U.S. Pat. No. 5,989,463; U.S. Pat. No. 5,128,326; PCT Publication No. WO 99/15154; and PCT Publication No. WO 99/20253. Examples of polymers used in sustained release formulations include, but are not limited to, poly(2-hydroxy ethyl methacrylate), poly(methyl methacrylate), poly(acrylic acid), poly(ethylene-co-vinyl acetate), poly(methacrylic acid), polyglycolides (PLG), polyanhydrides, poly(N-vinyl pyrrolidone), poly(vinyl alcohol), polyacrylamide, poly(ethylene glycol), polylactides (PLA), poly(lactide-co-glycolides) (PLGA), and polyorthoesters. In one embodiment, the polymer used in a sustained release formulation is inert, free of leachable impurities, stable on storage, sterile, and biodegradable. A controlled or sustained release system can be placed in proximity of the prophylactic or therapeutic target, thus requiring only a fraction of the systemic dose (see, e.g., Goodson, in Medical Applications of Controlled Release, *supra*, vol. 2, pp. 115-138 (1984)).

[0491] Controlled release systems are discussed in the review by Langer (1990, Science 249:1527-1533). Any technique known to one of skill in the art can be used to produce sustained release formulations comprising one or more TBMs of the disclosure. See, e.g., U.S. Pat. No. 4,526,938, PCT publication WO 91/05548, PCT publication WO 96/20698, Ning *et al.*, 1996, Radiotherapy & Oncology 39:179-189, Song *et al.*, 1995, PDA Journal of Pharmaceutical Science & Technology 50:372-397, Cleek *et al.*, 1997, Pro. Int'l. Symp. Control. Rel. Bioact. Mater. 24:853-854, and Lam *et al.*, 1997, Proc. Int'l. Symp. Control Rel. Bioact. Mater. 24:759-760, each of which is incorporated herein by reference in their entirety.

[0492] If the TBMs are administered topically, they can be formulated in the form of an ointment, cream, transdermal patch, lotion, gel, shampoo, spray, aerosol, solution, emulsion, or other form well-known to one of skill in the art. See, e.g., Remington's Pharmaceutical Sciences and Introduction to Pharmaceutical Dosage Forms, 19th ed., Mack Pub. Co., Easton, Pa. (1995). For non-sprayable topical dosage forms, viscous to semi-solid or solid forms comprising a carrier or one or more excipients compatible with topical application and having a dynamic viscosity, in some instances, greater than water are typically employed. Suitable formulations include, without limitation, solutions, suspensions, emulsions, creams, ointments,

powders, liniments, salves, and the like, which are, if desired, sterilized or mixed with auxiliary agents (e.g., preservatives, stabilizers, wetting agents, buffers, or salts) for influencing various properties, such as, for example, osmotic pressure. Other suitable topical dosage forms include sprayable aerosol preparations wherein the active ingredient, in some instances, in combination with a solid or liquid inert carrier, is packaged in a mixture with a pressurized volatile (e.g., a gaseous propellant, such as freon) or in a squeeze bottle. Moisturizers or humectants can also be added to pharmaceutical compositions and dosage forms if desired. Examples of such additional ingredients are well-known in the art.

[0493] If the compositions comprising the TBMs are administered intranasally, the TBMs can be formulated in an aerosol form, spray, mist or in the form of drops. In particular, prophylactic or therapeutic agents for use according to the present disclosure can be conveniently delivered in the form of an aerosol spray presentation from pressurized packs or a nebulizer, with the use of a suitable propellant (e.g., dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, carbon dioxide or other suitable gas). In the case of a pressurized aerosol the dosage unit may be determined by providing a valve to deliver a metered amount. Capsules and cartridges (composed of, e.g., gelatin) for use in an inhaler or insufflator may be formulated containing a powder mix of the compound and a suitable powder base such as lactose or starch.

[0494] The TBMs of the disclosure can be administered in combination therapy regimens, as described in Section 6.13, *infra*.

[0495] In certain embodiments, the TBMs can be formulated to ensure proper distribution in vivo. For example, the blood-brain barrier (BBB) excludes many highly hydrophilic compounds. To ensure that the therapeutic compounds of the disclosure cross the BBB (if desired), they can be formulated, for example, in liposomes. For methods of manufacturing liposomes, see, e.g., U.S. Pat. Nos. 4,522,811; 5,374,548; and 5,399,331. The liposomes may comprise one or more moieties which are selectively transported into specific cells or organs, thus enhance targeted drug delivery (see, e.g., Ranade, 1989, J. Clin. Pharmacol. 29:685). Exemplary targeting moieties include folate or biotin (see, e.g., U.S. Pat. No. 5,416,016 to Low *et al.*); mannosides (Umezawa *et al.*, 1988, Biochem. Biophys. Res. Commun. 153:1038); antibodies (Bloeman *et al.*, 1995, FEBS Lett. 357:140; Owais *et al.*, 1995, Antimicrob. Agents Chemother. 39:180); surfactant protein A receptor (Briscoe *et al.*, 1995, Am. J. Physiol. 1233:134); p 120 (Schreier *et al.*, 1994, J. Biol. Chem. 269:9090); see also Keinanen and Laukkanen, 1994, FEBS Lett. 346:123; Killion and Fidler, 1994, Immunomethods 4:273.

[0496] When used in combination therapy, e.g., as described in Section 6.13, *infra*, a TBM of the disclosure and one or more additional agents can be administered to a subject in the same pharmaceutical composition. Alternatively, the TBM and the additional agent(s) of the

combination therapies can be administered concurrently to a subject in separate pharmaceutical compositions.

[0497] The therapeutic methods described herein may further comprise carrying a “companion diagnostic” test whereby a sample from a subject who is a candidate for therapy with a TBM of the disclosure is tested for the expression of the TAA targeted by ABM3. The companion diagnostic test can be performed prior to initiating therapy with a TBM of the disclosure and/or during a therapeutic regimen with a TBM of the disclosure to monitor the subject’s continued suitability for TBM therapy. The agent used in the companion diagnostic can be the TBM itself or another diagnostic agent, for example a labeled monospecific antibody against the TAA recognized by ABM3 or a nucleic acid probe to detect TAA RNA. The sample that can be tested in a companion diagnostic assay can be any sample in which the cells targeted by the TBM may be present, from example a tumor (e.g., a solid tumor) biopsy, lymph, stool, urine, blood or any other bodily fluid that might contain circulating tumor cells.

6.12. Therapeutic Indications

[0498] The TBMs of the disclosure can be used in the treatment of any proliferative disorder (e.g., cancer) that expresses a TAA. In particular embodiments, the cancer is HER2+ cancer, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), adrenocortical carcinoma, anal cancer, appendix cancer, astrocytoma, basal cell carcinoma, brain tumor, bile duct cancer, bladder cancer, bone cancer, breast cancer, bronchial tumor, Burkitt Lymphoma, carcinoma of unknown primary origin, cardiac tumor, cervical cancer, chordoma, chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), chronic myeloproliferative neoplasm, colon cancer, colorectal cancer, craniopharyngioma, cutaneous T-cell lymphoma, ductal carcinoma, embryonal tumor, endometrial cancer, ependymoma, esophageal cancer, esthesioneuroblastoma, fibrous histiocytoma, Ewing sarcoma, eye cancer, germ cell tumor, gallbladder cancer, gastric cancer, gastrointestinal carcinoid tumor, gastrointestinal stromal tumor, gestational trophoblastic disease, glioma, head and neck cancer, hairy cell leukemia, hepatocellular cancer, histiocytosis, Hodgkin lymphoma, hypopharyngeal cancer, intraocular melanoma, islet cell tumor, Kaposi sarcoma, kidney cancer, Langerhans cell histiocytosis, laryngeal cancer, leukemia, lip and oral cavity cancer, liver cancer, lobular carcinoma in situ, lung cancer, lymphoma, macroglobulinemia, malignant fibrous histiocytoma, melanoma, Merkel cell carcinoma, mesothelioma, metastatic squamous neck cancer with occult primary, midline tract carcinoma involving NUT gene, mouth cancer, multiple endocrine neoplasia syndrome, multiple myeloma, mycosis fungoides, myelodysplastic syndrome, myelodysplastic/myeloproliferative neoplasm, nasal cavity and para-nasal sinus cancer, nasopharyngeal cancer, neuroblastoma, non-Hodgkin lymphoma, non-small cell lung cancer, oropharyngeal cancer, osteosarcoma, ovarian cancer, pancreatic cancer, papillomatosis,

paraganglioma, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytomas, pituitary tumor, pleuropulmonary blastoma, primary central nervous system lymphoma, prostate cancer, rectal cancer, renal cell cancer, renal pelvis and ureter cancer, retinoblastoma, rhabdoid tumor, salivary gland cancer, Sezary syndrome, skin cancer, small cell lung cancer, small intestine cancer, soft tissue sarcoma, spinal cord tumor, stomach cancer, T-cell lymphoma, teratoid tumor, testicular cancer, throat cancer, thymoma and thymic carcinoma, thyroid cancer, urethral cancer, uterine cancer, vaginal cancer, vulvar cancer, or Wilms tumor.

[0499] Table 14 below shows exemplary indications that TBMs targeting particular TAAs can be used against.

TABLE 14 Examples of Tumor-Associated Antigen Indications	
Target	Exemplary Indication(s)
ADRB3	Ewing sarcoma
ALK	NSCLC, ALCL, IMT, neuroblastoma
B7H3	melanoma, osteosarcoma, leukemia, breast, prostate, ovarian, pancreatic, colorectal cancers
BCMA	multiple myeloma, leukemia (e.g., acute lymphoblastic leukemia ("ALL"), acute myeloid leukemia ("AML"), chronic lymphocytic leukemia ("CLL"), chronic myeloid leukemia ("CML") and hairy cell leukemia ("HCL")); lymphoma (e.g., Hodgkin's lymphoma, non-Hodgkin's lymphoma, including diffuse large B-cell lymphoma ("DLBCL"))
Cadherin 17	gastric, pancreatic, and colorectal adenocarcinomas
CAIX	clear-cell renal cell carcinoma, hypoxic solid tumors, head and neck squamous carcinoma
CD123	leukemia (e.g., ALL, CLL, AML, CML, HCL); lymphoma (e.g., Hodgkin's lymphoma, non-Hodgkin's lymphoma, e.g., DLBCL); multiple myeloma. In a preferred embodiment, the indication is AML.
CD171	neuroblastoma, paraganglioma
CD179a	B cell malignancies
CD19	leukemia (e.g., ALL, CLL, AML, CML, HCL); lymphoma (e.g., Hodgkin's lymphoma, non-Hodgkin's lymphoma, e.g., DLBCL); multiple myeloma.
CD20	leukemia (e.g., ALL, CLL, AML, CML, HCL); lymphoma (e.g., Hodgkin's lymphoma, non-Hodgkin's lymphoma, e.g., DLBCL); multiple myeloma.
CD22	leukemia (e.g., ALL, CLL, AML, CML, HCL); lymphoma (e.g., Hodgkin's lymphoma, non-Hodgkin's lymphoma, e.g., DLBCL); multiple myeloma; lung cancer
CD24	ovarian, breast, prostate, bladder, renal, non-small cell carcinomas
CD30	anaplastic large cell lymphoma, embryonal carcinoma, Hodgkin Lymphoma
CD32b	B cell malignancies, gastric, pancreatic, esophageal, glioblastoma, breast, colorectal
CD33	leukemia (e.g., ALL, CLL, AML, CML, HCL); lymphoma (e.g., Hodgkin's

TABLE 14 Examples of Tumor-Associated Antigen Indications	
Target	Exemplary Indication(s)
	lymphoma, non-Hodgkin's lymphoma, e.g., DLBCL); multiple myeloma. In a preferred embodiment, the indication is AML.
CD38	leukemia (e.g., ALL, CLL, AML, CML, HCL); lymphoma (e.g., Hodgkin's lymphoma, non-Hodgkin's lymphoma, e.g., DLBCL); multiple myeloma
CD44v6	colon cancer, head and neck small cell carcinoma
CD97	B cell malignancies, gastric, pancreatic, esophageal, glioblastoma, breast, colorectal
CEA	colorectal carcinoma, gastric carcinoma, pancreatic carcinoma, lung cancer, breast cancer, medullary thyroid carcinoma
CLDN6	ovarian, breast, lung cancer
CLL-1	leukemia (e.g., ALL, CLL, AML, CML, HCL); lymphoma (e.g., Hodgkin's lymphoma, non-Hodgkin's lymphoma, e.g., DLBCL); multiple myeloma. In a preferred embodiment, the indication is AML.
CS1	multiple myeloma
EGFR	squamous cell carcinoma of lung, anal cancer, glioblastoma, epithelial tumors of head and neck, colon cancer
EGFRvIII	Glioblastoma
EPCAM	gastrointestinal carcinoma, colorectal cancer
EphA2	kaposi's sarcoma, glioblastoma, solid tumors, glioma
Ephrin B2	thyroid cancer, breast cancer, malignant melanoma
ERBB2 (Her2/neu)	breast, ovarian, gastric cancers, lung adenocarcinoma, non-small cell lung cancer, uterine cancer, uterine serous endometrial carcinoma, salivary duct carcinoma,
FAP	pancreatic cancer, colorectal cancer, metastasis, epithelial cancers, soft tissue sarcomas
FCRL5	multiple myeloma
FLT3	leukemia (e.g., ALL, CLL, AML, CML, HCL); lymphoma (e.g., Hodgkin's lymphoma, non-Hodgkin's lymphoma, e.g., DLBCL); multiple myeloma. In a preferred embodiment, the indication is AML.
Folate receptor alpha	ovarian, breast, renal, lung, colorectal, brain cancers
Folate receptor beta	ovarian cancer
Fucosyl GM1	AML, myeloma
GD2	malignant melanoma, neuroblastoma
GD3	Melanoma
GloboH	ovarian, gastric, prostate, lung, breast, and pancreatic cancers
gp100	Melanoma

TABLE 14 Examples of Tumor-Associated Antigen Indications	
Target	Exemplary Indication(s)
GPNMB	breast cancer, head and neck cancers
GPR20	GIST
GPR64	Ewing sarcoma, prostate, kidney and lung sarcomas
GPRC5D	multiple myeloma
HAVCR1	renal cancer
HER3	colon and gastric cancers
HMWMAA	melanoma, glioblastoma, breast cancer
IGF-I receptor	breast, prostate, lung cancers
IL-11Ra	papillary thyroid cancer, osteosarcoma, colorectal adenocarcinoma, lymphocytic leukemia
IL-13Ra2	renal cell carcinoma, prostate cancer, gliomas, head and neck cancer, astrocytoma
KIT	myeloid leukemia, kaposi's sarcoma, erythroleukemia, gastrointestinal stromal tumors
KLRG2	breast cancers, lung cancers and ovarian cancers.
LewisY	squamous cell lung carcinoma, lung adenocarcinoma, ovarian carcinoma, and colorectal adenocarcinoma
LMP2	prostate cancer, Hodgkin's lymphoma, nasopharyngeal carcinoma
LRP6	breast cancer
LY6K	breast, lung, ovarian, and cervical cancer
LYPD8	colorectal and gastric cancers
Mesothelin	mesothelioma, pancreatic cancer, ovarian cancer, stomach cancer, lung cancer, endometrial cancer.
MUC1	breast and ovarian cancers, lung, stomach, pancreatic, prostate cancers
NCAM	melanoma, Wilms' tumor, small cell lung cancer, neuroblastoma, myeloma, paraganglioma, pancreatic acinar cell carcinoma, myeloid leukemia
NY-BR-1	breast cancer
o-acetyl GD2	neuroblastoma, melanoma
OR51E2	prostate cancer
PANX3	osteosarcoma
PLAC1	hepatocellular carcinoma
Polysialic acid	small cell lung cancer
PDGFR-beta	myelomonocytic leukemia, chronic myeloid leukemia, acute myelogenous leukemia, acute lymphoblastic leukemia
PRSS21	colon cancer, testicular cancer, ovarian cancer
PSCA	prostate cancer, gastric and bladder cancers

TABLE 14 Examples of Tumor-Associated Antigen Indications	
Target	Exemplary Indication(s)
PSMA	prostate cancer,
ROR1	metastatic cancers, chronic lymphocytic leukemia, solid tumors in lung, breast, ovarian, colon, pancreatic, sarcoma
SLC34A2	bladder cancer
SLC39A6	breast cancer, esophageal cancer
SLITRK6	breast cancer, urothelial cancer, lung cancer
SSEA-4	breast cancer, cancer stem cells, epithelial ovarian carcinoma
TACSTD2	carcinomas, e.g., non-small-cell lung cancer
TAG72	ovarian, breast, colon, lung, pancreatic cancers, gastric cancer
TEM1/CD248	colorectal cancer
TEM7R	colorectal cancer
Tn	colorectal, breast cancers, cervical, lung, stomach cancers
TSHR	thyroid cancer, multiple myeloma
Tyrosinase	prostate cancer, melanoma
UPK2	bladder cancer
VEGFR2	ovarian and pancreatic cancers, renal cell carcinoma, colorectal cancer, medullary thyroid carcinoma

[0500] Accordingly, the present disclosure provides methods of treating cancer comprising administering to a subject suffering from cancer a TBM in which ABM3 (*i.e.*, the TAA ABM) binds to a TAA expressed on that type of cancer. In some embodiments, a TBM that targets a TAA identified in Table 14 is can be administered to a subject afflicted with a cancer that Table 14 indicates expressed the TAA. By way of example and not limitation, a TBM that targets EPCAM or folate receptor alpha can be administered to a subject afflicted with colorectal cancer, a TBM that targets BCMA or CD19 can be administered to a subject afflicted with a blood cancer such as multiple myeloma, a TBM that targets PSCA or PCMA can be administered a subject afflicted with prostate cancer, a TBM that targets tyrosinase or GP3 can be administered to a subject afflicted with melanoma, a TBM that targets CD33, CLL-1 or FLT3 can be administered to a subject afflicted with a blood cancer such as acute myeloid leukemia.

6.13. Combination Therapy

[0501] A TBM of the disclosure may be used in combination other known agents and therapies. For example, the TBMs of the disclosure can be used in treatment regimens in combination with surgery, chemotherapy, antibodies, radiation, peptide vaccines, steroids, cytotoxins, or a combination thereof.

[0502] For convenience, an agent that is used in combination with a TBM of the disclosure is referred to herein as an “additional” agent.

[0503] 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”. The term “concurrently” is not limited to the administration of therapies (e.g., a TBM and an additional agent) at exactly the same time, but rather it is meant that a pharmaceutical composition comprising a TBM of the disclosure is administered to a subject in a sequence and within a time interval such that the TBMs of the disclosure can act together with the additional therapy(ies) to provide an increased benefit than if they were administered otherwise. For example, each therapy may be administered to a subject at the same time or sequentially in any order at different points in time; however, if not administered at the same time, they should be administered sufficiently close in time so as to provide the desired therapeutic effect.

[0504] A TBM of the disclosure and one or more additional agents can be administered simultaneously, in the same or in separate compositions, or sequentially. For sequential administration, the TBM can be administered first, and the additional agent can be administered second, or the order of administration can be reversed.

[0505] The TBM and the additional agent(s) can be administered to a subject in any appropriate form and by any suitable route. In some embodiments, the routes of administration are the same. In other embodiments the routes of administration are different.

[0506] In other embodiments, the delivery of one treatment ends before the delivery of the other treatment begins.

[0507] 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.

[0508] The TBMs of the disclosure and/or additional agents can be administered during periods of active disorder, or during a period of remission or less active disease. A TBM can be administered before the treatment with the additional agent(s), concurrently with the treatment with the additional agent(s), post-treatment with the additional agent(s), or during remission of the disorder.

[0509] When administered in combination, the TBM and/or the additional agent(s) can be administered in an amount or dose that is higher, lower or the same than the amount or dosage of each agent used individually, *e.g.*, as a monotherapy.

[0510] The additional agent(s) of the combination therapies of the disclosure can be administered to a subject concurrently. The term “concurrently” is not limited to the administration of therapies (*e.g.*, prophylactic or therapeutic agents) at exactly the same time, but rather it is meant that a pharmaceutical composition comprising a TBM of the disclosure is administered to a subject in a sequence and within a time interval such that the molecules of the disclosure can act together with the additional therapy(ies) to provide an increased benefit than if they were administered otherwise. For example, each therapy may be administered to a subject at the same time or sequentially in any order at different points in time; however, if not administered at the same time, they should be administered sufficiently close in time so as to provide the desired therapeutic or prophylactic effect. Each therapy can be administered to a subject separately, in any appropriate form and by any suitable route.

[0511] The TBM and the additional agent(s) may be administered to a subject by the same or different routes of administration.

[0512] The TBMs and the additional agent(s) may be cyclically administered. Cycling therapy involves the administration of a first therapy (*e.g.*, a first prophylactic or therapeutic agent) for a period of time, followed by the administration of a second therapy (*e.g.*, a second prophylactic or therapeutic agent) for a period of time, optionally, followed by the administration of a third therapy (*e.g.*, prophylactic or therapeutic agent) for a period of time and so forth, and repeating this sequential administration, *i.e.*, the cycle in order to reduce the development of resistance to one of the therapies, to avoid or reduce the side effects of one of the therapies, and/or to improve the efficacy of the therapies.

[0513] In certain instances, the one or more additional agents, are other anti-cancer agents, anti-allergic agents, anti-nausea agents (or anti-emetics), pain relievers, cytoprotective agents, and combinations thereof.

[0514] In one embodiment, a TBM of the disclosure can be used in combination with a chemotherapeutic agent. Exemplary chemotherapeutic agents include an anthracycline (*e.g.*, doxorubicin (*e.g.*, liposomal doxorubicin)), a vinca alkaloid (*e.g.*, vinblastine, vincristine,

vindesine, vinorelbine), an alkylating agent (e.g., cyclophosphamide, decarbazine, melphalan, ifosfamide, temozolomide), an immune cell antibody (e.g., alemtuzumab, gemtuzumab, rituximab, tositumomab, obinutuzumab, ofatumumab, daratumumab, elotuzumab), an antimetabolite (including, e.g., folic acid antagonists, pyrimidine analogs, purine analogs and adenosine deaminase inhibitors (e.g., fludarabine)), an mTOR inhibitor, a TNFR glucocorticoid induced TNFR related protein (GITR) agonist, a proteasome inhibitor (e.g., aclacinomycin A, gliotoxin or bortezomib), an immunomodulator such as thalidomide or a thalidomide derivative (e.g., lenalidomide).

[0515] General chemotherapeutic agents considered for use in combination therapies include anastrozole (Arimidex®), bicalutamide (Casodex®), bleomycin sulfate (Blenoxane®), busulfan (Myleran®), busulfan injection (Busulfex®), capecitabine (Xeloda®), N4-pentoxycarbonyl-5-deoxy-5-fluorocytidine, carboplatin (Paraplatin®), carmustine (BiCNU®), chlorambucil (Leukeran®), cisplatin (Platinol®), cladribine (Leustatin®), cyclophosphamide (Cytoxan® or Neosar®), cytarabine, cytosine arabinoside (Cytosar-U®), cytarabine liposome injection (DepoCyt®), dacarbazine (DTIC-Dome®), dactinomycin (Actinomycin D, Cosmegen), daunorubicin hydrochloride (Cerubidine®), daunorubicin citrate liposome injection (DaunoXome®), dexamethasone, docetaxel (Taxotere®), doxorubicin hydrochloride (Adriamycin®, Rubex®), etoposide (Vepesid®), fludarabine phosphate (Fludara®), 5-fluorouracil (Acrucil®, Efudex®), flutamide (Eulexin®), tezacitibine, Gemcitabine (difluorodeoxycytidine), hydroxyurea (Hydrea®), Idarubicin (Idamycin®), ifosfamide (IFEX®), irinotecan (Camptosar®), L-asparaginase (ELSPAR®), leucovorin calcium, melphalan (Alkeran®), 6-mercaptopurine (Purinethol®), methotrexate (Folex®), mitoxantrone (Novantrone®), mylotarg, paclitaxel (Taxol®), phoenix (Yttrium90/MX-DTPA), pentostatin, polifeprosan 20 with carmustine implant (Gliadel®), tamoxifen citrate (Nolvadex®), teniposide (Vumon®), 6-thioguanine, thiotepa, tirapazamine (Tirazone®), topotecan hydrochloride for injection (Hycamtin®), vinblastine (Velban®), vincristine (Oncovin®), and vinorelbine (Navelbine®).

[0516] Anti-cancer agents of particular interest for combinations with the TBMs of the present disclosure include: anthracyclines; alkylating agents; antimetabolites; drugs that inhibit either the calcium dependent phosphatase calcineurin or the p70S6 kinase FK506) or inhibit the p70S6 kinase; mTOR inhibitors; immunomodulators; anthracyclines; vinca alkaloids; proteasome inhibitors; GITR agonists; protein tyrosine phosphatase inhibitors; a CDK4 kinase inhibitor; a BTK inhibitor; a MKN kinase inhibitor; a DGK kinase inhibitor; or an oncolytic virus.

[0517] Exemplary alkylating agents include, without limitation, nitrogen mustards, ethylenimine derivatives, alkyl sulfonates, nitrosoureas and triazenes): uracil mustard (Aminouracil Mustard®, Chlorethaminacil®, Demethyldopan®, Desmethyldopan®, Haemanthamine®,

Nordopan®, Uracil nitrogen mustard®, Uracillost®, Uracilmostaza®, Uramustin®, Uramustine®, chlormethine (Mustargen®), cyclophosphamide (Cytoxan®, Neosar®, Clafen®, Endoxan®, Procytox®, Revimmune™), ifosfamide (Mitoxana®), melphalan (Alkeran®), Chlorambucil (Leukeran®), pipobroman (Amedel®, Vercyte®), triethylenemelamine (Hemel®, Hexalen®, Hexastat®), triethylenethiophosphoramine, Temozolomide (Temodar®), thiotepa (Thioplex®), busulfan (Busilvex®, Myleran®), carmustine (BiCNU®), lomustine (CeeNU®), streptozocin (Zanosar®), and Dacarbazine (DTIC-Dome®). Additional exemplary alkylating agents include, without limitation, Oxaliplatin (Eloxatin®); Temozolomide (Temodar® and Temodal®); Dactinomycin (also known as actinomycin-D, Cosmegen®); Melphalan (also known as L-PAM, L-sarcolysin, and phenylalanine mustard, Alkeran®); Altretamine (also known as hexamethylmelamine (HMM), Hexalen®); Carmustine (BiCNU®); Bendamustine (Treanda®); Busulfan (Busulfex® and Myleran®); Carboplatin (Paraplatin®); Lomustine (also known as CCNU, CeeNU®); Cisplatin (also known as CDDP, Platinol® and Platinol®-AQ); Chlorambucil (Leukeran®); Cyclophosphamide (Cytoxan® and Neosar®); Dacarbazine (also known as DTIC, DIC and imidazole carboxamide, DTIC-Dome®); Altretamine (also known as hexamethylmelamine (HMM), Hexalen®); Ifosfamide (Ifex®); Prednumustine; Procarbazine (Matulane®); Mechlorethamine (also known as nitrogen mustard, mustine and mechlorethamine hydrochloride, Mustargen®); Streptozocin (Zanosar®); Thiotepa (also known as thiophosphoamide, TESP and TSPA, Thioplex®); Cyclophosphamide (Endoxan®, Cytoxan®, Neosar®, Procytox®, Revimmune®); and Bendamustine HCl (Treanda®).

[0518] Exemplary mTOR inhibitors include, *e.g.*, temsirolimus; ridaforolimus (formally known as deferolimus, (1R,2R,4S)-4-[(2R)-2 [(1R,9S,12S,15R,16E,18R,19R,21R,23S,24E,26E,28Z,30S,32S,35R)-1,18-dihydroxy-19,30-dimethoxy-15,17,21,23,29,35-hexamethyl-2,3,10,14,20-penta-oxo-11,36-dioxo-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, and described in PCT Publication No. WO 03/064383); everolimus (Afinitor® or RAD001); rapamycin (AY22989, Sirolimus®); simapimod (CAS 164301-51-3); emsirolimus, (5-{2,4-Bis[(3S)-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(8H)-one (PF04691502, CAS 1013101-36-4); and N2-[1,4-dioxo-4-[[4-(4-oxo-8-phenyl-4H-1-benzopyran-2-yl)morpholinium-4-yl]methoxy]butyl]-L-arginylglycyl-L- α -aspartyl-L-serine- (SEQ ID NO: 718), inner salt (SF1126, CAS 936487-67-1), and XL765.

[0519] Exemplary immunomodulators include, *e.g.*, afutuzumab (available from Roche®); pegfilgrastim (Neulasta®); lenalidomide (CC-5013, Revlimid®); thalidomide (Thalomid®), actimid (CC4047); and IRX-2 (mixture of human cytokines including interleukin 1, interleukin 2, and interferon γ , CAS 951209-71-5, available from IRX Therapeutics).

[0520] Exemplary anthracyclines include, e.g., doxorubicin (Adriamycin® and Rubex®); bleomycin (lenoxane®); daunorubicin (daunorubicin hydrochloride, daunomycin, and rubidomycin hydrochloride, Cerubidine®); daunorubicin liposomal (daunorubicin citrate liposome, DaunoXome®); mitoxantrone (DHAD, Novantrone®); epirubicin (Ellence™); idarubicin (Idamycin®, Idamycin PFS®); mitomycin C (Mutamycin®); geldanamycin; herbimycin; ravidomycin; and desacetylravidomycin.

[0521] Exemplary vinca alkaloids include, e.g., vinorelbine tartrate (Navelbine®), Vincristine (Oncovin®), and Vindesine (Eldisine®); vinblastine (also known as vinblastine sulfate, vincaleukoblastine and VLB, Alkaban-AQ® and Velban®); and vinorelbine (Navelbine®).

[0522] Exemplary proteasome inhibitors include bortezomib (Velcade®); carfilzomib (PX-171-007, (S)-4-Methyl-N-(((S)-1-(((S)-4-methyl-1-((R)-2-methyloxiran-2-yl)-1-oxopentan-2-yl)amino)-1-oxo-3-phenylpropan-2-yl)-2-((S)-2-(2-morpholinoacetamido)-4-phenylbutanamido)-pentanamide); marizomib (NPI-0052); ixazomib citrate (MLN-9708); delanzomib (CEP-18770); and O-Methyl-N-[(2-methyl-5-thiazolyl)carbonyl]-L-seryl-O-methyl-N-[(1S)-2-[(2R)-2-methyl-2-oxiranyl]-2-oxo-1-(phenylmethyl)ethyl]-L-serinamide (ONX-0912).

[0523] In certain aspects, “cocktails” of different chemotherapeutic agents are administered as the additional agent(s).

7. EXAMPLES

7.1. Example 1: Production and characterization of Anti-CD19-Anti-CD3-Anti-CD2 human IgG1 bi- and tri-specific antibodies

7.1.1. Materials and Methods

7.1.1.1. Gene construction, expression and purification of bi- and tri-specific binding molecules

[0524] Gene synthesis with mammalian expression codon optimization was performed externally for constructs represented in FIG. 2. Amino acid sequences for the constructs represented in FIG. 2 are shown in Table 15.

TABLE 15 Amino Acid Sequences of Bi- and Tri-specific Constructs		
Component	Sequence	SEQ ID NO:
Bispecific Ab1 (CD19 scFV/hCD3 scFv 1x1 format)		
Anti-CD19 scFv		
HCDR1 (Kabat)	DYGVS	689
HCDR2 (Kabat)	VIWGSETTYQSSLKS	692
HCDR3 (Kabat)	HYYYGGSYAMDY	694

TABLE 15 Amino Acid Sequences of Bi- and Tri-specific Constructs		
Component	Sequence	SEQ ID NO:
HCDR1 (Chothia)	GVSLPDY	719
HCDR2 (Chothia)	WGSET	720
HCDR3 (Chothia)	HYYYGGSYAMDY	694
HCDR1 (IMGT)	GVSLPDY	719
HCDR2 (IMGT)	WGSET	720
HCDR3 (IMGT)	HYYYGGSYAMDY	694
VH	QVQLQESGPGLVKPSSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYQQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTV SS	700
LCDR1 (Kabat)	RASQDISKYLN	695
LCDR2 (Kabat)	HTSRLHS	696
LCDR3 (Kabat)	QQGNTLPYT	697
LCDR1 (Chothia)	SQDISKY	721
LCDR2 (Chothia)	HTS	722
LCDR3 (Chothia)	GNTLPY	723
LCDR1 (IMGT)	QDISKY	724
LCDR2 (IMGT)	HTS	722
LCDR3 (IMGT)	QQGNTLPYT	697
VL	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE DFAVYFCQQGNTLPYTFGQGTKLEIK	703
Linker	GGGGSGGGGSGGGGS	1
scFv (VH-linker-VL)	QVQLQESGPGLVKPSSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYQQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTV SSGGGGSGGGGSGGGGSEIVMTQSPATLSLSPGERATL SCRASQDISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPAR FSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYTFGQ GTKLEIK	707
Anti-CD3 scFv		
HCDR1 (Kabat)	TYAMN	131
HCDR2 (Kabat)	RIRSKYNNYATYYADSVKD	151

TABLE 15 Amino Acid Sequences of Bi- and Tri-specific Constructs		
Component	Sequence	SEQ ID NO:
HCDR3 (Kabat)	HGNFGNSYVSWFAY	175
HCDR1 (Chothia)	GFTFNTY	199
HCDR2 (Chothia)	RSKYNNYA	212
HCDR3 (Chothia)	HGNFGNSYVSWFAY	175
HCDR1 (IMGT)	GFTFNTYA	725
HCDR2 (IMGT)	IRSKYNNYAT	726
HCDR3 (IMGT)	VRHGNFGNSYVSWFAY	182
VH	EVQLVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWVR QASGKGLEWWGRIRSKYNNYATYYADSVKDRFTISRDDS KSTLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYW GQGTLLTVSS	114
LCDR1 (Kabat)	RSSTGAVTTSNYAN	132
LCDR2 (Kabat)	GTNKRAP	152
LCDR3 (Kabat)	ALWYSNLWW	176
LCDR1 (Chothia)	STGAVTTSNY	200
LCDR2 (Chothia)	GTN	213
LCDR3 (Chothia)	WYSNLW	223
LCDR1 (IMGT)	TGAVTTSNY	727
LCDR2 (IMGT)	GTNKRAPWTP	728
LCDR3 (IMGT)	ALWYSNLWW	176
VL	QAVVTQEPSTLVSPGGTVTLTCRSSTGAVTTSNYANWWQ QKPGQAPRGLIGGTNKRAPWTPARFSGSLLGDKAALTLS GAQPEDEAEYFCALWYSNLWWFGGGTKLTVL	115
Linker	GGGGSGGGGSGGGGSGGGGS	48
scFv (VH-linker-VL)	EVQLVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWVR QASGKGLEWWGRIRSKYNNYATYYADSVKDRFTISRDDS KSTLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYW GQGTLLTVSSGGGGSGGGGSGGGGSGGGGSQAVVTQ EPSTLVSPGGTVTLTCRSSTGAVTTSNYANWWQQKPGQA PRGLIGGTNKRAPWTPARFSGSLLGDKAALTLGAQPED EAEYFCALWYSNLWWFGGGTKLTVL	116
Full Ab region		
Linker CD19 arm	GGGGS	25

TABLE 15 Amino Acid Sequences of Bi- and Tri-specific Constructs		
Component	Sequence	SEQ ID NO:
Fc-HC CD19 arm	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPCRDELTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV MHEALHNHYTQKSLSLSPGK	729
Full CD19 arm	QVQLQESGPGLVKPSSETLSLTCTVSGVSLPDYGVSWIRQPPGKGLEWIGVIWGSETTYQSSSLKSRVTISKDNSKNQVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGT LTVTVSSGGGGSGGGGGSGGGGGSEIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLIYHTSRLHSGIPARFSGSGSGTDYTLTISSSLQPEDFAVYFCQQGNTLPYTFGQGTKLEIKGGGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPCRDELTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNV FSCSV MHEALHNHYTQKSLSLSPGK	730
Linker CD3 arm	GGGGS	25
Fc-HC CD3 arm	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVCTLPSPRDELTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLVSKLTVDKSRWQQGNV FSCSV MHEALHNHYTQKSLSLSPGK	731
Full CD3 arm	EVQLVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWVRQASGKGLEWVGRIIRSKYNNYATYYADSVKDRFTISRDDS KSTLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYWGQGT LTVTVSSGGGGSGGGGGSGGGGGSGGGGSAVVTQEPSTLVSPGGTVTLTCRSSTGAVTTSNYANWWQQKPGQA PRGLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQPED EAEYFCALWYSNLWFGGGTKLTVLGGGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVCTLPSPRDELTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLVSKLTVDKSRWQQGNV FSCSV MHEALHNHYTQKSLSLSPGK	732
Bispecific Ab2 (hCD19 scFv/hCD58 ligand 1x1 format)		
Anti-CD19 scFv		
HCDR1 (Kabat)	DYGVS	689
HCDR2 (Kabat)	VIWGSETTYQSSSLKS	692
HCDR3 (Kabat)	HYYYGGSYAMDY	694
HCDR1 (Chothia)	GVSLPDY	719
HCDR2 (Chothia)	WGSET	720
HCDR3 (Chothia)	HYYYGGSYAMDY	694

TABLE 15 Amino Acid Sequences of Bi- and Tri-specific Constructs		
Component	Sequence	SEQ ID NO:
HCDR1 (IMGT)	GVSLPDY	719
HCDR2 (IMGT)	WGSET	720
HCDR3 (IMGT)	HYYYGGSYAMDY	694
VH	QVQLQESGPGGLVKPSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYYYQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTV SS	700
LCDR1 (Kabat)	RASQDISKYLN	695
LCDR2 (Kabat)	HTSRLHS	696
LCDR3 (Kabat)	QQGNTLPYT	697
LCDR1 (Chothia)	SQDISKY	721
LCDR2 (Chothia)	HTS	722
LCDR3 (Chothia)	GNTLPY	723
LCDR1 (IMGT)	QDISKY	724
LCDR2 (IMGT)	HTS	722
LCDR3 (IMGT)	QQGNTLPYT	697
VL	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE DFAVYFCQQGNTLPYTFGQGTKLEIK	703
Linker	GGGGSGGGGSGGGGS	1
scFv (VH-linker-VL)	QVQLQESGPGGLVKPSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYYYQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTV SSGGGGSGGGGSGGGGSEIVMTQSPATLSLSPGERATL SCRASQDISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPAR FSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYTFGQ GTKLEIK	707
CD58 ligand		
CD58 ligand	FSQQIYGVVYGNVTFHVPSNVPLKEVLWKKQKDKVAELE NSEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMES PNITDTMKFFLYVLESPLSPPTLTALTNNGSIEVQCMIEHY NSHRGLIMYSWDCPMEQCKRNSTSIYFKMENDLPQKIQC TLNPLFNTTSSIILTTCPSSGHSRHR	733
Full Ab region		
Linker CD19 arm	GGGGS	25
Fc-HC CD19 arm	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNS TYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISK AKGQPREPQVYTLPPCRDELTKNQVSLWCLVKGFYPSDI AVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSR WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	729
Full CD19 arm	QVQLQESGPGGLVKPSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYYYQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTV SSGGGGSGGGGSGGGGSEIVMTQSPATLSLSPGERATL SCRASQDISKYLNWYQQKPGQAPRLLIYHTSRLHSGIPAR FSGSGSGTDYTLTISSLQPEDFAVYFCQQGNTLPYTFGQ GTKLEIKGGGGSDKTHTCPPCPAPELLGGPSVFLFPPKPK DTLMISRTPEVTCVVAVSHEDPEVKFNWYVDGVEVHNA KTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK ALAAPIEKTISKAKGQPREPQVYTLPPCRDELTKNQVSLW	730

TABLE 15 Amino Acid Sequences of Bi- and Tri-specific Constructs		
Component	Sequence	SEQ ID NO:
	CLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFF LYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS PGK	
Linker CD58 arm	GGGGS	25
Fc-HC CD3 arm	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNS TYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISK AKGQPREPQVCTLPSPRDELTKNQVSLSCAVKGFYPSDI AVEWESNGQPENNYKTTTPVLDSDGSFFLVSKLTVDKSR WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	731
Full CD58 arm	FSQQIYGVVYGNVTFHVPSNVPLKEVLWKKQKDKVAELE NSEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMES PNITDTMKFFLYVLESPLSPTLTCAITNGSIEVQCMIPHY NSHRGLIMYSWDCPMEQCKRNSTSIYFKMENDLPQKIQC TLNPLFNTTSSIILTTCPSSGHSRHRGGGGSDKTHTCPP CPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVAVSH EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQ VCTLPSPRDELTKNQVSLSCAVKGFYPSDIAVEWESNGQ PENNYKTTTPVLDSDGSFFLVSKLTVDKSRWQQGNVFSC SVMHEALHNHYTQKSLSLSPGK	734
Trispecific Ab1 (CD19Fab/hCD3 scFv-CD58 ligand 1x1 format)		
Anti-CD19 Fab		
HCDR1 (Kabat)	DYGVS	689
HCDR2 (Kabat)	VIWGSETTYQSSLKS	692
HCDR3 (Kabat)	HYYYGGSYAMDY	694
HCDR1 (Chothia)	GVSLPDY	719
HCDR2 (Chothia)	WGSET	720
HCDR3 (Chothia)	HYYYGGSYAMDY	694
HCDR1 (IMGT)	GVSLPDY	719
HCDR2 (IMGT)	WGSET	720
HCDR3 (IMGT)	HYYYGGSYAMDY	694
VH	QVQLQESGPGLVKPSSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTV SS	700
VH-CH1 Fab fragment	QVQLQESGPGLVKPSSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLG TQTYICNVNHKPSNTKVDKRVEPKSC	735
LCDR1 (Kabat)	RASQDISKYLN	695
LCDR2 (Kabat)	HTSRLHS	696
LCDR3 (Kabat)	QQGNTLPYT	697
LCDR1 (Chothia)	SQDISKY	721
LCDR2 (Chothia)	HTS	722

TABLE 15 Amino Acid Sequences of Bi- and Tri-specific Constructs		
Component	Sequence	SEQ ID NO:
LCDR3 (Chothia)	GNTLPY	723
LCDR1 (IMGT)	QDISKY	724
LCDR2 (IMGT)	HTS	722
LCDR3 (IMGT)	QQGNTLPYT	697
VL	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE DFAVYFCQQGNTLPYTFGQGTKLEIK	703
Light chain	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE DFAVYFCQQGNTLPYTFGQGTKLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSLSSLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	736
Anti-CD3 scFv		
HCDR1 (Kabat)	TYAMN	131
HCDR2 (Kabat)	RIRSKYNNYATYYADSVKD	151
HCDR3 (Kabat)	HGNFGNSYVSWFAY	175
HCDR1 (Chothia)	GFTFNTY	199
HCDR2 (Chothia)	RSKYNNYA	212
HCDR3 (Chothia)	HGNFGNSYVSWFAY	175
HCDR1 (IMGT)	GFTFNTYA	725
HCDR2 (IMGT)	IRSKYNNYAT	726
HCDR3 (IMGT)	VRHGNFGNSYVSWFAY	182
VH	EVQLVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWVR QASGKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDS KSTLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYW GQGTLLTVSS	114
LCDR1 (Kabat)	RSSTGAVTTSNYAN	132
LCDR2 (Kabat)	GTNKRAP	152
LCDR3 (Kabat)	ALWYSNLWW	176
LCDR1 (Chothia)	STGAVTTSNY	200
LCDR2 (Chothia)	GTN	213
LCDR3 (Chothia)	WYSNLW	223
LCDR1 (IMGT)	TGAVTTSNY	727
LCDR2 (IMGT)	GTNKRAPWTP	728
LCDR3 (IMGT)	ALWYSNLWW	176
VL	QAVVTQEPSLTVSPGGTVTLTCSRSTGAVTTSNYANWWQ QKPGQAPRGLIGGTNKRAPWTPARFSGSLLGDKAALTLS GAQPEDEAEYFCALWYSNLWWFGGGGTKLTVL	115
Linker	GGGGSGGGGSGGGGSGGGGS	48
scFv (VH-linker-VL)	EVQLVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWVR QASGKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDS KSTLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYW GQGTLLTVSSGGGGSGGGGSGGGGSGGGGSGGGGSGQAVVTQ EPSLTVSPGGTVTLTCSRSTGAVTTSNYANWWQQKPGQA PRGLIGGTNKRAPWTPARFSGSLLGDKAALTLSSGAQPED EAEYFCALWYSNLWWFGGGGTKLTVL	116
CD58 ligand		
CD58 ligand	FSQQIYGVVYGNVTFHVPSNVPLKEVLWKKQKDKVAELE NSEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMES	733

TABLE 15 Amino Acid Sequences of Bi- and Tri-specific Constructs		
Component	Sequence	SEQ ID NO:
	PNITDTMKFFLYVLES LPSPTLTCA LTNGSIEVQCM IPEHY NSHRGLIMYSWDCPMEQCKRNSTSIYFKMENDLPQKIQ C TLNPLFNTTSSIILTT CIPSSGHSRHR	
Full Ab region		
Linker CD19-CD3	GGGGSGGGGS	47
Linker CD3-Fc	GGGS	25
Fc-HC CD19 arm	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVAVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYGS TYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTISK AKGQPREPQVCTLPSSRDELTKNQVSLSCAVKGFYPSDI AVEWESNGQPENNYKTTTPVLDSDGSFFLVSKLTVDKSR WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	737
Full CD19-CD3 arm	QVQLQESGPGLVKPSSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYYQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGLTVTV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLG TQTYICNVNHKPSNTKVDKRVEPKSCGGGGSGGGGSEV QLVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWVRQA SGKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDSKS TLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYWGQ GTLTVTVSSGGGGSGGGGSGGGGSGGGGSGQAVVTQEPS LTVSPGGTVTLTCRSSTGAVTTSNYANWWQKPGQAPR GLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQPEDEA EYFCALWYSNLWVFGGGTKLTVLGGGGSDKTHTCPPCP APPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVAVSHED PEVKFNWYVDGVEVHNAKTKPREEQYGSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQV CTLPSSRDELTKNQVSLSCAVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	738
Linker CD58 ligand	GGGS	739
Fc CD58 ligand arm	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYAS TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK AKGQPREPQVYTLPPCREEMTKNQVSLWCLVKGFYPSDI AVEWESNGQPENNYKTTTPVLDSDGSFFLVSKLTVDKSR WQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	740
Full CD58 ligand arm	FSQQIYGVVYGNVTFHVPSNVPLKEVLWKKQKDKVAELE NSEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMES PNITDTMKFFLYVLES LPSPTLTCA LTNGSIEVQCM IPEHY NSHRGLIMYSWDCPMEQCKRNSTSIYFKMENDLPQKIQ C TLNPLFNTTSSIILTT CIPSSGHSRHRGGGSDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH DPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTV LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV YTLPPCREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNRYTQKSLSLSPGK	741

[0525] Hetero-dimerization of Fc for the trispecific antibody was achieved by the 'knobs-into-holes' engineering (Ridgway *et al.* 1999, Protein Eng. 9(7):617-21). The extracellular domain of human CD58 was fused to human IgG1 Fc with a short flexible linker, while the other arm was encoded with a target binding Fab followed by a short flexible linker, followed by an anti-CD3 scFv, fused to human IgG1 Fc with a short flexible linker such as GGGGS (SEQ ID NO: 25). The corresponding full target light chain plasmid was also synthesized. Constant human IgG1 Fc sequence contained modifications that silence antibody dependent cellular cytotoxicity and facilitate purification of heterodimeric Fc multi-specific antibodies.

[0526] TBMs were expressed transiently in Human Embryonic Kidney (HEK293) cells. Briefly, transfection was performed using PEI (Polyethylenimine, MW 25,000 linear, Cat No. 23966-1, Polysciences, USA) as the transfection reagent. For small scale (≤ 1 L) transfections, cells were grown in flat-bottomed shake flasks on an orbital shaker (125 rpm) in a 37 °C humidified incubator at 8% CO₂. Plasmids were combined with PEI at a final ratio of 1 : 3 = DNA : PEI. 1 mg of plasmid per L culture was used for transfection at 2.0 million cells/mL media. After 5 days of expression, the antibody was harvested by clarification of the media via centrifugation and filtration. Purification was performed via Protein A affinity chromatography (rProtein A Sepharose Fast Flow, GE Healthcare Life Sciences, Uppsala, Sweden) by batch-binding using approximately 5 mL resin / L harvested supernatant. The batch-bound resin slurry was poured over Econo Pac® Chromatography Columns (Cat No. 7321010, BioRad Laboratories, Hercules, CA), and the resin bed washed with 10 CV of dPBS. Protein was eluted with 4 CV of 20 mM citrate, 125 mM NaCl, 50 mM sucrose, pH 3.0. The eluted protein was titrated to pH 5.5 with 1 M Sodium Citrate, pH 8.2. If the antibody contained aggregates, preparative size exclusion chromatography was performed using Superdex200 (GE Healthcare Life Sciences, Uppsala, Sweden) as a final polishing step with a mobile phase of 20 mM citrate, 125 mM NaCl, 50 mM sucrose, pH 5.5. Antibody titer, monomer content, and sample endotoxin levels were measured prior to assaying.

7.1.1.2. Re-directed T cell cytotoxicity (Quantitative luciferase assay)

[0527] In a series of studies, a trispecific construct targeting human CD3, human CD2 and human CD19 was compared with a bispecific construct targeting human CD3 and human CD19 as well as a non-targeting control construct targeting human CD3 and human growth hormone (gH). The constructs were all analyzed for their potential to induce T cell-mediated apoptosis in tumor target cells. The amino acid sequences of the non-targeting control construct targeting human CD3 and gH are shown in Table 16.

TABLE 16 Amino Acid Sequences of anti-CD3 x anti-gH control antibody		
Component	Sequence	SEQ ID NO:

TABLE 16 Amino Acid Sequences of anti-CD3 x anti-gH control antibody		
Component	Sequence	SEQ ID NO:
<i>anti-gH scFv-Fc</i>	EVQLVESGGGLVVKPGGSLRLSCAASGFTFSPYSVFWWRQ APGKGLEWVSSINTDSTYKYYADSVKGRFTISRDN AENSI FLQMNSLRAEDTAVYYCARDRSYYAFSSGSLSDY YYGLD VWGQGT LVT VSSGGGGSGGGGSGGGGSGGGGSD IVMT QSPLSLSVTPGEPASISCRSSQSLLHTNLYNYLDW YVQKP GQSPQLLIYLASNRASGVDPDRFSGSGSGTDFTL KISRVE EDVG VYYCMQALQIPRTFGQG TKLEIKGGGGSD KTHTCP PCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTC VVAVS HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR VVSV LTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKG QPRE PQVYTLPPCRDELTKNQVSLWCLVKGFYPSDIAVEW ESNGQ GPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQG NVF SCSVMHEALHNHYTQKSLSLSPGK	742
<i>anti-CD3 scFv-Fc</i>	EVQLVESGGGLVQPGGSLKLSAASGFTFNTYAMNWR QASGKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDS KSTLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYW GQGT LVT VSSGGGGSGGGGSGGGGSGGGGSGGGGSGQAV VTQ EPSLTVSPGGTVTLTCRSSTGAVTTSNYANWWQQKPG QA PRGLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQPED EA EYFCALWYSNLWFGGGTKLTVLGGGGSDKTHTCP CPP CPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVA VSH EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREP Q VCTLPPSRDELTKNQVSLSCAVKGFYPSDIAVEWESNGQ PENNYKTTTPVLDSDGSFFLVSKLTVDKSRWQQGNVFS C SVMHEALHNHYTQKSLSLSPGK	732

[0528] The purified constructs were compared across multiple donor effector cells. Briefly, target cells (huCD19-expressing Nalm6 cells, huCD19-expressing Daudi cells, and human K562 cells (negative control)) were engineered to overexpress firefly luciferase. Cells were harvested and resuspended in RPMI medium (Invitrogen # 11875-093) with 10% FBS. 10,000 target cells per well were plated in a flat-bottom 96-well plate. Human pan T effector cells were isolated via MACS negative selection (Miltenyi Biotec #130-096-535) from donors from cryopreserved PBMC (Cellular Technologies Limited #CTL-UP1; Hemacare #PB009C-1-AML) then added to the plate to obtain a final E:T ratio of 5:1 or 10:1. Co-cultured cells were incubated with a serial dilution of all constructs and controls. For normalization, average maximum luminescence refers to target cells co-incubated with effector cells, but without any test construct. After an incubation of either 24 or 48 hr at 37°C, 5% CO₂, OneGlo luciferase substrate (Promega #E6120) was added to the plate. Luminescence was measured on an

Envision plate reader after a 10 minute incubation. Percent specific lysis was calculated using the following equation:

$$\text{Specific lysis (\%)} = (1 - (\text{sample luminescence} / \text{average maximum luminescence})) * 100$$

[0529] Studies were also performed in which 10,000 additional target cells were added to the co-cultures to mimic T cell exhaustion at 48 hr, 72 hr, and 96 hr with luciferase based cytotoxicity measurements being made at 48 hr, 72 hr, 96 hr and 120 hr. Additionally, the live cell populations at 48 and 96 hours were analyzed for by FACS for activation markers, checkpoint molecules, and phenotypic markers. Cells treated with 1 nM of the bispecific or trispecific construct were harvested via centrifugation after the first challenge at 48 hours or after the third challenge at 96 hours, and the live cell population was gated through either CD4 or CD8 and analyzed for the activation markers CD25 and CD69 (after the 96 hour challenge), checkpoint molecules PD1, LAG3, and TIM3 (after the 48 hour and 96 hour challenges), and the phenotypic markers CCR7 and CD45RO (after the 48 hour and 96 hour challenges).

7.1.1.3. Proliferation Assay

[0530] The purified TBM was tested by flow cytometry for its potential to induce proliferation of CD8+ or CD4+ T cells in the presence of human CD19-expressing Nalm6 tumor cells.

[0531] Briefly, freshly isolated human pan T cells were adjusted to 1 mio cells per ml in warm PBS and stained with 1 μ M CellTrace Far Red (Invitrogen #C34564) at 37°C for 20 minutes. The staining volume was quadrupled by addition of RPMI1640 medium, containing 10% FBS. After incubation at 37°C for an additional 5 min, the cells were washed once with pre-warmed medium to remove remaining dye. The stained effector T cells were adjusted to 1.111×10^6 viable cells per ml in RPMI1640 medium containing 10% FBS and BME. 180 μ L of the cell suspension was added per well into a tissue culture treated 24-well plate. Nalm6 target cells were harvested, counted and checked for viability. Cells were adjusted to 0.222×10^6 viable cells per ml in RPMI1640 medium, containing 10% FBS and BME. 180 μ L of the cell suspension was added to the plated effector T cells to obtain a final E:T ratio of 5:1. 40 μ L of the test constructs were added to the cell-containing wells to obtain a final concentration of either 100, 10, 1 or 0.1 nM. As a positive control, effector T cells were plated in the absence of target cells or test construct with the addition of CD3/CD28 conjugated T-Activator DynaBeads (Invitrogen #111.41D). T cells plated alone with no stimuli served as a negative control.

[0532] After a four day incubation at 37°C, 5% CO₂, cells were centrifuged (5 min, 300 x g) and washed twice with 150 μ L/well PBS, including 0.5% FBS.

[0533] Surface staining for CD8 (mouse IgG1.K; clone HIT8a; BD #555635) or CD4 (mouse IgG1.K; clone RPA-T4 ; BD #557695) was performed on ice for 1 hr, according to the supplier's suggestions. Cells were washed three times with 200 μ L/well PBS containing 0.5% FBS,

resuspended in 150 μ L/well PBS with 0.5% FBS, and analyzed using a Beckman-Coulter FACS Cytotflex machine (CytExpert Software).

[0534] The live cell population was gated through either CD4 or CD8 for determination of subsequent proliferation of indicated cell type.

7.1.1.4. Cytokine release assay

[0535] The purified TBM targeting human CD3, human CD2 and human CD19 was analyzed for its ability to induce T cell-mediated de novo secretion of cytokines in the presence or absence of tumor target cells.

[0536] Briefly, huCD19-expressing Nalm6 target cells were harvested and resuspended in RPMI medium with 10% FBS. 20 000 target cells per well were plated in a flat-bottom 96-well plate. Human pan T effector cells were isolated via MACS negative selection from cryopreserved PBMC then added to the plate to obtain a final E:T ratio of 5:1. Co-cultured cells were incubated with two concentrations of all constructs and controls. After an incubation of 24 hr at 37°C, 5% CO₂ the supernatants were harvested by centrifugation at 300 x g for 5 min for subsequent analysis.

[0537] A multiplexed ELISA was performed according to the manufacturer's instructions using a V-PLEX Proinflammatory Panel 1 Kit (MesoScale Discovery #K15049D).

7.1.1.5. Granzyme B ELISpot Assay

[0538] The purified TBM targeting human CD3, human CD2 and human CD19 was analyzed for its ability to induce Granzyme B secretion in the presence or absence of tumor target cells.

[0539] Briefly, Human pan T effector cells were isolated via MACS negative selection from cryopreserved PBMC. 50 000 effector cells per well were added to an ELISpot plate precoated with anti-Granzyme B antibody (MABTech #3485-4APW) and allowed to settle for 30 min at room temperature. 10 000 huCD19-expressing Nalm6 target cells were harvested and added carefully to the plate so as not to disturb the T cell layer. Co-cultured cells were incubated with two concentrations of all constructs and controls. After an incubation of 48 hr at 37°C, 5% CO₂ the plate was washed and detection performed according to the manufacturer's instructions. The plate was dried and submitted for analysis to ZellNet consulting.

7.1.2. Results

7.1.2.1. Results: Re-directed T cell cytotoxicity assay

[0540] FIG. 3 shows that the TBM construct induced superior cytotoxicity in huCD19-expressing Nalm6 target cells compared to the bispecific construct in an assay performed with a final E:T ratio of 5:1 and either 24 or 48 hour incubation.

[0541] FIG. 4 shows that the TBM construct induced superior cytotoxic activity in huCD19-expressing Daudi target cells compared to the bispecific construct in an assay performed with a

final E:T ratio of 5:1 and 48 hour incubation. As expected, the non-targeting anti-gH showed negligible cytotoxic activity.

[0542] FIG. 5 shows that the bispecific and TBM constructs do not induce apoptosis of the negative control K562 cell line, which does not express human CD19, in an assay performed with a final E:T ratio of 5:1 and 48 hour incubation.

[0543] FIG. 6 shows that the TBM exhibited comparable or superior potency and efficacy compared to the bispecific construct in huCD19-expressing Nalm6 target cells when using human cryopreserved PBMCs that were thawed and rested overnight prior to use and with a final E:T ratio of 10:1 and 24 hour incubation.

[0544] FIG. 7 shows that the TBM construct induced superior cytotoxic activity in huCD19-expressing Nalm6 target cells compared to the bispecific when using human cryopreserved PBMCs from a patient diagnosed with acute myeloid leukemia (Hemacare #PB009C-1-AML) that were thawed and rested overnight prior to use and with a final E:T ratio of 10:1 and 24 hour incubation. As expected, the non-targeting anti-gH showed negligible cytotoxic activity.

[0545] FIGS. 8A-8D shows that in a rechallenge assay with huCD19 expressing Nalm6 target cells, the TBM continued to induce apoptosis up to 120 hours with little apparent loss in activity across each rechallenge while the bispecific construct loses significant potency and activity with each subsequent target cell addition.

[0546] As expected, the non-targeting anti-gH showed negligible cytotoxic activity in each assay.

[0547] Table 17 shows the results of the FACS analysis for the activation markers CD25 and CD69 performed after the third challenge at 96 hours. The trispecific construct mediated higher levels of CD25 and double positive expression (CD25 and CD69) compared to the bispecific construct in both the CD4 and CD8 compartments. Values in Table 17 are expressed as percentage of positive cells.

TABLE 17			
CD4			
Activation Marker	No Treatment	Bispecific at 1 nM	Trispecific at 1 nM
CD25+	4	3	54
CD69+	2	5	10
Double Positive	0	0	19
Double Negative	94	92	17

TABLE 17			
CD8			
Activation Marker	No Treatment	Bispecific at 1 nM	Trispecific at 1 nM
CD25+	0	7	78
CD69+	2	13	4
Double Positive	0	4	6
Double Negative	98	76	12

[0548] Table 18 shows the results of the FACS analysis for the checkpoint molecules PD1, LAG3 and TIM3 performed after either the first challenge at 48 hours or the third challenge at 96 hours. The trispecific construct mediated higher levels of PD1, LAG3 and TIM3 compared to the bispecific construct in both the CD4 and CD8 compartments. Values in Table 18 are expressed as percentage of positive cells.

TABLE 18						
CD4						
	Post Challenge 1 at 48 hours			Post Challenge 3 at 96 hours		
Checkpoint Marker	No Treatment	Bispecific at 1 nM	Trispecific at 1 nM	No Treatment	Bispecific at 1 nM	Trispecific at 1 nM
PD1+	7	12	25	7	5	40
TIM3+	5	10	5	0	0	3
Double Positive	0	2	17	0	0	26
Double Negative	88	76	53	93	95	31
CD8						
	Post Challenge 1 at 48 hours			Post Challenge 3 at 96 hours		
Activation Marker	No Treatment	Bispecific at 1 nM	Trispecific at 1 nM	No Treatment	Bispecific at 1 nM	Trispecific at 1 nM
PD1+	6	12	18	7	18	24
LAG3+	0	0	1	0	0	4

TABLE 18						
Double Positive	0	0	23	0	1	10
Double Negative	94	88	58	93	81	62
CD8						
	Post Challenge 1 at 48 hours			Post Challenge 3 at 96 hours		
Checkpoint Marker	No Treatment	Bispecific at 1 nM	Trispecific at 1 nM	No Treatment	Bispecific at 1 nM	Trispecific at 1 nM
PD1+	8	16	22	13	26	28
TIM3+	6	9	8	0	0	12
Double Positive	0	3	12	0	2	17
Double Negative	86	72	58	87	72	43
CD8						
	Post Challenge 1 at 48 hours			Post Challenge 3 at 96 hours		
Activation Marker	No Treatment	Bispecific at 1 nM	Trispecific at 1 nM	No Treatment	Bispecific at 1 nM	Trispecific at 1 nM
PD1+	11	22	24	7	19	24
LAG3+	1	1	1	0	0	4
Double Positive	0	0	13	0	0	10
Double Negative	88	77	62	93	81	62

[0549] Table 19 shows the results of the FACS analysis for the phenotypic markers CCR7 and CD45RO performed after the first challenge at 48 hours and the third challenge at 96 hours. The trispecific construct mediated a greater amount of central memory T cells compared to the bispecific construct. Values in Table 19 are expressed as percentage of positive cells.

TABLE 19
CD4

TABLE 19						
	Post Challenge 1 at 48 hours			Post Challenge 3 at 96 hours		
Phenotype	No Treatment	Bispecific at 1 nM	Trispecific at 1 nM	No Treatment	Bispecific at 1 nM	Trispecific at 1 nM
T _{effector} (CCR7- CD45RO-)	1	0	0	1	3	2
T _{effector memory} (CCR7- CD45RO+)	28	25	12	46	43	26
T _{central memory} (CCR7+ CD45RO+)	38	47	61	25	18	62
T _{naive} (CCR7+ CD45RO-)	33	28	27	28	36	10

7.1.2.2. Proliferation assay

[0550] FIG. 9 shows that the TBM induces proliferation of CD4+ T cells or CD8+ T cells in the presence of target cells in a dose dependent manner. The TBM also appears to induce proliferation of CD8+ T cells to a greater extent than the CD3/CD28 conjugated T-Activator DynaBeads.

7.1.2.3. Cytokine Release Assay

[0551] FIG. 10 shows levels of the different cytokine measured in the supernatant. The results show that the trispecific molecule induced production of IFN γ , TNF α , IL2, IL6 and IL10 in human pan T effector cells in the presence of huCD19-expressing Nalm6 target cells. The induction by the CD2-CD3-CD19-targeting TBM was several fold greater than the CD3-CD19 bispecific antibody.

7.1.2.4. Results: Granzyme B ELISpot Assay

[0552] FIG. 11 shows that the number of Granzyme B spotforming T cells is much higher upon treatment with the CD2-CD3-CD19-targeting TBM than with the CD3-CD19 bispecific antibody.

7.2. Example 2: Anti-CD19-Anti-CD3-Anti-CD2 TBMs with different CD2 binding arms

[0553] Trispecific binding molecules with different anti-human CD2 binding arms were generated and analyzed for their potential to induce T cell-mediated apoptosis in tumor target cells and for their potential to induce nuclear factor of activated T-cells (NFAT) in the absence of target cells.

7.2.1. Materials and Methods

7.2.1.1. Constructs

[0554] TBM constructs included the TBM of Example 1 having a full length CD58 moiety (AB2-1 in this Example), a TBM having a truncated CD58 comprising the IgV-like domain of CD58 (AB2-2 in this Example), and TBM having an scFv corresponding to the anti-CD2 antibody Medi 507 (AB2-3 in this Example). Amino acid sequences of the TBMs are shown in Table 20. The TBMs are schematically shown in FIG. 12.

TABLE 20 Amino Acid Sequences of TBMs of Example 2		
Component	Sequence	SEQ ID NO:
AB2-1 (FIG. 12A) (αCD19-CD58-αCD3)		
αCD19 Light Chain	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE DFAVYFCQQGNTLPYTFGQGTKLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	736
CD58-Fc	FSQQIYGVVYGNVTFHVPSNVPLKEVLWKKQKDKVAELE NSEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMES PNITDTMKFFLYVLESLPSPTLTCALTNGSIEVQCMIPHEY NSHRGLIMYSWDCPMEQCKRNSTSIYFKMENDLPQKIQC TLNPLFNTTSSIILTCIPSSGHSRHRGGGSDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHE DPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTV LHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV YTLPPCREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS VMHEALHNRYTQKSLSLSPGK	741
αCD19_Fab- αCD3_scFv-Fc	QVQLQESGPGLVKPSSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYYQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGLTVTV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLG TQTYICNVNHKPSNTKVDKRVEPKSCGGGGSGGGGSEV QLVESGGGLVQPGGSLKLSKAASGFTFTNYAMNWVRQA SGKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDSKS TLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYWGQ GTLVTVSSGGGGSGGGGSGGGGSGGGGSGQAVVTQEPS LTVSPGGTVTLTCRSSTGAVTTSNYANWWQQKPGQAPR GLIGGTNKRAPWTPARFSGSLLGDKAALTLGAQPEDEA EYFCALWYSNLWVFGGGTKLTVLGGGGSDKTHTCPPCP APELLGGPSVFLFPPKPKDTLMISRTPEVTCVVAVSHED PEVKFNWYVDGVEVHNAKTKPREEQYGSTYRVVSVLTVL LHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQV	738

TABLE 20 Amino Acid Sequences of TBMs of Example 2		
Component	Sequence	SEQ ID NO:
	CTLPPSRDELTKNQVSLSCAVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSGDSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	
AB2-2 (FIG. 12B) (α CD19-CD58(IgV)- α CD3)		
α CD19 Light Chain	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE DFAVYFCQQGNTLPYTFGQGTKLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSLSSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	736
α CD19_Fab- α CD3_scFv-Fc	QVQLQESGPGLVKPSSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYQSSLSKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTTLVTV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLG TQTYICNVNHKPSNTKVDKRVEPKSCGGGGSGGGGSEV QLVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWVRQA SGKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDSKS TLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYWGQ GTLVTVSSGGGGSGGGGSGGGGSGGGGSSQAVVTQEPS LTVSPGGTVTLTCRSSTGAVTTSNYANWWQKPGQAPR GLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQPEDEA EYFCALWYSNLWVFGGGTKLTVLGGGGSDKTHTCPPCP APELLGGPSVFLFPPKPKDTLMISRTPEVTCVAVSHED PEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVL HQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQV CTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSGDSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	743
CD58 IgV-Fc	SQQIYGVVYGNVTFHVPNSVPLKEVLWKKQKDKVAELEN SEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMESP NITDTMKFFLYVLESGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVAVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEY KCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPCREEMT KNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL DSGDSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNRY TQKSLSLSPGK	744
AB2-3 (FIG. 12C) (α CD19-Medi507- α CD3)		
α CD19 Light Chain	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE DFAVYFCQQGNTLPYTFGQGTKLEIKRTVAAPSVFIFPPS	736

TABLE 20 Amino Acid Sequences of TBMs of Example 2		
Component	Sequence	SEQ ID NO:
	DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSLSSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	
αCD19_Fab- αCD3_scFv-Fc	QVQLQESGPGGLVKKPSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYQSSLSKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLLTV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLG TQTYICNVNHKPSNTKVDKRVEPKSCGGGGSGGGGSEV QLVESGGGLVQPGGSLKLSKAASGFTFNTYAMNWVRQA SGKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDSKS TLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYWGQ GTLVTVSSGGGGSGGGGSGGGGSGGGGSGQAVVTQEPS LTVSPGGTVTLTCRSSTGAVTTSNYANWVQKPGQAPR GLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQPEDEA EYFCALWYSLNWVFGGGTKLTVLGGGGSDKTHTCPPCP APPELLGGPSVFLFPPKPKDTLMISRTPEVTCVAVSHED PEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVL HQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQV CTLPPSRREEMTKNQVSLTSCAVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSGDSFLLVSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	743
Medi 507 scFv-Fc	QVQLVQSGAEVQRPGASVKVSCKASGYIFTEYYMYWVR QAPGQGLELVGRIDPEDGSIDYVEKFKKKVTLTADTSSST AYMELSSLTSDDTAVYYCARGKFNYRFAYWGQGTLLTVS SGGGGSGGGGSGGGGSGGGGSDVVMQSPPSLLVTLG QPASISCRSSQSLHSSGNTYLNWLLQRPQGSPQPLIYLV SKLESGVPDRFSGSGSGTDFTLKISGVEAEDVGVYYCMQ FTHYPYTFGQGTKLEIKGGGGSDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVAVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN GKEYKCKVSNKALAAPIEKTISKAKGQPREPQVCTLPPSR DELTKNQVSLTSCAVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSGDSFLLVSKLTVDKSRWQQGNVFSCSVMHEALH NHYTQKSLSLSPGK	745

7.2.1.2. Re-directed T cell cytotoxicity assay

[0555] A re-directed T cell cytotoxicity assay was performed on the TBMs as described in Example 1, using human CD-19 expressing Nalm6 target cells at an E:T ratio of 5:1 and an incubation time of 48 hours.

[0556] A re-directed T cell cytotoxicity assay was also performed with AB2-2 using cynomolgus monkey pan T effector cells isolated via MACS negative selection (Miltenyi Biotec #130-091-

993) from cryopreserved PBMC (iQ Biosciences # IQB-MnPB102). The cynomolgus monkey pan T effector cells were used in the assay at an E:T ratio of 5:1 and an incubation time of 48 hr.

7.2.1.3. NFAT activation assay

[0557] A Jurkat-NFAT reporter cell line can be used to evaluate the functional activity of trispecific constructs, specifically the non-specific activation of NFAT. Jurkat cells (cell line E6-1) stably expressing a NFAT-LUC reporter (JNL) were grown in RPMI-1640 media containing 2mM glutamine and 10% fetal bovine serum with puromycin at 0.5 ug/ml. 100,000 JNL cells per well were plated in a flat-bottom 96-well plate and were incubated with a serial dilution of all constructs and controls. After an incubation of 6 hr at 37°C, 5% CO₂, OneGlo luciferase substrate (Promega #E6120) was added to the plate. Luminescence was measured on an Envision plate reader after a 10 minute incubation.

7.2.2. Results

[0558] The results of the re-directed T cell cytotoxicity assay performed with Nalm6 target cells and human Pan T effector cells are shown in FIG. 13. The trispecific construct with the truncated CD58 IgV only domain (AB2-2) was observed to have similar cytotoxic activity to the trispecific construct having the full length CD58 molecule (AB2-1). The trispecific construct comprising a Medi 507 scFv (AB2-3) was observed in this assay to have superior cytotoxic activity compared to the trispecific constructs comprising a CD58 moiety.

[0559] The results of the re-directed T cell cytotoxicity assay performed with Nalm6 target cells and cynomolgus monkey pan T effector cells are shown in FIG. 14. TBM AB2-2 exhibited superior cytotoxic activity in huCD19-expressing Nalm6 target cells compared to the bispecific molecule.

[0560] The results of the NFAT activation assay are shown in FIG. 15. The construct with truncated CD58 IgV only domain (AB2-2) was observed to induce less NFAT activation compared to the construct with the full length CD58 molecule (AB2-1). The construct having a scFv corresponding to the anti-CD2 antibody Medi 507 (AB2-3) showed a much greater induction of NFAT, indicating a higher potential for non-specific activation compared to the CD58 comprising trispecifics.

7.3. Example 3: Alternative format Anti-CD19-Anti-CD3-Anti-CD2 TBMs

7.3.1. Materials and Methods

[0561] Trispecific binding molecules with various TBM formats were generated and analyzed for their potential to induce T cell-mediated apoptosis in tumor target cells. The TBM constructs included the TBM having the CD58 IgV domain from Example 2 (AB3-1 in this Example), a TBM having CD58 IgV domain N-terminal to an anti-CD3 scFab and an anti-CD19Fab (AB3-2), a TBM having CD58 IgV domain N-terminal to an anti-CD3 scFv, and an anti-CD19Fab (AB3-

3), a TBM having an anti-CD3 scFv N-terminal to a CD58 IgV domain, and an anti-CD19 Fab (AB4-4), and a TBM having an anti-CD3 scFV, a C-terminal CD58 IgV domain, and an anti-CD19 Fab (AB4-5). Amino acid sequences of the TBMs of this Example are shown in Table 21. The TBMs are schematically shown in FIG. 16.

TABLE 21 Amino Acid Sequences of TBMs of Example 3		
Component	Sequence	SEQ ID NO:
AB3-1 (FIG. 16A) (αCD19-CD58(IgV)-αCD3)		
Anti-CD19 Light Chain	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE DFAVYFCQQGNTLPYTFGQGTKLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSLSSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	736
Anti-CD19 Fab-Anti-CD3_scFv-Fc	QVQLQESGPGGLVKPSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYQQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLLTV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSSVTVPSSSLG TQTYICNVNHKPSNTKVDKRVEPKSCGGGGSGGGGSEV QLVESGGGLVQPGGSLKLSCAASGFTFTNYAMNWVRQA SGKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDSKS TLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYWGQ GTLVTVSSGGGGSGGGGSGGGGSGGGGSSQAVVTQEPS LTVSPGGTVTLTCRSSTGAVTTSNYANWWQQKPGQAPR GLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQPEDEA EYFCALWYSNLWVFGGGTKLTVLGGGGSDKTHTCPPCP APELLGGPSVFLFPPKPKDTLMISRTPEVTCVAVVAVSHED PEVKFNWYVDGVEVHNAKTKPREEQYGSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQV CTLPPSRDELTKNQVSLSCAVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	738
CD58 IgV-Fc	FSQQIYGVVYGNVTFHVPSNVPLKEVLWKKQKDKVAELE NSEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMES PNITDTMKFFLYVLESGGGGSDKTHTCPPCPAPELLGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV DGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKE YKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCREEM TKNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPV LDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNR YTQKSLSLSPGK	746
AB3-2 (FIG. 16B) (CD58-αCD3Fab-αCD19Fab)		
Anti-CD19 Heavy	QVQLQESGPGGLVKPSETLSLTCTVSGVSLPDYGVSWIRQ	747

TABLE 21 Amino Acid Sequences of TBMs of Example 3		
Component	Sequence	SEQ ID NO:
Chain	PPGKGLEWIGVIWGSETTYQQSSLSKSRVTISKDNSKNOVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGLTVTV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLG TQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEL LGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVCTLP PSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSFFLVSKLTVDKSRWQQGNVFSFSVMHE ALHNHYTQKSLSLSPGK	
CD58-CD3_Fab-Fc	SQQIYGVVYGNVTFHVPSNVPLKEVLWKKQKDKVAELEN SEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMESP NITDTMKFFLYVLESLPSPTLTALTNNGSIEVQCMIPHEYN SHRGLIMYSWDCPMEQCKRNSTSIYFKMENDLPQKIQCT LSNPLFNTTSSIIILTCIPSSGHSRHRGGGGSGGGGSQAV VTQEPLSLTVSPGGTVTLTCRSSTGAVTTSNYANWWQKQP GQAPRGLIGGTNKRAPWTPARFSGSLLGDKAALTLGSAQ PEDEAEYFCALWYSNLWFGGGTKLTVLGQPKAAPSVTL FPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKA GVETTTPSKQSNKYAASSYLSLTPEQWKSQRSYSCQVT HEGSTVEKTVAPTECSGSDKHTHTCPPCPAPELLGGPSVF LFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCREEMT KNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL DSDGSFFLYSKLTVDKSRWQQGNVFSFSVMHEALHNRY TQKSLSLSPGK	748
Anti-CD19 Light Chain	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE DFAVYFCQQGNTLPYTFGQGTKLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	736
Anti-CD3 Light Chain	EVQLVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWVR QASGKGLEWVGRIIRSKYNNYATYYADSVKDRFTISRDDS KSTLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYW GQGTSLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLV KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSC	749
AB3-3 (FIG. 16C) (CD58- α CD3scFv- α CD19Fab)		
Anti-CD19 Light Chain	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE DFAVYFCQQGNTLPYTFGQGTKLEIKRTVAAPSVFIFPPS	736

TABLE 21 Amino Acid Sequences of TBMs of Example 3		
Component	Sequence	SEQ ID NO:
	DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSLSSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	
Anti-CD19 Heavy Chain	QVQLQESGPGGLVKPSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYQSSLSRVTSISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLLTVV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLG TQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEL LGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVCTLP PSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPGK	747
CD58_AntiCD3scFv-Fc	SQQIYGVVYGNVTFHVPNSVPLKEVLWKKQKDKVAELEN SEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMESP NITDTMKFFLYVLESLPSPTLTALTNESIEVQCMIPHYN SHRGLIMYSWDCPMEQCKRNSTSIYFKMENDLPQKIQCT LSNPLFNTTSSIIITTCIPSSGHSRHRGGGGSGGGGSEVQ LVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWRQAS GKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDSKSTL YLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYWGQGT LTVVSSGGGGSGGGGGSGGGGGSGGGGSAVVVTQEPSTL VSPGGTVTLTCRSSTGAVTTSNYANWWQKPGQAPRGLI GGTNKRAPWTPARFSGSLLGDKAALTLGAQPEDEAEYF CALWYSNLWVFGGGTKLTVLGGGGSDKHTCPPCPAPE LLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLTP PCREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNRYTQKSLSLSPGK	750
AB3-4 (FIG. 16D) (α CD3-CD58- α CD19Fab)		
Anti-CD19 Light Chain	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE DFAVYFCQQGNTLPYTFGQGTKLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSLSSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	736
Anti-CD19 Heavy Chain	QVQLQESGPGGLVKPSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYQSSLSRVTSISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLLTVV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT	747

TABLE 21 Amino Acid Sequences of TBMs of Example 3		
Component	Sequence	SEQ ID NO:
	VSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEL LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVCTLP PSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNY KTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPGK	
AntiCD3scFv-CD58-Fc	EVQLVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWVR QASGKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDS KSTLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYW GQGTLLTVSSGGGGSGGGGSGGGGSGGGGSGQAVVTQ EPSLTVSPGGTVTLTCRSSTGAVTTSNYANWWQQKPGQA PRGLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQPED EAIFYCALWYSNLWVFGGGTKLTVLGGGGSGGGGSSQ QIYGVVYGNVTFHVPSNVPLKEVLWKKQKDKVAELENSE FRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMESPNIT DTMKFFLYVLESLPSPTLTCAITNGSIEVQCMIPHEYNHR GLIMYSWDCPMEQCKRNSTSIYFKMENDLPQKIQCTLSN PLFNTTSSILTTICIPSSGHSRHRGSDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF NWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP CREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQPENNY KTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHE ALHNRYTQKSLSLSPGK	751
AB3-5 (FIG. 16E) (αCD3scFv-αCD19Fab-Fc-CD58)		
Anti-CD19 Light Chain	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLOPE DFAVYFCQQGNTLPYTFGQGTKLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKSTYSLSSLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	736
Anti-CD19 Heavy Chain	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYQQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLLTV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEL LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVCTLP PSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNY KTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHE	747

TABLE 21 Amino Acid Sequences of TBMs of Example 3		
Component	Sequence	SEQ ID NO:
	ALHNHYTQKSLSLSPGK	
AntiCD3 scFv-Fc-CD58	EVQLVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWVR QASGKGLEWWGRIRSKYNNYATYYADSVKDRFTISRDDS KSTLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYW GQGTLVTVSSGGGGSGGGGSGGGGSGGGGSGQAVVTQ EPSLTVSPGGTVTLTCRSSTGAVTTSNYANWWQQKPGQA PRGLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQPED EAEIFCALWYSNLWWFGGGTKLTVLGGGGSDKTHTCPP CPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSH EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPCREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQ PENNYKTTTPVLDSGSSFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGS GGGGSSQIYGVVYGNVTFHVPSNVPLKEVLWKKQKDK VAELENSEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDE YEMESPNITDTMKFFLYVLESLSPTLTALTNNGSIEVQCM IPEHYNSHRGLIMYSWDCPMEQCKRNSTSIYFKMENDLP QKIQCTLSNPLFNTTSSIILTTICIPSSGHSRHR	752

[0562] Re-directed T cell cytotoxicity assays were performed on the TBMs as described in Example 1, using human CD-19 expressing Nalm6 target cells at an E:T ratio of 5:1 and an incubation time of 48 hours.

[0563] A NFAT activation assay to assess non-specific NFAT activation of the constructs was performed as described in Example 2.

7.3.2. Results

[0564] The results of the re-directed T cell cytotoxicity assay are shown in FIG. 17. The TBM with the truncated CD58 IgV only domain on the C-terminus (AB3-5) displayed similar cytotoxic activity to trispecific AB3-1. The other alternative formats showed inferior activity.

[0565] The results of the NFAT activation assay are shown in FIG. 18. The trispecific construct with the truncated CD58 IgV only domain on the C-terminus (AB3-5) displayed greater induction of NFAT compared to the other constructs. The original format (AB3-1) showed the lowest induction of NFAT.

7.4. Example 4: Anti-CD19-Anti-CD3-Anti-CD2 TBMs with different CD19 binding arm configurations

7.4.1. Materials and Methods

[0566] Trispecific binding molecules with different anti-CD19 arm configurations were analyzed for their potential to induce T cell-mediated apoptosis in tumor target cells. Constructs included the TBM having an anti-CD19 Fab N-terminal to an anti-CD3 scFv, and a CD58 IgV domain (the same construct as AB2-2 and AB3-1, labeled AB4-1 in this Example), a TBM having an anti-CD3scFv, a C-terminal anti-CD19 scFv, and a CD58 IgV domain (AB4-2), and a TBM having an anti-CD3scFv, a C-terminal anti-CD19 Fab, and a CD58 IgV domain (AB4-3). Amino acid sequences of the TBMs of this Example are shown in Table 22. The TBMs are schematically shown in FIG. 19.

TABLE 22 Amino Acid Sequences of TBMs of Example 4		
Component	Sequence	SEQ ID NO:
AB4-1 (FIG. 19A) (αCD19$\times$CD58(IgV)$\times$$\alpha$CD3)		
αCD19 Light Chain	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGGTDTLTISLQPE DFAVYFCQQGNTLPYTFGQGTKLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	736
αCD19_Fab- αCD3_scFv-Fc	QVQLQESGPGLVKPSSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYQQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLLTV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLG TQTYICNVNHKPSNTKVDKRVEPKSCGGGGSGGGGSEV QLVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWVRQA SGKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDSKS TLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYWGQ GTLVTVSSGGGGSGGGGSGGGGSGGGGSGQAVVTQEPS LTVSPGGTVTLTCRSSTGAVTTSNYANWWQKPGQAPR GLIGGTNKRAPWTPARFSGSLLGDKAALTLGAQPEDEA EYFCALWYSNLWVFGGGTKLTVLGGGGSDKTHTCPPCP APELLGGPSVFLFPPKPKDTLMISRTPEVTCVAVSHED PEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVL HQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQV CTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSDGSFFLVSKLTVDKSRWQQGNVFCSS VMHEALHNHYTQKSLSLSPGK	743
CD58 IgV-Fc	SQQIYGVVYGNVTFHVPNSNVPLKEVLWKKQKDKVAELEN SEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMESP NITDTMKFFLYVLESGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVAVSHEDPEVKFNWYVD	744

TABLE 22 Amino Acid Sequences of TBMs of Example 4		
Component	Sequence	SEQ ID NO:
	GVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEY KCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPCREEMT KNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLD SDGSFFLYSKLTVDKSRWQQGNVFSVMSVMHEALHNR TQKSLSLSPGK	
AB4-2 (FIG. 19B) (αCD3xCD58xαCD19scFv)		
αCD3_scFv-Fc- αCD19_scFv	EVQLVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWVR QASGKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDS KSTLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYW GQGTLTVTSSGGGGSGGGGSGGGGSGGGGSGQAVVTQ EPSLTVSPGGTVTLTCRSSTGAVTTSNYANWWQQKPGQA PRGLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQPED EAEIFCALWYSNLWVFGGGTKLTVLGGGGSDKHTCPP CPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVAVVAVSH EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQ VYTLPPCREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQ PENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSV SVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGS GGGGSQVQLQESGPGLVKPSSETLSLTCTVSGVSLPDYGV SWIRQPPGKGLEWIGVIWGSETTYQSSLSRVTSKDNS KNQVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQ GTLVTVSSGGGGSGGGGSGGGGSGGGGSEIVMTQSPA TSLSPGERATLSCRASQDISKYLNWYQQKPGQAPRLLIY HTSRLHSGIPARFSGSGSGTDYTLTISSLQPEDFAVYFCQ QGNTLPYTFGQGTKLEIK	753
CD58 IgV-Fc	SQQIYGVVYGNVTFHVPNSVPLKEVLWKKQKDKVAELEN SEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMESP NITDTMKFFLYVLESGGGSDKHTCPPCPAPELLGGPSVF LFPPKPKDTLMISRTPEVTCVAVVAVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYGSTYRVVSVLTVLHQDWLNGKE YKCKVSNKALAAPIEKTISKAKGQPREPQVCTLPSSRDEL TKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTPPV LDSDGSFFLVSKLTVDKSRWQQGNVFSVMSVMHEALHNR YTQKSLSLSPGK	754
AB4-3 (FIG. 19C) (αCD3xCD58xαCD19Fab)		
αCD19 Light Chain	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE FAVYFCQQGNTLPYTFGQGTKLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSSTLSLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	736

TABLE 22 Amino Acid Sequences of TBMs of Example 4		
Component	Sequence	SEQ ID NO:
αCD3_scFv-Fc- αCD19_VH-CH1	EVQLVESGGGLVQPGGSLKLSAASGFTFNTYAMNWVR QASGKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDS KSTLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYW GQGTLVTVSSGGGGSGGGGSGGGGSGGGGSQAVVTQ EPSLTVSPGGTVTLTCRSSTGAVTTSNYANWWQQKPGQA PRGLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQPED EAEIFCALWYSNLWFGGGTKLTVLGGGSDKTHTCPP CPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVAVSH EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQ VYTLPPCREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQ PENNYKTTTPVLDSGGSFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNHYTQKSLSLSPGKGGGGSGGGGSGGGGS GGGGSQVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGV SWIRQPPGKGLEWIGVIWGSETTYQSSLSKSRVTISKDNS KNQVSLKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQ GTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTV PSSSLGTQTYICNVNHKPSNTKVDKRVEPKSC	755
CD58 IgV-Fc	SQIYGVVYGNVTFHVP SNVPLKEVLWKKQKDKVAELEN SEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMESP NITDTMKFFLYVLESGGGSDKTHTCPPCPAPELLGGPSVF LFPPKPKDTLMISRTPEVTCVAVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYGSTYRVVSVLTVLHQDWLNGKE YKCKVSNKALAAPIEKTISKAKGQPREPQVCTLPSSRDEL TKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTTPV LDSGGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNR YTQKSLSLSPGK	754

[0567] Re-directed T cell cytotoxicity assays were performed on the TBMs as described in Example 1, using human CD-19 expressing Nalm6 target cells at an E:T ratio of 5:1 and an incubation time of 48 hours.

[0568] A NFAT activation assay to assess non-specific NFAT activation of the constructs was performed as described in Example 2.

[0569] A cytokine release assay as performed in Example 1 was performed using TBMs AB4-1, AB4-2, AB3-3, an anti-CD3-anti-CD19 bispecific construct, and an anti-gH-anti-CD3-CD58 trispecific construct.

7.4.2. Results

[0570] The results of the re-directed T cell cytotoxicity assay are shown in FIG. 20. TBMs with the CD19 binding arm on the C-terminus (AB4-2 and AB4-3) were observed to have less cytotoxic activity compared to the N-terminus format (AB4-1).

[0571] The results of the NFAT activation assay are shown in FIG. 21. Constructs with the CD19 binding arm on the C-terminus (AB4-2 and AB4-3) induced a higher induction of NFAT compared to the the N-terminus format (AB4-1).

[0572] The results of the cytokine release assay are shown in FIG. 22. The AB4-1 construct format induced the highest cytokine levels. The other trispecific scaffolds tested stimulated cytokine levels that were relatively comparable to the bispecific format.

7.5. Example 5: Anti-CD19-Anti-CD3-Anti-CD2 TBMs with different CD3 binding arms

7.5.1. Materials and Methods

[0573] Trispecific binding molecules with different anti-CD3 binding arms, namely scFvs corresponding to anti-CD3 antibodies BMA031 and OKT3, were generated and analyzed for their potential to induce T cell-mediated apoptosis in tumor target cells. The TBMs were compared to bispecific constructs targeting CD3 and CD19. Amino acid sequences of the bispecific and trispecific constructs used in this example are shown in Table 23. The bispecific and trispecific constructs used in this Example are schematically shown in FIG. 23.

TABLE 23A Amino Acid Sequences of BMA031 Constructs of Example 5		
Component	Sequence	SEQ ID NO:
Bispecific (FIG. 23A) αCD19-αCD3 (BMA031)		
αCD19 Light Chain	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE DFAVYFCQQGNTLPYTFGQGTKLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNFPYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSTLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	736
αCD19 Heavy Chain	QVQLQESGPGLVKPSSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYYQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLLTV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLG TQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPEL LGGPSVFLFPPKPKDTLMISRTPEVTCVAVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQD WLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVCTLP PSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNY	756

TABLE 23A Amino Acid Sequences of BMA031 Constructs of Example 5		
Component	Sequence	SEQ ID NO:
	KTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPGK	
BMA031 scFv-Fc		
HCDR1 (Combined)	GYKFTSYVMH	757
HCDR2 (Combined)	YINPYNDVTKYNEKFKG	758
HCDR3 (Combined)	GSYYDYDGFVY	243
HCDR1 (Kabat)	SYVMH	759
HCDR2 (Kabat)	YINPYNDVTKYNEKFKG	758
HCDR3 (Kabat)	GSYYDYDGFVY	243
HCDR1 (Chothia)	GYKFTSY	760
HCDR2 (Chothia)	NPYNDV	761
HCDR3 (Chothia)	GSYYDYDGFVY	243
HCDR1 (IMGT)	GYKFTSYV	762
HCDR2 (IMGT)	INPYNDVT	763
HCDR3 (IMGT)	ARGSYDYDGFVY	764
VH	EVQLQQSGPELVKPGASVKMSCKASGYKFTSYVMHWWK QKPGQGLEWIGYINPYNDVTKYNEKFKGKATLTSDKSSST AYMELSSLTSEDSAVHYCARGSYDYDGFVYWGQGTLV TVSA	245
LCDR1 (Combined)	SATSSVSYMH	244
LCDR2 (Combined)	DTSKLAS	150
LCDR3 (Combined)	QQWSSNPLT	179
LCDR1 (Kabat)	SATSSVSYMH	244
LCDR2 (Kabat)	DTSKLAS	150
LCDR3 (Kabat)	QQWSSNPLT	179
LCDR1 (Chothia)	TSSVSY	765
LCDR2 (Chothia)	DTS	211
LCDR3 (Chothia)	WSSNPL	225

TABLE 23A Amino Acid Sequences of BMA031 Constructs of Example 5		
Component	Sequence	SEQ ID NO:
LCDR1 (IMGT)	SSVSY	766
LCDR2 (IMGT)	DTS	211
LCDR3 (IMGT)	QQWSSNPLT	179
VL	QIVLTQSPAIMASASPGEKVTMTCSATSSVSVMHWWYQQKS GTSPKRWIYDTSKLGASGVPARFSGSGSGTSYSLTISSMEA EDAATYYCQQWSSNPLTFGAGTKLELK	246
BMA031 scFv-Fc full sequence	EVQLQQSGPELVKPGASVKMSCKASGYKFTSYVMHWWK QKPGQGLEWIGYINPYNDVTKYNEKFKGKATLTSDKSSST AYMELSSLTSEDSAVHYCARGSYDYDGFVYWGQGTLLV TVSAGGGGSGGGGSGGGGSGGGGSGQIVLTQSPAIMASAS PGEKVTMTCSATSSVSVMHWWYQQKSGTSPKRWIYDTSK LASGVPARFSGSGSGTSYSLTISSMEAEDAATYYCQQWS SNPLTFGAGTKLELKGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPCREEMT KNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL DSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMHEALHNHY TQKSLSLSPGK	767
Trispecific (FIG. 23B) α CD19- α CD3(BMA031)-CD58IgV		
αCD19Light Chain	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE DFAVYFCQQGNTLPYTFGQGTLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	736
αCD19_Fab-BMA031_scFv-Fc	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYYQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLLVTV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLG TQTYICNVNHKPSNTKVDKRVKPKSCGGGGSGGGGSEV QLQQSGPELVKPGASVKMSCKASGYKFTSYVMHWWKQK PGQGLEWIGYINPYNDVTKYNEKFKGKATLTSDKSSSTAY MELSSLTSEDSAVHYCARGSYDYDGFVYWGQGTLLVTV SAGGGGSGGGGSGGGGSGGGGSGQIVLTQSPAIMASASP EVTMTCSATSSVSVMHWWYQQKSGTSPKRWIYDTSKLG ASGVPARFSGSGSGTSYSLTISSMEAEDAATYYCQQWSSNP LTFGAGTKLELKGGGGSDKTHTCPPCPAPELLGGPSVFL FPPKPKDTLMISRTPEVTCVVAVVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYGSTYRVVSVLTVLHQDWLNGKEYK	768

TABLE 23A Amino Acid Sequences of BMA031 Constructs of Example 5		
Component	Sequence	SEQ ID NO:
	CKVSNKALAAPIEKTISKAKGQPREPQVCTLPSPRDELTK NQVSLSCAVKGFYPSDIAVEWESNGQPENNYKTTTPVLD SDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEALHNHYT QKSLSLSPGK	
CD58 IgV-Fc	SQQIYGVVYGNVTFHVPSNVPLKEVLWKKQKDKVAELEN SEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMESP NITDTMKFFLYVLESGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVAVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEY KCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPCREEMT KNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNRY TQKSLSLSPGK	744

TABLE 23B Amino Acid Sequences of OKT3 Constructs of Example 5		
Component	Sequence	SEQ ID NO:
Bispecific (FIG. 23A) αCD19-αCD3(OKT3)		
αCD19Light Chain	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE DFAVYFCQQGNTLPYTFGGGTKLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	736
αCD19 Heavy Chain	QVQLQESGPGLVKPSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYYQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLVTV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLG TQTYICNVNHKPSNTKVDKRVEPKSCDKHTHTCPPCPAPEL LGGPSVFLFPPKPKDTLMISRTPEVTCVAVSHEDPEVK FNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQD WLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVCTLP PSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNY KTTTPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHE ALHNHYTQKSLSLSPGK	756
OKT3 scFv-Fc		
HCDR1 (Combined)	GYTFTRYTMH	231

TABLE 23B Amino Acid Sequences of OKT3 Constructs of Example 5		
Component	Sequence	SEQ ID NO:
HCDR2 (Combined)	YINPSRGYTNYNQKVVD	156
HCDR3 (Combined)	YYDDHYSLDY	188
HCDR1 (Kabat)	RYTMH	129
HCDR2 (Kabat)	YINPSRGYTNYNQKVVD	156
HCDR3 (Kabat)	YYDDHYSLDY	188
HCDR1 (Chothia)	GYTFTRY	197
HCDR2 (Chothia)	NPSRGY	210
HCDR3 (Chothia)	YYDDHYSLDY	188
HCDR1 (IMGT)	GYTFTRYT	769
HCDR2 (IMGT)	INPSRGYT	770
HCDR3 (IMGT)	ARYDDHYSLDY	771
VH	QVQLVQSGGGVVPGRSLRLSCKASGYTFTRYTMHWVR QAPGKGLEWIGYINPSRGYTNYNQKVVDKDRFTISRDNKNT AFLQMDSLRLPEDTGVYFCARYDDHYSLDYWGQGTPVT VSS	111
LCDR1 (Combined)	SASSSVSYM	130
LCDR2 (Combined)	DTSKLAS	150
LCDR3 (Combined)	QQWSSNPFT	174
LCDR1 (Kabat)	SASSSVSYM	130
LCDR2 (Kabat)	DTSKLAS	150
LCDR3 (Kabat)	QQWSSNPFT	174
LCDR1 (Chothia)	SSSVSY	198
LCDR2 (Chothia)	DTS	211
LCDR3 (Chothia)	WSSNPF	222
LCDR1 (IMGT)	SSSVSY	766
LCDR2 (IMGT)	DTS	211
LCDR3 (IMGT)	QQWSSNPFT	174
VL	DIQMTQSPSSLSASVGDRTITCSASSSVSYMNWYQQTP GKAPKRWIYDTSKLASGVPSRFSGSGSGTDYFTISSLP	87

TABLE 23B Amino Acid Sequences of OKT3 Constructs of Example 5		
Component	Sequence	SEQ ID NO:
	EDIATYYCQQWSSNPFTFGQGTKLQIT	
OKT3 scFv-Fc full sequence	QVQLVQSGGGVVPGRSLRLSCKASGYTFTRYTMHWVR QAPGKGLEWIGYINPSRGYTNYNQVKDRFTISRDN SKNT AFLQMDSL RPEDTGVYFCARYYDDHYS LDYWGQGTPVT VSSGGGGSGGGGSKKGGSGGGGSDIQMTQSPSSLSASV GDRVITICSASSSVSYMNWYQQTPGKAPKRWIYDTSKLA SGVPSRFSGSGSGTDYFTFTISSLQPEDIATYYCQQWSSN PFTFGQGTKLQITGGGGSDKTHTCPPCPAPELLGGPSVF LPPKPKDTLMISRTPEVTCVAVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEY KCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPCREEMT KNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY TQKSLSLSPGK	772
Trispecific (FIG. 23B) αCD19-αCD3(OKT3)-CD58IgV		
αCD19Light Chain	EIVMTQSPATLSLSPGERATLSCRASQDISKYL N WYQQKP GQAPRL LIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE DFAVYFCQQGNTLPYTFGQGTKLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	736
αCD19_Fab- OKT3_scFv-Fc	QVQLQESGPGLVKPSSETLSLTCTVSGVSLPDYGVSWIRQ PPGKGLEWIGVIWGSETTYQSSLSKSRVTISKDN SKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGT LVTV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLG TQTYICNVNHKPSNTKVDKRVEPKSCGGGGSGGGGSQV QLVQSGGGVVPGRSLRLSCKASGYTFTRYTMHWVRQA PGKGLEWIGYINPSRGYTNYNQVKDRFTISRDN SKNTAF LQMDSL RPEDTGVYFCARYYDDHYS LDYWGQGTPVTVS SGGGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSASV GDRVITICSASSSVSYMNWYQQTPGKAPKRWIYDTSKLAS GVPSRFSGSGSGTDYFTFTISSLQPEDIATYYCQQWSSNP FTFGQGTKLQITGGGGSDKTHTCPPCPAPELLGGPSVFLF PPKPKDTLMISRTPEVTCVAVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYG STYRVVSVLTVLHQDWLNGKEYKCKVSNKALAAPIEKTIS KAKGQPREPQVCTLPSSRDELTKNQVSLSCAVKGFYPSD IAVEWESNGQPENNYKTTTPVL DSDGSFFLVSKLTVDKSR WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK	773
CD58 IgV-Fc	SQQIYGVVYGNVTFHVPSNVPLKEVLWKKQKDKVAELEN SEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMESP	744

TABLE 23B Amino Acid Sequences of OKT3 Constructs of Example 5		
Component	Sequence	SEQ ID NO:
	NITDTMKFFLYVLESGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVAVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEY KCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPCREEMT KNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTPPV LDS DGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNR YTQKSLSLSPGK	

[0574] Re-directed T cell cytotoxicity assays were performed using the constructs as described in Example 1, using human CD-19 expressing Nalm6 target cells at an E:T ratio of 5:1 and an incubation time of 48 hours.

[0575] Cytokine release assays were also performed as in Example 1.

7.5.2. Results

[0576] The results of the re-directed T cell cytotoxicity assay are shown in FIG. 24A and FIG. 24B. The two trispecific constructs exhibited superior cytotoxicity in target cells compared to the bispecific constructs.

[0577] Results of the cytokine release assay are shown in FIG. 25. The trispecific constructs were observed to elicit a stronger cytokine response when compared to their bispecific counterpart.

7.6. Example 6: Production and characterization of an Anti-Her2-Anti-CD3-Anti-CD2 TBM

7.6.1. Materials and Methods

[0578] A trispecific binding molecules targeting Her2, CD3 and CD2 was generated and analyzed for its potential to induce T cell-mediated apoptosis in tumor target cells. The TBM was compared to a bispecific construct targeting CD3 and Her2. Amino acid sequences of the bispecific and trispecific constructs used in this Example are shown in Table 24. The bispecific and trispecific constructs used in this Example are schematically shown in FIG. 26.

TABLE 24 Amino Acid Sequences of Constucts of Example 6		
Component	Sequence	SEQ ID NO:
Bispecific (FIG. 26A) α Her2 $\times\alpha$ CD3		
α Her2 Fab		
HCDR1 (Combined)	GFNIKDTYIH	774

TABLE 24 Amino Acid Sequences of Constructs of Example 6		
Component	Sequence	SEQ ID NO:
HCDR2 (Combined)	RIYPTNGYTRYADSVKG	775
HCDR3 (Combined)	WGGDGFYAMDY	776
HCDR1 (Kabat)	DTYIH	777
HCDR2 (Kabat)	RIYPTNGYTRYADSVKG	775
HCDR3 (Kabat)	WGGDGFYAMDY	776
HCDR1 (Chothia)	GFNIKDT	778
HCDR2 (Chothia)	YPTNGY	779
HCDR3 (Chothia)	WGGDGFYAMDY	776
HCDR1 (IMGT)	GFNIKDTY	780
HCDR2 (IMGT)	IYPTNGYT	781
HCDR3 (IMGT)	SRWGGDGFYAMDY	782
VH	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQ APGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKNTA YLQMNSLR AEDTAVYYCSRWGGDGFYAMDYWGQGLV TVSS	783
LCDR1 (Combined)	RASQDVNTAVA	784
LCDR2 (Combined)	SASFLYS	785
LCDR3 (Combined)	QQHYTTPPT	786
LCDR1 (Kabat)	RASQDVNTAVA	784
LCDR2 (Kabat)	SASFLYS	785
LCDR3 (Kabat)	QQHYTTPPT	786
LCDR1 (Chothia)	SQDVNTA	504
LCDR2 (Chothia)	SAS	518
LCDR3 (Chothia)	HYTTPP	787
LCDR1 (IMGT)	QDVNTA	788
LCDR2 (IMGT)	SAS	518
LCDR3 (IMGT)	QQHYTTPPT	786
VL	DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQK PGKAPKLLIYSASFLYSGVPSRFSRSGTDFTLTISLQP EDFATYYCQQHYTTPPTFGQGKVEIK	789
αHer2 Light Chain	DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQK PGKAPKLLIYSASFLYSGVPSRFSRSGTDFTLTISLQP EDFATYYCQQHYTTPPTFGQGKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN SQESVTEQDSKSTYSLSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	790

TABLE 24 Amino Acid Sequences of Constructs of Example 6		
Component	Sequence	SEQ ID NO:
αHer2 Heavy Chain	EVQLVESGGGLVQPGGSLRLSCAASGFTNIDYIHWWRQ APGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKNTA YLQMNSLRLEDTAVYYCSRWGGDGFYAMDYWGQGTLLV TVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSL GTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAP ELLGGPSVFLFPPKPKDTLMISRTPEVTCVAVVAVSHEDPE VKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQ DWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVCTL PPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPGK	791
αCD3 scFv-Fc	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWWR QASGKGLEWVGRIIRSKYNNYATYYADSVKDRFTISRDDS KSTLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYW GQGTLLVTVSSGGGGSGGGGSGGGGSGGGGSGQAVVTQ EPSLTVSPGGTVTLTCRSSTGAVTTSNYANWWQQKPGQA PRGLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQPED EAEYFCALWYSNLWFGGGTKLTVLGGGGSDKTHTCPP CPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVAVVAVSH EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLT VLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQ VYTLPPCREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQ PENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNRYTQKSLSLSPGK	792
Trispecific (FIG. 26B) αHer2αCD3αCD58IgV		
αHer2 Light Chain	DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQK PGKAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQP EDFATYYCQQHYTTPPTFGQGTKEIKRTVAAPSVFIFPP SDEQLKSGTASVCLLNNFYPREAKVQWKVDNALQSGN SQESVTEQDSKSTYSLSSLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	790
αHer2_Fab- αCD3_scFv-Fc	EVQLVESGGGLVQPGGSLRLSCAASGFTNIDYIHWWRQ APGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKNTA YLQMNSLRLEDTAVYYCSRWGGDGFYAMDYWGQGTLLV TVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSL GTQTYICNVNHKPSNTKVDKRVEPKSCGGGGSGGGGSE VQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWWRQ ASGKGLEWVGRIIRSKYNNYATYYADSVKDRFTISRDDSK STLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYWG QGTLLVTVSSGGGGSGGGGSGGGGSGGGGSGQAVVTQEP SLTVSPGGTVTLTCRSSTGAVTTSNYANWWQQKPGQAP RGLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQPEDE	793

TABLE 24 Amino Acid Sequences of Constructs of Example 6		
Component	Sequence	SEQ ID NO:
	AEYFCALWYSNLWWFGGGTKLTVLGGGGSDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVAVSHE DPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTV LHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQV CTLPPSREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSGDSFFLVSKLTVDKSRWQQGNVFSCS VMHEALHNHYTQKSLSLSPGK	
CD58 IgV-Fc	SQQIYGVVYGNVTFHVPSNVPLKEVLWKKQKDKVAELEN SEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMESP NITDTMKFFLYVLESGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVAVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEY KCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPCREEMT KNQVSLWCLVKGFPYPSDIAVEWESNGQPENNYKTTTPVL DSGDSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNR Y TQKSLSLSPGK	744

[0579] Re-directed T cell cytotoxicity assays were performed using the constructs as described in Example 1, using human huHer2-expressing HCC1954 target cells (cultured in RPMI medium with 10% FBS) and human pan T effector cells at an E:T ratio of 5:1 and an incubation of 48 hours.

[0580] Cytokine release assays were also performed. Secreted cytokines were measured in the supernatant of trispecific or bispecific treated effector and target cell co-cultures using huHer2-expressing HCC1954 target cells (cultured in RPMI medium with 10% FBS) and human pan T effector cells at an E:T ratio of 5:1 and an incubation of 24 hr.

7.6.2. Results

[0581] The results of the re-directed T cell cytotoxicity assay are shown in FIG. 27. The TBM showed equivalent to superior cytotoxic activity compared to the bispecific construct.

[0582] Results of the cytokine release assay are shown in FIG. 28. The trispecific construct targeting human CD3, human CD2 and human Her2 produced cytokine levels that were at least comparable to the bispecific molecule targeting human CD3 and human Her2.

7.7. Example 7: Production and characterization of an Anti-mesothelin-Anti-CD3-Anti-CD2 TBM

7.7.1. Materials and Methods

[0583] A trispecific binding molecules targeting mesothelin, CD3 and CD2 was generated and analyzed for its potential to induce T cell-mediated apoptosis in tumor target cells. The TBM was compared to a bispecific construct targeting CD3 and mesothelin. Amino acid sequences

of the bispecific and trispecific constructs used in this Example are shown in Table 25. The bispecific and trispecific constructs used in this Example are schematically shown in FIG. 29.

TABLE 25 Amino Acid Sequences of Constructs of Example 7		
Component	Sequence	SEQ ID NO:
Bispecific (FIG. 29A) αMesoxαCD3		
αMesothelin Fab		
HCDR1 (Combined)	GYTFTDYMH	794
HCDR2 (Combined)	WINPNSGGTNYAQKFQG	795
HCDR3 (Combined)	GWDFDY	796
HCDR1 (Kabat)	DYYMH	797
HCDR2 (Kabat)	WINPNSGGTNYAQKFQG	795
HCDR3 (Kabat)	GWDFDY	796
HCDR1 (Chothia)	GYTFTDY	644
HCDR2 (Chothia)	NPNSGG	798
HCDR3 (Chothia)	GWDFDY	796
HCDR1 (IMGT)	GYTFTDYY	799
HCDR2 (IMGT)	INPNSGGT	800
HCDR3 (IMGT)	ASGWDFDY	801
VH	QVQLVQSGAEVEKPGASVKVSCKASGYTFTDYMHWR QAPGQGLEWMGWNPNSGGTNYAQKFQGRVTMTRDTSI STAYMELSRRLSDDTAVYYCASGWDFDYWGQGTLLVTS S	802
LCDR1 (Combined)	RASQSIRYYLS	803
LCDR2 (Combined)	TASILQN	804
LCDR3 (Combined)	LQTYTTPD	805
LCDR1 (Kabat)	RASQSIRYYLS	803
LCDR2 (Kabat)	TASILQN	804
LCDR3 (Kabat)	LQTYTTPD	805
LCDR1 (Chothia)	SQSIRYY	806
LCDR2 (Chothia)	TAS	807
LCDR3 (Chothia)	TYTTP	808
LCDR1 (IMGT)	QSIRYY	809
LCDR2 (IMGT)	TASILQNGVP	810
LCDR3 (IMGT)	LQTYTTPD	805
VL	DIVMTQSPSSLSASVGDRVTITCRASQSIRYYLSWYQQKP GKAPKLLIYTASILQNGVPSRFSGSGSGTDFTLTISLQPE DFATYYCLQTYTTPDFGPGTKVEIK	811

TABLE 25 Amino Acid Sequences of Constructs of Example 7		
Component	Sequence	SEQ ID NO:
αMesothelin Light Chain	DIVMTQSPSSLSASVGDRVTITCRASQSIRYYLSWYQQKP GKAPKLLIYTASILQNGVPSRFSGSGSGTDFTLTISLQPE DFATYYCLQTYTTPDFGPGTKVEIKRTVAAPSVFIFPPSDE QLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGL SSPVTKSFNRGEC	812
αMesothelin Heavy Chain	QVQLVQSGAEVEKPGASVKVSCKASGYTFTDYYMHWR QAPGQGLEWMGWINPNSGGTNYAQKFQGRVTMTRDTSI STAYMELSRRLSDDTAVYYCASGWDFDYWGQGTLLTVS SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT SWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGT QTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLMISRTPEVTCVAVSHEDPEVKF NWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLHQDW LNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVCTLP SREEMTKNQVSLSCAVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPGK	813
αCD3 scFv-Fc	EVQLVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWVR QASGKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDS KSTLYLQMNLSKTEDTAVYYCVRHGNFGNSYVSWFAYW GQGTLLTVVSSGGGGSGGGGSGGGGSGGGGSQAVVTQ EPSLTVSPGGTVTLTCSRSTGAVTTSNYANWWQQKPGQA PRGLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQPED EAIFYCALWYSNLWVFGGGTKLTVLGGGGSDKTHTCPP CPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVAVSH EDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLT VLHQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQ VYTLPPCREEMTKNQVSLWCLVKGFYPSDIAVEWESNGQ PENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNRYTQKSLSLSPGK	792
Trispecific (FIG. 29B) αMesoxαCD3xCD58IgV		
αMesothelin Light Chain	DIVMTQSPSSLSASVGDRVTITCRASQSIRYYLSWYQQKP GKAPKLLIYTASILQNGVPSRFSGSGSGTDFTLTISLQPE DFATYYCLQTYTTPDFGPGTKVEIKRTVAAPSVFIFPPSDE QLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQE SVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGL SSPVTKSFNRGEC	812
αMesothelin_Fab-αCD3_scFv-Fc	QVQLVQSGAEVEKPGASVKVSCKASGYTFTDYYMHWR QAPGQGLEWMGWINPNSGGTNYAQKFQGRVTMTRDTSI STAYMELSRRLSDDTAVYYCASGWDFDYWGQGTLLTVS SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT SWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGT QTYICNVNHKPSNTKVDKRVEPKSCGGGGSGGGGSEVQ	814

TABLE 25 Amino Acid Sequences of Constructs of Example 7		
Component	Sequence	SEQ ID NO:
	LVESGGGLVQPGGSLKLSCAASGFTFNTYAMNWRQAS GKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDSKSTL YLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYWGQGT LVTVSSGGGGSGGGGSGGGGSGGGGSSQAVVTQEPSLT VSPGGTVTLTCRSSTGAVTTSNYANWWQQKPGQAPRGLI GGTNKRAPWTPARFSGSLLGDKAALTLGAQPEDEAEYF CALWYSNLWWFGGGTKLTVLGGGGSDKTHTCPPCPAPE LLGGPSVFLFPPKPKDTLMISRTPEVTCVAVSHEDPEV KFNWYVDGVEVHNAKTKPREEQYGSTYRVVSVLTVLHQ DWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQVCTL PPSRDELTKNQVSLSCAVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSDGSFFLVSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPGK	
CD58 IgV-Fc	SQQIYGVVYGNVTFHVPSTNPLKEVLWKKQKDKVAELEN SEFRAFSSFKNRVYLDTVSGSLTIYNLTSSDEDEYEMESP NITDTMKFFLYVLESGGGGSDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVAVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYASTYRVVSVLTVLHQDWLNGKEY KCKVSNKALAAPIEKTISKAKGQPREPQVYTLPPCREMT KNQVSLWCLVKGFYPSDIAVEWESNGQPENNYKTTTPVL DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNRY TQKSLSLSPGK	744

[0584] Re-directed T cell cytotoxicity assays were performed using the constructs as described in Example 1, using human huMesothelin-expressing OVCAR8 target cells (cultured in DMEM medium with 10% FBS) and human pan T effector cells at an E:T ratio of 5:1 and an incubation of 48 hours.

[0585] Cytokine release assays were also performed. Secreted cytokines were measured in the supernatant of trispecific or bispecific treated effector and target cell co-cultures using huMesothelin-expressing Ovar8 target cells (cultured in DMEM medium with 10% FBS) and human pan T effector cells at an E:T ratio of 5:1 and an incubation of 24 hr.

7.7.2. Results

[0586] The results of the re-directed T cell cytotoxicity assay are shown in FIG. 30. The TBM showed superior cytotoxic activity compared to the bispecific construct.

[0587] Results of the cytokine release assay are shown in FIG. 31. The trispecific construct targeting human CD3, human CD2 and human mesothelin produced cytokine levels that are at least comparable to the bispecific molecule targeting human CD3 and human mesothelin.

7.8. Example 8: Production and characterization of an Anti-CD19-Anti-CD3-Anti-CD2 TBM with CD48 as the CD2 binding arm

7.8.1. Materials and Methods

7.8.1.1. Gene construction, expression and purification of bi- and tri-specific binding molecules

[0588] A trispecific construct is made as in Example 1, but with a CD48 moiety substituted for the CD58 moiety. The trispecific construct is represented schematically in FIG. 32. Amino acid sequences for the construct are shown in Table 26.

TABLE 26 Amino Acid Sequences of the Tri-specific Construct of Example 8 (CD19Fab/hCD3 scFv-CD48 ligand 1x1 format)		
Component	Sequence	SEQ ID NO:
CD48 ligand (positions 27-220 of UniProt identifier P09326)	QGHVHMTVVSGSNVTNLNISESLPENYKQLTWFYTFDQKI VEWDSRKSIFYESKFGRVRLDPQSGALYISKVQKEDNS TYIMRVLKKTGNEQEWKIKLQVLDVPKPKVIEKIEDMDD NCYLKLSVCIPGESVNYTWYGDKRPFKELQNSVLETTLM PHNYSRCYTCQVSNSVSSKNGTVCLSPPTLARS	815
αCD19 Light chain	EIVMTQSPATLSLSPGERATLSCRASQDISKYLNWYQQKP GQAPRLLIYHTSRLHSGIPARFSGSGSGTDYTLTISSLQPE DFAVYFCQQGNTLPYTFGQGTKLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC	736
Full CD19-CD3 arm	QVQLQESGPGLVKPSSETLSLTCTVSGVSLPDYGVSWMRQ PPGKGLEWIGVIWGSETTYQQSSLKSRVTISKDNSKNQVS LKLSSVTAADTAVYYCAKHYYYGGSYAMDYWGQGTLLTV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT VSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLG TQTYICNVNHKPSNTKVDKRVEPKSCGGGGSGGGGSEV QLVESGGGLVQPGGSLKLSKAASGFTFTNYAMNWVRQA SGKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDSKS TLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYWGQ GTLVTVSSGGGGSGGGGSGGGGSGGGGSGQAVVTQEPS LTVSPGGTVTLTCSRSTGAVTTSNYANWWQKPGQAPR GLIGGTNKRAPWTPARFSGSLLGDKAALTLSGAQPEDEA EYFCALWYSNLWVFGGGTKLTVLGGGGSDKTHTCPPCP APPELLGGPSVFLFPPKPKDTLMISRTPEVTCVAVVSHED PEVKFNWYVDGVEVHNAKTKPREEQYGSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALAAPIEKTISKAKGQPREPQV CTLPPSRDELTKNQVSLSCAVKGFYPSDIAVEWESNGQP ENNYKTTTPVLDSDGSFFLVSKLTVDKSRWQQGNVFCSS VMHEALHNHYTQKSLSLSPGK	738
Full CD48 ligand arm	QGHVHMTVVSGSNVTNLNISESLPENYKQLTWFYTFDQKI VEWDSRKSIFYESKFGRVRLDPQSGALYISKVQKEDNS TYIMRVLKKTGNEQEWKIKLQVLDVPKPKVIEKIEDMDD NCYLKLSVCIPGESVNYTWYGDKRPFKELQNSVLETTLM PHNYSRCYTCQVSNSVSSKNGTVCLSPPTLARS DKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYAS TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISK	816

TABLE 26 Amino Acid Sequences of the Tri-specific Construct of Example 8 (CD19Fab/hCD3 scFv-CD48 ligand 1x1 format)		
Component	Sequence	SEQ ID NO:
	AKGQPREPQVYTLPPCREEMTKNQVSLWCLVKGFYPSDI AVEWESNGQPENNYKTTTPVLDSGSSFFLYSKLTVDKSR WQQGNVFSCSVMHEALHNRYTQKSLSLSPGK	

[0589] The TBM is expressed and purified according to the protocol described in Example 1.

[0590] A re-directed T cell cytotoxicity assay, proliferation assay, cytokine release assay, and granzyme B ELISpot assay are performed as in Example 1, with the anti-CD19-anti-CD3 bispecific construct described in Example 1 as comparator molecule.

7.8.2. Results

7.8.2.1. Results

[0591] The TBM construct induces superior cytotoxicity in huCD19-expressing Nalm6 target cells compared to the bispecific construct in an assay performed with a final E:T ratio of 5:1 and either 24 or 48 hour incubation.

[0592] The TBM construct induces superior cytotoxic activity in huCD19-expressing Daudi target cells compared to the bispecific construct in an assay performed with a final E:T ratio of 5:1 and 48 hour incubation.

[0593] The TBM construct does not induce apoptosis of the negative control K562 cell line, which does not express human CD19, in an assay performed with a final E:T ratio of 5:1 and 48 hour incubation.

[0594] The TBM exhibits comparable or superior potency and efficacy compared to the bispecific construct in huCD19-expressing Nalm6 target cells when using human cryopreserved PBMCs that are thawed and rested overnight prior to use and with a final E:T ratio of 10:1 and 24 hour incubation.

[0595] The TBM construct induces superior cytotoxic activity in huCD19-expressing Nalm6 target cells compared to the bispecific when using human cryopreserved PBMCs from a patient diagnosed with acute myeloid leukemia (Hemacare #PB009C-1-AML) that are thawed and rested overnight prior to use and with a final E:T ratio of 10:1 and 24 hour incubation.

[0596] In a rechallenge assay with huCD19 expressing Nalm6 target cells, the TBM continues to induce apoptosis up to 120 hours with little apparent loss in activity across each rechallenge while the bispecific construct loses significant potency and activity with each subsequent target cell addition.

[0597] The trispecific construct mediates higher levels of CD25 and double positive expression (CD25 and CD69) compared to the bispecific construct in both the CD4 and CD8 compartments.

[0598] The trispecific construct mediates higher levels of PD1, LAG3 and TIM3 compared to the bispecific construct in both the CD4 and CD8 compartments.

[0599] The trispecific construct mediates a greater amount of central memory T cells compared to the bispecific construct.

[0600] The TBM induces proliferation of CD8+ T cells.

[0601] The trispecific molecule induces production of IFN γ , TNF α , IL2, IL6 and IL10 in human pan T effector cells in the presence of huCD19-expressing Nalm6 target cells.

[0602] The number of Granzyme B spotforming T cells is higher upon treatment with the CD2-CD3-CD19-targeting TBM than with the bispecific construct.

8. SPECIFIC EMBODIMENTS, CITATION OF REFERENCES

[0603] While various specific embodiments have been illustrated and described, it will be appreciated that various changes can be made without departing from the spirit and scope of the disclosure(s). The present disclosure is exemplified by the numbered embodiments set forth below.

1. A trispecific binding molecule (TBM), comprising:

(a) an antigen-binding module 1 (ABM1) that binds specifically to human CD2;

(b) an antigen-binding module 2 (ABM2) that binds specifically to a component of a human T-cell receptor (TCR) complex; and

(c) an antigen-binding module 3 (ABM3) that binds specifically to a human tumor-associated antigen (TAA),

optionally wherein each antigen-binding module is capable of binding its respective target at the same time as each of the other antigen-binding modules is bound to its respective target.

2. The TBM of embodiment 1, wherein ABM1 comprises a receptor binding domain of a CD2 ligand.

3. The TBM of embodiment 2, wherein the CD2 ligand is CD58.

4. The TBM of embodiment 2, wherein the CD2 ligand is CD48.
5. The TBM of embodiment 1, wherein ABM1 is a CD58 moiety.
6. The TBM of embodiment 5, wherein the CD58 moiety comprises the amino acid sequence of CD58-5.
7. The TBM of embodiment 6, wherein the amino acid designated as J is a valine.
8. The TBM of embodiment 6, wherein the amino acid designated as J is a lysine.
9. The TBM of any one of embodiments 6 to 8, wherein the amino acid designated as O is a valine.
10. The TBM of any one of embodiments 6 to 8, wherein the amino acid designated as O is a glutamine.
11. The TBM of embodiment 5, wherein the CD58 moiety comprises the amino acid sequence of CD58-3.
12. The TBM of embodiment 11, wherein the amino acid designated as B is a phenylalanine.
13. The TBM of embodiment 11, wherein the amino acid designated as B is a serine.
14. The TBM of any one of embodiments 11 to 13, wherein the amino acid designated as J is a valine.
15. The TBM of any one of embodiments 11 to 13, wherein the amino acid designated as J is a lysine.
16. The TBM of any one of embodiments 11 to 15, wherein the amino acid designated as O is a valine.
17. The TBM of any one of embodiments 11 to 15, wherein the amino acid designated as O is a glutamine.
18. The TBM of any one of embodiments 11 to 17, wherein the amino acid designated as U is a valine.
19. The TBM of any one of embodiments 11 to 17, wherein the amino acid designated as U is a lysine.

20. The TBM of any one of embodiments 11 to 19, wherein the amino acid designated as X is a threonine.

21. The TBM of any one of embodiments 11 to 19, wherein the amino acid designated as X is a serine.

22. The TBM of any one of embodiments 11 to 21, wherein the amino acid designated as Z is a leucine.

23. The TBM of any one of embodiments 11 to 21, wherein the amino acid designated as X is a glycine.

24. The TBM of embodiment 2, wherein the CD58 moiety comprises amino acids 1-94 of CD58-2.

25. The TBM of embodiment 1, wherein ABM1 is a CD48 moiety.

26. The TBM of embodiment 25, wherein the CD48 moiety has at least 70% sequence identity to amino acids 27-220 of the amino acid sequence of Uniprot identifier P09326.

27. The TBM of embodiment 25, wherein the CD48 moiety has at least 80% sequence identity to amino acids 27-220 of the amino acid sequence of Uniprot identifier P09326.

28. The TBM of embodiment 25, wherein the CD48 moiety has at least 90% sequence identity to amino acids 27-220 of the amino acid sequence of Uniprot identifier P09326.

29. The TBM of embodiment 25, wherein the CD48 moiety has at least 95% sequence identity to amino acids 27-220 of the amino acid sequence of Uniprot identifier P09326.

30. The TBM of embodiment 25, wherein the CD48 moiety has at least 99% sequence identity to amino acids 27-220 of the amino acid sequence of Uniprot identifier P09326.

31. The TBM of embodiment 1, wherein ABM1 is an anti-CD2 antibody or an antigen-binding domain thereof.

32. The TBM of embodiment 31, wherein ABM1 comprises the CDR sequences of CD2-1.

33. The TBM of embodiment 32, wherein ABM1 comprises the heavy and light chain variable sequences of CD2-1.
34. The TBM of embodiment 32, wherein ABM1 comprises the heavy and light chain variable sequences of hu1CD2-1.
35. The TBM of embodiment 32, wherein ABM1 comprises the heavy and light chain variable sequences of hu2CD2-1.
36. The TBM of embodiment 31, wherein ABM1 comprises the CDR sequences of Medi 507.
37. The TBM of embodiment 36, wherein ABM1 comprises the heavy and light chain variable sequences of Medi 507.
38. The TBM of any one of embodiments 1 to 37, wherein the component of the TCR complex is CD3.
39. The TBM of embodiment 38, wherein ABM2 is an anti-CD3 antibody or an antigen-binding domain thereof.
40. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-1.
41. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-2.
42. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-3.
43. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-4.
44. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-5.
45. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-6.
46. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-7.

47. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-8.
48. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-9.
49. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-10.
50. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-11.
51. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-12.
52. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-13.
53. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-14.
54. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-15.
55. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-16.
56. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-17.
57. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-18.
58. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-19.
59. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-20.
60. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of CD3-21.

61. The TBM of any one of embodiment 40 to embodiment 60, wherein the CDRs are defined by Kabat numbering, as set forth in Table 7B.

62. The TBM of any one of embodiment 40 to embodiment 60, wherein the CDRs are defined by Chothia numbering, as set forth in Table 7C.

63. TBM of any one of embodiment 40 to embodiment 60, wherein the CDRs are defined by a combination of Kabat and Chothia numbering, as set forth in Table 7D.

64. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-1, as set forth in Table 7A.

65. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-2, as set forth in Table 7A.

66. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-3, as set forth in Table 7A.

67. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-4, as set forth in Table 7A.

68. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-5, as set forth in Table 7A.

69. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-6, as set forth in Table 7A.

70. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-7, as set forth in Table 7A.

71. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-8, as set forth in Table 7A.

72. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-9, as set forth in Table 7A.

73. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-10, as set forth in Table 7A.

74. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-11, as set forth in Table 7A.

75. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-12, as set forth in Table 7A.

76. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-13, as set forth in Table 7A.

77. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-14, as set forth in Table 7A.

78. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-15, as set forth in Table 7A.

79. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-16, as set forth in Table 7A.

80. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-17, as set forth in Table 7A.

81. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-18, as set forth in Table 7A.

82. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-19, as set forth in Table 7A.

83. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-20, as set forth in Table 7A.

84. The TBM of embodiment 39, wherein ABM2 comprises the heavy and light chain variable sequences of CD3-21, as set forth in Table 7A.

85. The TBM of embodiment 39, wherein ABM2 comprises the CDR sequences of OKT3.

86. The TBM of embodiment 85, wherein the CDRs are defined by Kabat numbering, as set forth in Table 23B.

87. The TBM of embodiment 85, wherein the CDRs are defined by Chothia numbering, as set forth in Table 23B.

88. The TBM of embodiment 85, wherein the CDRs are defined by IMGT numbering, as set forth in Table 23B.

89. TBM of embodiment 85, wherein the CDRs are defined by a combination of Kabat and Chothia numbering, as set forth in Table 23B.

90. TBM of embodiment 85, wherein ABM2 comprises the heavy and light chain variable sequences of OKT3, as set forth in Table 23B.

91. The TBM of any one of embodiments 1 to 35, wherein the component of the TCR complex is TCR- α , TCR- β , or a TCR- α/β dimer.

92. The TBM of embodiment 91, wherein ABM2 is an antibody or an antigen-binding domain thereof.

93. The TBM of embodiment 92, wherein ABM2 comprises the CDR sequences of BMA031.

94. The TBM of embodiment 93, wherein the CDR sequences are defined as in Table 8.

95. The TBM of embodiment 93, wherein the CDR sequences are defined by Kabat numbering, as set forth in Table 23A.

96. The TBM of embodiment 93, wherein the CDR sequences are defined by IMGT numbering, as set forth in Table 23A.

97. The TBM of embodiment 93, wherein the CDR sequences are defined by Chothia numbering, as set forth in Table 23A.

98. The TBM of embodiment 93, wherein the CDR sequences are defined by a combination of Kabat and Chothia numbering, as set forth in Table 23A.

99. The TBM of embodiment 93, wherein ABM2 comprises the heavy and light chain variable sequences of BMA031.

100. The TBM of any any one of embodiments 1 to 35, wherein the component of the TCR complex is TCR- γ , TCR- δ , or a TCR- γ/δ dimer.

101. The TBM of embodiment 100, wherein ABM2 is an antibody or an antigen-binding domain thereof.

102. The TBM of embodiment 101 wherein ABM2 comprises the CDR sequences of δ TCS1.

103. The TBM of embodiment 102, wherein the CDR sequences are defined by Kabat numbering.

104. The TBM of embodiment 102, wherein the CDR sequences are defined by Chothia numbering.

105. The TBM of embodiment 102, wherein the CDR sequences are defined by a combination of Kabat and Chothia numbering.

106. The TBM of embodiment 102, wherein ABM2 comprises the heavy and light chain variable sequences of δ TCS1.

107. The TBM of any one of embodiments 1 to 106 wherein ABM3 is an anti-TAA antibody or an antigen-binding domain thereof.

108. The TBM of embodiment 107, wherein the TAA is TSHR, CD171, CS-1, CLL-1, GD3, Tn Ag, FLT3, CD38, CD44v6, B7H3, KIT, IL-13Ra2, IL-11Ra, PSCA, PRSS21, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, MUC1, EGFR, NCAM, CAIX, LMP2, EphA2, fucosyl GM1, sLe, GM3, TGS5, HMWMAA, α -acetyl-GD2, GD2, folate receptor alpha, 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, TAARP, WT1, ETV6-AML, sperm protein 17, XAGE1, Tie 2, MAD-CT-1, MAD-CT-2, Fos-related antigen 1, p53 mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP-4, SSX2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3, FCRL5, IGLL1, CD19, CD20, CD30, ERBB2, ROR1, FLT3, TAAG72, CD22, CD33, GD2, BCMA, gp100Tn, FAP, tyrosinase, EPCAM, CEA, Igf-I receptor, EphB2, mesothelin, Cadherin17, CD32b, EGFRvIII, GPNMB, GPR64, HER3, LRP6, LYPD8, NKG2D, SLC34A2, SLC39A6, SLITRK6, or TACSTD2.

109. The TBM of embodiment 108, wherein the anti-TAA antibody or antigen-binding domain thereof has the CDR sequences of an antibody set forth in Table 11.

110. The TBM of embodiment 108, wherein the anti-TAA antibody or antigen-binding domain thereof has the heavy and light chain variable region sequences of an antibody set forth in Table 11.

111. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to CD22.

112. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to CS1.

113. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to CD33.

114. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to GD2.

115. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to BCMA.

116. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to Tn.

117. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to PSMA.

118. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to ROR1.

119. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to FLT3.

120. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to TAAG72.

121. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to FAP.

122. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to CD38.

123. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to CD44v6.

124. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to CEA.

125. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to EPCAM.

126. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to PRSS21.

127. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to B7H3.

128. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to KIT.

129. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to IL-13Ra2.

130. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to CD30.

131. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to GD3.

132. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to CD171.

133. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to IL-11Ra.

134. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to PSCA.

135. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to VEGFR2.

136. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to LewisY.

137. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to CD24.

138. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to PDGFR-beta.

139. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to SSEA-4.

140. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to CD20.

141. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to folate receptor alpha.

142. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to ERBB2.

143. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to MUC1.

144. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to EGFR.

145. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to NCAM.

146. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to ephrin B2

147. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to IGF-I receptor.

148. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to CAIX.

149. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to LMP2.

150. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to gp100.

151. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to tyrosinase.

152. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to ephA2.

153. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to mesothelin.

154. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to ALK.

155. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to CD19.

156. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to CD97.

157. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to CLDN6.

158. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to EGFRvIII.

159. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to folate receptor beta.

160. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to GloboH.

161. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to GPRC5D.

162. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to HMWMAA.

163. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to LRP6.

164. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to NY-BR-1.

165. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to PLAC1.

166. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to polysialic acid.

167. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to TEM1/CD248.

168. The TBM of embodiment 109 or embodiment 110, wherein the anti-TAA antibody or antigen-binding domain thereof binds to TSHR.

169. The TBM of embodiment 107, wherein the TAA is CD19.

170. The TBM of embodiment 169, wherein the anti-TAA antibody or antigen-binding domain thereof comprises heavy chain CDRs having the amino acid sequences of CD19-H1, CD19-H2A, and CD19-H3 as set forth in Table 13 and light chain CDRs having the amino acid sequences of CD19-L1, CD19-L2, and CD19-L3 as set forth in Table 13.

171. The TBM of embodiment 170, wherein the anti-TAA antibody or antigen-binding domain thereof comprises a heavy chain variable region having the amino acid sequences of VHA as set forth in Table 13 and a light chain variable region having the amino acid sequences of VLA as set forth in Table 13.

172. The TBM of embodiment 169, wherein the anti-TAA antibody or antigen-binding domain thereof comprises heavy chain CDRs having the amino acid sequences of CD19-H1, CD19-H2B, and CD19-H3 as set forth in Table 13 and light chain CDRs having the amino acid sequences of CD19-L1, CD19-L2, and CD19-L3 as set forth in Table 13.

173. The TBM of embodiment 172, wherein the anti-TAA antibody or antigen-binding domain thereof comprises a heavy chain variable region having the amino acid sequences of VHB as set forth in Table 13 and a light chain variable region having the amino acid sequences of VLB as set forth in Table 13.

174. The TBM of embodiment 169, wherein the anti-TAA antibody or antigen-binding domain thereof comprises heavy chain CDRs having the amino acid sequences of CD19-H1, CD19-H2C, and CD19-H3 as set forth in Table 13 and light chain CDRs having the amino acid sequences of CD19-L1, CD19-L2, and CD19-L3 as set forth in Table 13.

175. The TBM of embodiment 174, wherein the anti-TAA antibody or antigen-binding domain thereof comprises a heavy chain variable region having the amino acid sequences of VHC as set forth in Table 13 and a light chain variable region having the amino acid sequences of VLB as set forth in Table 13.

176. The TBM of embodiment 169, wherein the anti-TAA antibody or antigen-binding domain thereof comprises heavy chain CDRs having the amino acid sequences of CD19-H1, CD19-H2D, and CD19-H3 as set forth in Table 13 and light chain CDRs having the amino acid sequences of CD19-L1, CD19-L2, and CD19-L3 as set forth in Table 13.

177. The TBM of embodiment 176, wherein the anti-TAA antibody or antigen-binding domain thereof comprises a heavy chain variable region having the amino acid sequences of VHD as set forth in Table 13 and a light chain variable region having the amino acid sequences of VLB as set forth in Table 13.

178. The TBM of embodiment 107, wherein the TAA is Her2.

179. The TBM of embodiment 178, wherein ABM3 comprises the CDR sequences of the VH and VL sequences of the anti-Her2 Fab set forth in Table 24.

180. The TBM of embodiment 179, wherein the CDRs are defined by Kabat numbering, as set forth in Table 24.

181. The TBM of embodiment 179, wherein the CDRs are defined by Chothia numbering, as set forth in Table 24.

182. The TBM of embodiment 179, wherein the CDRs are defined by IMGT numbering, as set forth in Table 24.

183. The TBM of embodiment 179, wherein the CDRs are defined by a combination of Kabat and Chothia numbering, as set forth in Table 24.

184. The TBM of embodiment 178, wherein ABM3 comprises the VH and VL sequences of the anti-Her2 Fab set forth in Table 24.

185. The TBM of embodiment 107, wherein the TAA is mesothelin.

186. The TBM of embodiment 185, wherein ABM3 comprises the CDR sequences of the VH and VL sequences of the anti-mesothelin Fab set forth in Table 25.

187. The TBM of embodiment 186, wherein the CDRs are defined by Kabat numbering, as set forth in Table 25.

188. The TBM of embodiment 186, wherein the CDRs are defined by Chothia numbering, as set forth in Table 25.

189. The TBM of embodiment 186, wherein the CDRs are defined by IMGT numbering, as set forth in Table 25.

190. The TBM of embodiment 186, wherein the CDRs are defined by a combination of Kabat and Chothia numbering, as set forth in Table 25.

191. The TBM of embodiment 185, wherein ABM3 comprises the VH and VL sequences of the anti-mesothelin Fab set forth in Table 25.
192. The TBM of embodiment 107, wherein the TAA is BCMA.
193. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-1.
194. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-2.
195. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-3.
196. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-4.
197. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-5.
198. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-6.
199. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-7.
200. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-8.
201. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-9.
202. The TBM of embodiment 178, wherein ABM3 comprises the CDR sequences of BCMA-10.
203. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-11.
204. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-12.
205. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-13.

206. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-14.
207. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-15.
208. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-16.
209. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-17.
210. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-18.
211. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-19.
212. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-20.
213. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-21.
214. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-22.
215. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-23.
216. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-24.
217. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-25.
218. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-26.
219. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-27.

220. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-28.
221. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-29.
222. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-30.
223. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-31.
224. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-32.
225. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-33.
226. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-34.
227. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-35.
228. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-36.
229. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-37.
230. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-38.
231. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-39.
232. The TBM of embodiment 192, wherein ABM3 comprises the CDR sequences of BCMA-40.
233. The TBM of any one of embodiments 193 to 232, wherein the CDRs are defined by Kabat numbering, as set forth in Table 12B and 12E.

234. The TBM of any one of embodiments 193 to 232, wherein the CDRs are defined by Chothia numbering, as set forth in Table 12C and 12F.

235. TBM of any one of embodiments 193 to 232, wherein the CDRs are defined by a combination of Kabat and Chothia numbering, as set forth in Table 12D and 12G.

236. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-1, as set forth in Table 12A.

237. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-2, as set forth in Table 12A.

238. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-3, as set forth in Table 12A.

239. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-4, as set forth in Table 12A.

240. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-5, as set forth in Table 12A.

241. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-6, as set forth in Table 12A.

242. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-7, as set forth in Table 12A.

243. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-8, as set forth in Table 12A.

244. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-9, as set forth in Table 12A.

245. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-10, as set forth in Table 12A.

246. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-11, as set forth in Table 12A.

247. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-12, as set forth in Table 12A.

248. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-13, as set forth in Table 12A.

249. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-14, as set forth in Table 12A.

250. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-15, as set forth in Table 12A.

251. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-16, as set forth in Table 12A.

252. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-17, as set forth in Table 12A.

253. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-18, as set forth in Table 12A.

254. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-19, as set forth in Table 12A.

255. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-20, as set forth in Table 12A.

256. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-21, as set forth in Table 12A.

257. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-22, as set forth in Table 12A.

258. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-23, as set forth in Table 12A.

259. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-24, as set forth in Table 12A.

260. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-25, as set forth in Table 12A.

261. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-26, as set forth in Table 12A.

262. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-27, as set forth in Table 12A.

263. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-28, as set forth in Table 12A.

264. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-29, as set forth in Table 12A.

265. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-30, as set forth in Table 12A.

266. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-31, as set forth in Table 12A.

267. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-32, as set forth in Table 12A.

268. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-33, as set forth in Table 12A.

269. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-34, as set forth in Table 12A.

270. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-35, as set forth in Table 12A.

271. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-36, as set forth in Table 12A.

272. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-37, as set forth in Table 12A.

273. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-38, as set forth in Table 12A.

274. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-39, as set forth in Table 12A.

275. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-40, as set forth in Table 12A.

276. The TBM of embodiment 192, wherein ABM3 comprises the heavy and light chain variable sequences of BCMA-40, as set forth in Table 12A.

277. The TBM of any one of embodiments 1 to 106, wherein if TAA is a receptor, ABM3 comprises a receptor binding domain of a ligand of the receptor, and if TAA is a ligand, ABM3 comprises a ligand binding domain of a receptor of the ligand.

278. The TBM of embodiment 277, wherein the TAA is TSHR, CD171, CS-1, CLL-1, GD3, Tn Ag, FLT3, CD38, CD44v6, B7H3, KIT, IL-13Ra2, IL-11Ra, PSCA, PRSS21, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, MUC1, EGFR, NCAM, CAIX, LMP2, EphA2, fucosyl GM1, sLe, GM3, TGS5, HMWMAA, o-acetyl-GD2, GD2, folate receptor alpha, 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, TAARP, WT1, ETV6-AML, sperm protein 17, XAGE1, Tie 2, MAD-CT-1, MAD-CT-2, Fos-related antigen 1, p53 mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP-4, SSX2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3, FCRL5, IGLL1, CD19, CD20, CD30, ERBB2, ROR1, FLT3, TAAG72, CD22, CD33, GD2, BCMA, gp100Tn, FAP, tyrosinase, EPCAM, CEA, Igf-I receptor, EphB2, mesothelin, Cadherin17, CD32b, EGFRvIII, GPNMB, GPR64, HER3, LRP6, LYPD8, NKG2D, SLC34A2, SLC39A6, SLITRK6, or TACSTD2.

279. The TBM of embodiment 278, wherein the TAA is CD22.

280. The TBM of embodiment 278, wherein the TAA is CS1.

281. The TBM of embodiment 278, wherein the TAA is CD33.

282. The TBM of embodiment 278, wherein the TAA is GD2.

283. The TBM of embodiment 278, wherein the TAA is BCMA.

284. The TBM of embodiment 278, wherein the TAA is Tn.

285. The TBM of embodiment 278, wherein the TAA is PSMA.

286. The TBM of embodiment 278, wherein the TAA is ROR1.

287. The TBM of embodiment 278, wherein the TAA is FLT3.

288. The TBM of embodiment 278, wherein the TAA is TAAG72.

- 289. The TBM of embodiment 278, wherein the TAA is FAP.
- 290. The TBM of embodiment 278, wherein the TAA is CD38.
- 291. The TBM of embodiment 278, wherein the TAA is CD44v6.
- 292. The TBM of embodiment 278, wherein the TAA is CEA.
- 293. The TBM of embodiment 278, wherein the TAA is EPCAM.
- 294. The TBM of embodiment 278, wherein the TAA is PRSS21.
- 295. The TBM of embodiment 278, wherein the TAA is B7H3.
- 296. The TBM of embodiment 278, wherein the TAA is KIT.
- 297. The TBM of embodiment 278, wherein the TAA is IL-13Ra2.
- 298. The TBM of embodiment 278, wherein the TAA is CD30.
- 299. The TBM of embodiment 278, wherein the TAA is GD3.
- 300. The TBM of embodiment 278, wherein the TAA is CD171.
- 301. The TBM of 278, wherein the TAA is IL-11Ra.
- 302. The TBM of embodiment 278, wherein the TAA is PSCA.
- 303. The TBM of embodiment 278, wherein the TAA is VEGFR2.
- 304. The TBM of embodiment 278, wherein the TAA is LewisY.
- 305. The TBM of embodiment 278, wherein the TAA is CD24.
- 306. The TBM of embodiment 278, wherein the TAA is PDGFR-beta.
- 307. The TBM of embodiment 278, wherein the TAA is SSEA-4.
- 308. The TBM of embodiment 278, wherein the TAA is CD20.
- 309. The TBM of embodiment 278, wherein the TAA is folate receptor alpha.
- 310. The TBM of embodiment 278, wherein the TAA is ERBB2.
- 311. The TBM of embodiment 278, wherein the TAA is MUC1.

- 312. The TBM of embodiment 278, wherein the TAA is EGFR.
- 313. The TBM of embodiment 278, wherein the TAA is NCAM.
- 314. The TBM of embodiment 278, wherein the TAA is ephrin B2
- 315. The TBM of embodiment 278, wherein the TAA is IGF-I receptor.
- 316. The TBM of embodiment 278, wherein the TAA is CAIX.
- 317. The TBM of embodiment 278, wherein the TAA is LMP2.
- 318. The TBM of embodiment 278, wherein the TAA is gp100.
- 319. The TBM of embodiment 278, wherein the TAA is tyrosinase.
- 320. The TBM of embodiment 278, wherein the TAA is ephA2.
- 321. The TBM of embodiment 278, wherein the TAA is mesothelin.
- 322. The TBM of embodiment 278, wherein the TAA is ALK.
- 323. The TBM of embodiment 278, wherein the TAA is CD19.
- 324. The TBM of embodiment 278, wherein the TAA is CD97.
- 325. The TBM of embodiment 278, wherein the TAA is CLDN6.
- 326. The TBM of embodiment 278, wherein the TAA is EGFRvIII.
- 327. The TBM of embodiment 278, wherein the TAA is folate receptor beta.
- 328. The TBM of embodiment 278, wherein the TAA is GloboH.
- 329. The TBM of embodiment 278, wherein the TAA is GPRC5D.
- 330. The TBM of embodiment 278, wherein the TAA is HMWMAA.
- 331. The TBM of embodiment 278, wherein the TAA is LRP6.
- 332. The TBM of embodiment 278, wherein the TAA is NY-BR-1.
- 333. The TBM of embodiment 278, wherein the TAA is PLAC1.
- 334. The TBM of embodiment 278, wherein the TAA is polysialic acid.

335. The TBM of embodiment 278, wherein the TAA is TEM1/CD248.
336. The TBM of embodiment 278, wherein the TAA is TSHR.
337. The TBM of embodiment 278, wherein the TAA is CD19.
338. The TBM of embodiment 278, wherein the TAA is Her2.
339. The TBM of embodiment of any one of embodiments 31 to 338, wherein ABM1 is an antibody, an antibody fragment, an scFv, a dsFv, a Fv, a Fab, an scFab, a (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain.
340. The TBM of embodiment 339, wherein ABM1 is an scFv.
341. The TBM of embodiment of embodiment 339, wherein ABM1 is a Fab.
342. The TBM of any one of embodiments 1 to 341, wherein ABM2 is an antibody, an antibody fragment, an scFv, a dsFv, a Fv, a Fab, an scFab, a (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain.
343. The TBM of embodiment 342, wherein ABM2 is an scFv.
344. The TBM of embodiment 343, wherein the scFv comprises the amino acid sequence of the scFv binding domain designated as CD3-21.
345. The TBM of any of embodiment 342, wherein ABM2 is a Fab.
346. The TBM of any one of embodiments 1 to 345, except when depending from any one of embodiments 277 to 338, wherein ABM3 is an antibody, an antibody fragment, an scFv, a dsFv, a Fv, a Fab, an scFab, a (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain.
347. The TBM of embodiment 346, wherein ABM3 is an scFv.
348. The TBM of embodiment 347, wherein the TAA is CD19 and the scFv comprises the amino acid sequence of CD19-scFv1 as set forth in Table 13.
349. The TBM of embodiment 347, wherein the TAA is CD19 and the scFv comprises the amino acid sequence of CD19-scFv2 as set forth in Table 13.
350. The TBM of embodiment 347, wherein the TAA is CD19 and the scFv comprises the amino acid sequence of CD19-scFv3 as set forth in Table 13.

351. The TBM of embodiment 347, wherein the TAA is CD19 and the scFv comprises the amino acid sequence of CD19-scFv4 as set forth in Table 13.

352. The TBM of embodiment 347, wherein the TAA is CD19 and the scFv comprises the amino acid sequence of CD19-scFv5 as set forth in Table 13.

353. The TBM of embodiment 347, wherein the TAA is CD19 and the scFv comprises the amino acid sequence of CD19-scFv6 as set forth in Table 13.

354. The TBM of embodiment 347, wherein the TAA is CD19 and the scFv comprises the amino acid sequence of CD19-scFv7 as set forth in Table 13.

355. The TBM of embodiment 347, wherein the TAA is CD19 and the scFv comprises the amino acid sequence of CD19-scFv8 as set forth in Table 13.

356. The TBM of embodiment 347, wherein the TAA is CD19 and the scFv comprises the amino acid sequence of CD19-scFv9 as set forth in Table 13.

357. The TBM of embodiment 347, wherein the TAA is CD19 and the scFv comprises the amino acid sequence of CD19-scFv10 as set forth in Table 13.

358. The TBM of embodiment 347, wherein the TAA is CD19 and the scFv comprises the amino acid sequence of CD19-scFv11 as set forth in Table 13.

359. The TBM of embodiment 347, wherein the TAA is CD19 and the scFv comprises the amino acid sequence of CD19-scFv12 as set forth in Table 13.

360. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-1 as set forth in Table 12A.

361. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-2 as set forth in Table 12A.

362. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-3 as set forth in Table 12A.

363. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-4 as set forth in Table 12A.

364. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-5 as set forth in Table 12A.

365. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-6 as set forth in Table 12A.

366. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-7 as set forth in Table 12A.

367. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-8 as set forth in Table 12A.

368. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-9 as set forth in Table 12A.

369. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-10 as set forth in Table 12A.

370. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-11 as set forth in Table 12A.

371. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-12 as set forth in Table 12A.

372. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-13 as set forth in Table 12A.

373. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-14 as set forth in Table 12A.

374. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-15 as set forth in Table 12A.

375. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-16 as set forth in Table 12A.

376. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-17 as set forth in Table 12A.

377. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-18 as set forth in Table 12A.

378. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-19 as set forth in Table 12A.

379. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-20 as set forth in Table 12A.

380. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-21 as set forth in Table 12A.

381. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-22 as set forth in Table 12A.

382. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-23 as set forth in Table 12A.

383. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-24 as set forth in Table 12A.

384. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-25 as set forth in Table 12A.

385. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-26 as set forth in Table 12A.

386. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-27 as set forth in Table 12A.

387. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-28 as set forth in Table 12A.

388. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-29 as set forth in Table 12A.

389. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-30 as set forth in Table 12A.

390. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-31 as set forth in Table 12A.

391. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-32 as set forth in Table 12A.

392. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-33 as set forth in Table 12A.

393. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-34 as set forth in Table 12A.

394. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-35 as set forth in Table 12A.

395. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-36 as set forth in Table 12A.

396. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-37 as set forth in Table 12A.

397. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-38 as set forth in Table 12A.

398. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-39 as set forth in Table 12A.

399. The TBM of embodiment 347, wherein the TAA is BCMA and the scFv comprises the amino acid sequence of scFv corresponding to BCMA-40 as set forth in Table 12A.

400. The TBM of embodiment 346, wherein ABM3 is a Fab.

401. The TBM of any one of embodiments 1 to 400, which comprises:

(a) a first monomer or half antibody comprising:

(i) a first chain comprising a first variant Fc region and a first heavy chain variable domain;

(ii) a first scFv domain; and

(b) a second monomer or half antibody comprising:

(i) a second chain comprising a second variant Fc region and first heavy chain variable domain;

(ii) a second scFv domain; and

(c) a third chain comprising a light chain constant domain and a light chain variable domain; wherein:

- (1) the first and second variant Fc regions form a heterodimer,
- (2) the first heavy chain variable domain and the light chain variable domain form ABM1, provided that TBM1 is not a CD58 moiety,
- (3) the first scFv domain forms ABM2, and
- (4) the second scFv domain forms ABM3.

402. The TBM of any one of embodiments 1 to 400, which comprises:

- (a) a first monomer or half antibody comprising:
 - (i) a first chain comprising a first variant Fc region and a first heavy chain variable domain;
 - (ii) a first scFv domain; and
- (b) a second monomer or half antibody comprising:
 - (i) a second chain comprising a second variant Fc region and first heavy chain variable domain;
 - (ii) a second scFv domain; and
- (c) a third chain comprising a light chain constant domain and a light chain variable domain; wherein:
 - (1) the first and second variant Fc regions form a heterodimer,
 - (2) the first heavy chain variable domain and the light chain variable domain form ABM1, provided that TBM1 is not a CD58 moiety,
 - (3) the first scFv domain forms ABM3, and
 - (4) the second scFv domain forms ABM2.

403. The TBM of any one of embodiments 1 to 400, which comprises:

- (a) a first monomer or half antibody comprising:

- (i) a first chain comprising a first variant Fc region and a first heavy chain variable domain;
- (ii) a first scFv domain or CD58 moiety; and
- (b) a second monomer or half antibody comprising:
 - (i) a second chain comprising a second variant Fc region and first heavy chain variable domain;
 - (ii) a second scFv domain; and
- (c) a third chain comprising a light chain constant domain and a light chain variable domain; wherein
 - (1) the first and second variant Fc regions form a heterodimer,
 - (2) the first heavy chain variable domain and the light chain variable domain form ABM2,
 - (3) the first scFv domain or CD58 moiety forms ABM1, and
 - (4) the second scFv domain forms ABM3.

404. The TBM of any one of embodiments 1 to 400, which comprises:

- (a) a first monomer or half antibody comprising:
 - (i) a first chain comprising a first variant Fc region and a first heavy chain variable domain;
 - (ii) a first scFv domain; and
- (b) a second monomer or half antibody comprising:
 - (i) a second chain comprising a second variant Fc region and first heavy chain variable domain;
 - (ii) a second scFv domain or a CD58 moiety; and
- (c) a third chain comprising a light chain constant domain and a light chain variable domain; wherein
 - (1) the first and second variant Fc regions form a heterodimer,

(2) the first heavy chain variable domain and the light chain variable domain form ABM2,

(3) the first scFv domain forms ABM3, and

(4) the second scFv domain or CD58 moiety forms ABM1.

405. The TBM of any one of embodiments 1 to 400, which comprises:

(a) a first monomer or half antibody comprising:

(i) a first chain comprising a first variant Fc region and a first heavy chain variable domain;

(ii) a first scFv domain; and

(b) a second monomer or half antibody comprising:

(i) a second chain comprising a second variant Fc region and first heavy chain variable domain;

(ii) a second scFv domain or a CD58 moiety; and

a third chain comprising a light chain constant domain and a light chain variable domain; wherein:

(1) the first and second variant Fc regions form a heterodimer,

(2) the first heavy chain variable domain and the light chain variable domain form ABM3,

(3) the first scFv domain forms ABM2, and

(4) the second scFv domain or CD58 moiety forms ABM1.

406. The TBM of any one of embodiments 1 to 400, which comprises:

(a) a first monomer or half antibody comprising:

(i) a first chain comprising a first variant Fc region and a first heavy chain variable domain;

(ii) a first scFv domain or CD58 moiety; and

- (b) a second monomer or half antibody comprising:
 - (i) a second chain comprising a second variant Fc region and first heavy chain variable domain;
 - (ii) a second scFv domain; and
- (c) a third chain comprising a light chain constant domain and a light chain variable domain; wherein
 - (1) the first and second variant Fc regions form a heterodimer,
 - (2) the first heavy chain variable domain and the light chain variable domain form ABM3,
 - (3) the first scFv domain or CD58 moiety forms ABM1, and
 - (4) the second scFv domain forms ABM2.

407. The TBM of any one of embodiments 401 to 406, wherein the first and second variant Fc regions comprise the amino acid substitutions S364K/E357Q : L368D/K370S.

408. The TBM of any one of embodiments 401 to 406, wherein the first and second variant Fc regions comprise the amino acid substitutions L368D/K370S : S364.

409. The TBM of any one of embodiments 401 to 406, wherein the first and second variant Fc regions comprise the amino acid substitutions L368E/K370S : S364K.

410. The TBM of any one of embodiments 401 to 406, wherein the first and second variant Fc regions comprise the amino acid substitutions T411T/E360E/Q362E : D401K.

411. The TBM of any one of embodiments 401 to 406, wherein the first and second variant Fc regions comprise the amino acid substitutions L368D 370S : S364 /E357L.

412. The TBM of any one of embodiments 401 to 406, wherein the first and second variant Fc regions comprise the amino acid substitutions 370S : S364K/E357Q.

413. The TBM of any one of embodiments 401 to 406, wherein the first and second variant Fc regions comprise the amino acid substitutions of any of the steric variants listed in Figure 4 of WO 2014/110601 (reproduced in Table 2).

414. The TBM of any one of embodiments 401 to 406, wherein the first and second variant Fc regions comprise the amino acid substitutions of any of the variants listed in Figure 5 of WO 2014/110601 (reproduced in Table 2).

415. The TBM of any one of embodiments 401 to 406, wherein the first and second variant Fc regions comprise the amino acid substitutions of any of the variants listed in Figure 6 of WO 2014/110601 (reproduced in Table 2).

416. The TBM of any one of embodiments 401 to 415, wherein at least one of the monomers or half antibodies further comprises pl variant substitutions.

417. The TBM of embodiment 416 wherein said pl variant substitutions are selected from Table 2.

418. The TBM of embodiment 417, wherein the pl variant substitutions comprise the substitutions present in pl_ISO(-).

419. The TBM of embodiment 417, wherein the pl variant substitutions comprise the substitutions present in pl_(-)_isosteric_A.

420. The TBM of embodiment 417, wherein the pl variant substitutions comprise the substitutions present in pl_(-)_isosteric_B.

421. The TBM of embodiment 417, wherein the pl variant substitutions comprise the substitutions present in pl_ISO(+RR).

422. The TBM of embodiment 417, wherein the pl variant substitutions comprise the substitutions present in pl_ISO(+).

423. The TBM of embodiment 417, wherein the pl variant substitutions comprise the substitutions present in pl_(+)_isosteric_A.

424. The TBM of embodiment 417, wherein the pl variant substitutions comprise the substitutions present in pl_(+)_isosteric_B.

425. The TBM of embodiment 417, wherein the pl variant substitutions comprise the substitutions present in pl_(+)_isosteric_E269Q/E272Q.

426. The TBM of embodiment 417, wherein the pl variant substitutions comprise the substitutions present in pl_(+)_isosteric_E269Q/E283Q.

427. The TBM of embodiment 417, wherein the pl variant substitutions comprise the substitutions present in pl_(+)_isosteric_E2720/E283Q.

428. The TBM of embodiment 417, wherein the pl variant substitutions comprise the substitutions present in pl_(+)_isosteric_E269Q.

429. The TBM of embodiment any of embodiments 401 to 428, wherein said first and second scFv domains are covalently attached to the C-terminus of said first and second chains, respectively.

430. The TBM of embodiment any of embodiments 401 to 428, wherein said first and second scFv domains are covalently attached to the N-terminus of said first and second chains, respectively.

431. The TBM of embodiment any of embodiments 401 to 428, wherein each of the scFv domains is attached between said Fc region and the CH domain of said chain.

432. The TBM of embodiment any of embodiments 401 to 431, wherein the scFv domains are covalently attached using one or more domain linkers.

433. The TBM of embodiment any of embodiments 401 to 432, wherein the scFv domains comprise at least one scFv linker.

434. The TBM of embodiment 433, wherein at least one scFv linker is charged.

435. The TBM of embodiment 434, wherein the charged linker is selected from L1 through L54.

436. The TBM of embodiment any of embodiments 401 to 435, wherein the first and/or second Fc region further comprises one or more amino acid substitution(s) selected from 434A, 434S, 428L, 308F, 259I, 428L/434S, 259I/308F, 436I/428L, 436I or V/434S, 436V/428L, 252Y, 252Y/254T/256E, 259I/308F/428L, 236A, 239D, 239E, 332E, 332D, 239D/332E, 267D, 267E, 328F, 267E/328F, 236A/332E, 239D/332E/330Y, 239D, 332E/330L, 236R, 328R, 236R/328R, 236N/267E, 243L, 298A and 299T.

437. The TBM of embodiment any of embodiments 401 to 435, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 434A, 434S or 434V.

438. The TBM of embodiment 437, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 428L.

439. The TBM of any one of embodiments 437 to 438, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 308F.

440. The TBM of any one of embodiments 437 to 439, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 259I.

441. The TBM of any one of embodiments 437 to 440, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 436I.

442. The TBM of any one of embodiments 437 to 441, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 252Y.

443. The TBM of any one of embodiments 437 to 442, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 254T.

444. The TBM of any one of embodiments 437 to 443, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 256E.

445. The TBM of any one of embodiments 437 to 444, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 239D or 239E.

446. The TBM of any one of embodiments 437 to 445, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 332E or 332D.

447. The TBM of any one of embodiments 437 to 446, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 267D or 267E.

448. The TBM of any one of embodiments 437 to 447, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 330L.

449. The TBM of any one of embodiments 437 to 448, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 236R or 236N.

450. The TBM of any one of embodiments 437 to 449, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 328R.

451. The TBM of any one of embodiments 437 to 450, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 243L.

452. The TBM of any one of embodiments 437 to 451, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 298A.

453. The TBM of any one of embodiments 437 to 452, wherein the first and/or second Fc region further comprises one or more amino acid substitution comprises the amino acid substitution 299T.

454. The TBM of embodiment 1, which comprises the amino acid sequences of trispecific AB1 set forth in Table 15.

455. The TBM of embodiment 1, which comprises the amino acid sequences of AB2-2 set forth in Table 20.

456. The TBM of embodiment 1, which comprises the amino acid sequences of AB2-3 set forth in Table 20.

457. The TBM of embodiment 1, which comprises the amino acid sequences of AB3-2 set forth in Table 21.

458. The TBM of embodiment 1, which comprises the amino acid sequences of AB3-3 set forth in Table 21.

459. The TBM of embodiment 1, which comprises the amino acid sequences of AB3-4 set forth in Table 21.

460. The TBM of embodiment 1, which comprises the amino acid sequences of AB3-5 set forth in Table 21.

461. The TBM of embodiment 1, which comprises the amino acid sequences of AB4-2 set forth in Table 22.

462. The TBM of embodiment 1, which comprises the amino acid sequences of AB4-3 set forth in Table 22.

463. The TBM of embodiment 1, which comprises the amino acid sequences of the TBM set forth in Table 23A.

464. The TBM of embodiment 1, which comprises the amino acid sequences of the TBM set forth in Table 23B.

465. The TBM of embodiment 1, which comprises the amino acid sequences of the TBM set forth in Table 24.

466. The TBM of embodiment 1, which comprises the amino acid sequences of the TBM set forth in Table 25.

467. The TBM of embodiment 1, which comprises the amino acid sequences of the TBM set forth in Table 26.

468. The TBM of any one of embodiments 1 to 467, which has been recombinantly produced, optionally in a mammalian host cell, which is optionally selected from Vero cells, HeLa cells, COS cells, CHO cells, HEK293 cells, BHK cells and MDCKII cells.

469. A conjugate comprising the TBM of any one of embodiments 1 to 468 and an agent.

470. The conjugate of embodiment 469, wherein the agent is a therapeutic agent, a diagnostic agent, a masking moiety, a cleavable moiety, or any combination thereof.

471. The conjugate of embodiment 470, wherein the agent is any of the agents described in Section 4.9.

472. The conjugate of embodiment 470, wherein the agent is any of the agents described in Section 4.9.1.

473. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a radionuclide.

474. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to an alkylating agent.

475. The conjugate of any one of embodiments 469, wherein the TBM is conjugated to a topoisomerase inhibitor, which is optionally a topoisomerase I inhibitor or a topoisomerase II inhibitor.

476. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a DNA damaging agent.

477. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a DNA intercalating agent, optionally a groove binding agent such as a minor groove binding agent.

478. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a RNA/DNA antimetabolite.

479. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a kinase inhibitor.

480. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a protein synthesis inhibitor.

481. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a histone deacetylase (HDAC) inhibitor.

482. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a mitochondrial. Inhibitor, which is optionally an inhibitor of a phosphoryl transfer reaction in mitochondria.

483. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to an antimitotic agent.

484. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a maytansinoid.

485. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a kinesin inhibitor.

486. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a kinesin-like protein KIF11 inhibitor.

487. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a V-ATPase (vacuolar-type H⁺ -ATPase) inhibitor.

488. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a pro-apoptotic agent.

489. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a Bcl2 (B-cell lymphoma 2) inhibitor.

490. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to an MCL1 (myeloid cell leukemia 1) inhibitor.

491. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a HSP90 (heat shock protein 90) inhibitor.

492. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to an IAP (inhibitor of apoptosis) inhibitor.

493. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to an mTOR (mechanistic target of rapamycin) inhibitor.

494. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a microtubule stabilizer.

495. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a microtubule destabilizer.

496. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to an auristatin.

497. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a dolastatin.

498. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a MetAP (methionine aminopeptidase).

499. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a CRM1 (chromosomal maintenance 1) inhibitor.

500. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a DPPIV (dipeptidyl peptidase IV) inhibitor.

501. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a proteasome inhibitor.

502. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a protein synthesis inhibitor.

503. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a CDK2 (cyclin-dependent kinase 2) inhibitor.

504. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a CDK9 (cyclin-dependent kinase 9) inhibitor.

505. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a RNA polymerase inhibitor.

506. The conjugate of any one of embodiments 469 to 472, wherein the TBM is conjugated to a DHFR (dihydrofolate reductase) inhibitor.

507. The conjugate of any one of embodiments 469 to 506, wherein the agent is attached to the TBM with a linker, which is optionally a cleavable linker or a non-cleavable linker, *e.g.*, a linker as described in Section 4.9.2.

508. A preparation of TBMs comprising a plurality of TBM molecules according to any one of embodiments 1 to 468 or a plurality of conjugate molecules according to any one of embodiments 469 to 507, optionally wherein the plurality comprises at least 100, at least 1,000, at least 10,000, or at least 100,000 TBM molecules or conjugate molecules.

509. The preparation of embodiment 508, wherein at least 50% of the trispecific molecules in the preparation have the same primary amino acid sequence.

510. The preparation of embodiment 508, wherein at least 60% of the trispecific molecules in the preparation have the same primary amino acid sequence.

511. The preparation of embodiment 508, wherein at least 70% of the trispecific molecules in the preparation have the same primary amino acid sequence.

512. The preparation of embodiment 508, wherein at least 80% of the trispecific molecules in the preparation have the same primary amino acid sequence.

513. The preparation of embodiment 508, wherein at least 90% of the trispecific molecules in the preparation have the same primary amino acid sequence.

514. The preparation of embodiment 508, wherein at least 95% of the trispecific molecules in the preparation have the same primary amino acid sequence.

515. The preparation of embodiment 508, wherein at least 97% of the trispecific molecules in the preparation have the same primary amino acid sequence.

516. The preparation of embodiment 508, wherein at least 98% of the trispecific molecules in the preparation have the same primary amino acid sequence.

517. The preparation of embodiment 508, wherein at least 99% of the trispecific molecules in the preparation have the same primary amino acid sequence.

518. The preparation of embodiment 508, wherein 50% to 95% of the trispecific molecules in the preparation have the same primary amino acid sequence.

519. The preparation of embodiment 508, wherein 50% to 80% of the trispecific molecules in the preparation have the same primary amino acid sequence.

520. The preparation of embodiment 508, wherein 50% to 70% of the trispecific molecules in the preparation have the same primary amino acid sequence.

521. The preparation of embodiment 508, wherein 60% to 95% of the trispecific molecules in the preparation have the same primary amino acid sequence.

522. The preparation of embodiment 508, wherein 60% to 80% of the trispecific molecules in the preparation have the same primary amino acid sequence.

523. The preparation of embodiment 508, wherein 60% to 70% of the trispecific molecules in the preparation have the same primary amino acid sequence.

524. The preparation of embodiment 508, wherein 70% to 95% of the trispecific molecules in the preparation have the same primary amino acid sequence.

525. The preparation of embodiment 508, wherein 70% to 80% of the trispecific molecules in the preparation have the same primary amino acid sequence.

526. The preparation of embodiment 508, wherein 80% to 95% of the trispecific molecules in the preparation have the same primary amino acid sequence.

527. The preparation of embodiment 508, wherein 95% to 99% of the trispecific molecules in the preparation have the same primary amino acid sequence.

528. The preparation of any one of embodiments 508 to 527, wherein at least 50% of the trispecific molecules in the preparation have the same interchain crosslinks.

529. The preparation of any one of embodiments 508 to 527, wherein at least 60% of the trispecific molecules in the preparation have the same interchain crosslinks.

530. The preparation of any one of embodiments 508 to 527, wherein at least 70% of the trispecific molecules in the preparation have the same interchain crosslinks.

531. The preparation of any one of embodiments 508 to 527, wherein at least 80% of the trispecific molecules in the preparation have the same interchain crosslinks.

532. The preparation of any one of embodiments 508 to 527, wherein at least 90% of the trispecific molecules in the preparation have the same interchain crosslinks.

533. The preparation of any one of embodiments 508 to 527, wherein at least 95% of the trispecific molecules in the preparation have the same interchain crosslinks.

534. The preparation of any one of embodiments 508 to 527, wherein at least 97% of the trispecific molecules in the preparation have the same interchain crosslinks.

535. The preparation of any one of embodiments 508 to 527, wherein at least 98% of the trispecific molecules in the preparation have the same interchain crosslinks.

536. The preparation of any one of embodiments 508 to 527, wherein at least 99% of the trispecific molecules in the preparation have the same interchain crosslinks.

537. The preparation of any one of embodiments 508 to 527, wherein 50% to 95% of the trispecific molecules in the preparation have the same interchain crosslinks.

538. The preparation of any one of embodiments 508 to 527, wherein 50% to 80% of the trispecific molecules in the preparation have the same interchain crosslinks.

539. The preparation of any one of embodiments 508 to 527, wherein 50% to 70% of the trispecific molecules in the preparation have the same interchain crosslinks.

540. The preparation of any one of embodiments 508 to 527, wherein 60% to 95% of the trispecific molecules in the preparation have the same interchain crosslinks.

541. The preparation of any one of embodiments 508 to 527, wherein 60% to 80% of the trispecific molecules in the preparation have the same interchain crosslinks.

542. The preparation of any one of embodiments 508 to 527, wherein 60% to 70% of the trispecific molecules in the preparation have the same interchain crosslinks.

543. The preparation of any one of embodiments 508 to 527, wherein 70% to 95% of the trispecific molecules in the preparation have the same interchain crosslinks.

544. The preparation of any one of embodiments 508 to 527, wherein 70% to 80% of the trispecific molecules in the preparation have the same interchain crosslinks.

545. The preparation of any one of embodiments 508 to 527, wherein 80% to 95% of the trispecific molecules in the preparation have the same interchain crosslinks.

546. The preparation of any one of embodiments 508 to 527, wherein 95% to 99% of the trispecific molecules in the preparation have the same interchain crosslinks.

547. The preparation of any one of embodiments 508 to 546, wherein at least 50% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

548. The preparation of any one of embodiments 508 to 546, wherein at least 60% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

549. The preparation of any one of embodiments 508 to 546, wherein at least 70% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

550. The preparation of any one of embodiments 508 to 546, wherein at least 80% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

551. The preparation of any one of embodiments 508 to 546, wherein at least 90% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

552. The preparation of any one of embodiments 508 to 546, wherein at least 95% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

553. The preparation of any one of embodiments 508 to 546, wherein at least 97% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

554. The preparation of any one of embodiments 508 to 546, wherein at least 98% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

555. The preparation of any one of embodiments 508 to 546, wherein at least 99% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

556. The preparation of any one of embodiments 508 to 546, wherein 50% to 95% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

557. The preparation of any one of embodiments 508 to 546, wherein 50% to 80% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

558. The preparation of any one of embodiments 508 to 546, wherein 50% to 70% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

559. The preparation of any one of embodiments 508 to 546, wherein 60% to 95% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

560. The preparation of any one of embodiments 508 to 546, wherein 60% to 80% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

561. The preparation of any one of embodiments 508 to 546, wherein 60% to 70% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

562. The preparation of any one of embodiments 508 to 546, wherein 70% to 95% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

563. The preparation of any one of embodiments 508 to 546, wherein 70% to 80% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

564. The preparation of any one of embodiments 508 to 546, wherein 80% to 95% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

565. The preparation of any one of embodiments 508 to 546, wherein 95% to 99% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

566. A pharmaceutical composition comprising the TBM of any one of embodiments 1 to 468, the conjugate of any one of embodiments 469 to 507, or the preparation of any one of embodiments 508 to 565, and an excipient.

567. A method of treating a subject with cancer, comprising administering to a subject suffering from cancer an effective amount of the TBM of any one of embodiments 1 to 468, the

conjugate of any one of embodiments 469 to 507, the preparation of any one of embodiments 508 to 565, or the pharmaceutical composition of embodiment 566.

568. The method of embodiment 567, wherein the cancer is selected from HER2+ cancer, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), adrenocortical carcinoma, anal cancer, appendix cancer, astrocytoma, basal cell carcinoma, brain tumor, bile duct cancer, bladder cancer, bone cancer, breast cancer, bronchial tumor, Burkitt Lymphoma, carcinoma of unknown primary origin, cardiac tumor, cervical cancer, chordoma, chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), chronic myeloproliferative neoplasm, colon cancer, colorectal cancer, craniopharyngioma, cutaneous T-cell lymphoma, ductal carcinoma, embryonal tumor, endometrial cancer, ependymoma, esophageal cancer, esthesioneuroblastoma, fibrous histiocytoma, Ewing sarcoma, eye cancer, germ cell tumor, gallbladder cancer, gastric cancer, gastrointestinal carcinoid tumor, gastrointestinal stromal tumor, gestational trophoblastic disease, glioma, head and neck cancer, hairy cell leukemia, hepatocellular cancer, histiocytosis, Hodgkin lymphoma, hypopharyngeal cancer, intraocular melanoma, islet cell tumor, Kaposi sarcoma, kidney cancer, Langerhans cell histiocytosis, laryngeal cancer, leukemia, lip and oral cavity cancer, liver cancer, lobular carcinoma in situ, lung cancer, lymphoma, macroglobulinemia, malignant fibrous histiocytoma, melanoma, Merkel cell carcinoma, mesothelioma, metastatic squamous neck cancer with occult primary, midline tract carcinoma involving NUT gene, mouth cancer, multiple endocrine neoplasia syndrome, multiple myeloma, mycosis fungoides, myelodysplastic syndrome, myelodysplastic/myeloproliferative neoplasm, nasal cavity and para-nasal sinus cancer, nasopharyngeal cancer, neuroblastoma, non-Hodgkin lymphoma, non-small cell lung cancer, oropharyngeal cancer, osteosarcoma, ovarian cancer, pancreatic cancer, papillomatosis, paraganglioma, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytomas, pituitary tumor, pleuropulmonary blastoma, primary central nervous system lymphoma, prostate cancer, rectal cancer, renal cell cancer, renal pelvis and ureter cancer, retinoblastoma, rhabdoid tumor, salivary gland cancer, Sezary syndrome, skin cancer, small cell lung cancer, small intestine cancer, soft tissue sarcoma, spinal cord tumor, stomach cancer, T-cell lymphoma, teratoid tumor, testicular cancer, throat cancer, thymoma and thymic carcinoma, thyroid cancer, urethral cancer, uterine cancer, vaginal cancer, vulvar cancer, and Wilms tumor.

569. The method of any of embodiment 567 or embodiment 568, further comprising administering at least one further agent to the subject.

570. A cell engineered to express the TBM of any one of embodiments 1 to 468.

571. A cell transfected with one or more expression vectors comprising one or more nucleic acid sequences encoding the TBM of any one of embodiments 1 to 468 under the control of one or more promoters.

572. The cell of embodiment 570 or embodiment 571, wherein expression of the TBM is under the control of an inducible promoter.

573. The cell of any one of embodiments 570 to 572, wherein the TBM is produced in secretable form.

574. A method of producing a TBM, comprising:

(a) culturing the cell of any one of embodiments 570 to 573 in conditions under which the TBM is expressed; and

(b) recovering the TBM from the cell culture.

575. The TBM of embodiment 1, wherein ABM1 is

(a) an immunoglobulin scaffold-based ABM which is optionally an anti-CD2 antibody, an antibody fragment, an scFv, a dsFv, a Fv, a Fab, an scFab, a (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain; or

(b) a non-immunoglobulin scaffold-based ABM which is optionally a Kunitz domain, an Adnexin, an Affibody, a DARPin, an Avimer, an Anticalin, a Lipocalin, a Centyrin, a Versabody, a Knottin, an Adnectin, a Pronectin, an Affitin/Nanofitin, an Affilin, an Atrimer/Tetranectin, a bicyclic peptide, a cys-knot, a Fn3 scaffold, an Obody, a Tn3, an Aan Affimer, BD, an Adhiron, a Duocalin, an Alphabody, an Armadillo Repeat Protein, a Repebody, or a Fynomer.

576. The TBM of embodiment 575, wherein ABM1 is an scFv.

577. The TBM of embodiment 575, wherein ABM1 is a Fab.

578. The TBM of embodiment 577, wherein the Fab is a Fab heterodimer.

579. The TBM of any one of embodiments 575 to 578, wherein ABM1 comprises any of the binding sequences set forth in Table 9.

580. The TBM of embodiment 579, wherein ABM1 comprises the heavy and light chain CDRs of CD2-1.

581. The TBM of embodiment 579, wherein ABM1 comprises the VH and VL sequences of CD2-1.

582. The TBM of embodiment 579, wherein ABM1 comprises the VH and VL sequences of hu1CD2-1.

583. The TBM of embodiment 579, wherein ABM1 comprises the VH and VL sequences of hu2CD2-1.

584. The TBM of embodiment 1, wherein ABM1 is a CD58 moiety.

585. The TBM of embodiment 584, wherein ABM1 comprises any of the binding sequences set forth in Table 10.

586. The TBM of embodiment 585, wherein ABM1 comprises the amino acid sequence designated as CD58-2.

587. The TBM of embodiment 585, wherein ABM1 comprises the amino acid sequence designated CD58-2.

588. The TBM of embodiment 585, wherein ABM1 comprises the amino acid sequence designated as CD58-4.

589. The TBM of embodiment 585, wherein ABM1 comprises the amino acid sequence designated as CD58-5.

590. The TBM of any one of embodiments 1 to 589, wherein the component of a human TCR complex is CD3.

591. The TBM of embodiment 590, wherein ABM2 is:

(a) an immunoglobulin scaffold-based ABM which is optionally an anti-CD3 antibody, an antibody fragment, an scFv, a dsFv, a Fv, a Fab, an scFab, a (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain; or

(b) a non-immunoglobulin scaffold-based ABM which is optionally a Kunitz domain, an Adnexin, an Affibody, a DARPin, an Avimer, an Anticalin, a Lipocalin, a Centyrin, a Versabody, a Knottin, an Adnectin, a Pronectin, an Affitin/Nanofitin, an Affilin, an Atrimer/Tetranectin, a bicyclic peptide, a cys-knot, a Fn3 scaffold, an Obody, a Tn3, an Aan Affimer, BD, an Adhiron, a Duocalin, an Alphabody, an Armadillo Repeat Protein, a Repebody, or a Fynomer.

592. The TBM of embodiment 590 or embodiment 591, wherein ABM2 comprises any of the binding sequences set forth in any one of Tables 7A through 7D.

593. The TBM of embodiment 592, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of any one of the binding domains designated as CD3-1 through CD3-28.

594. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-1.

595. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-1.

596. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-2.

597. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-2.

598. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-3.

599. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-3.

600. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-4.

601. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-4.

602. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-5.

603. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-5.

604. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-6.

605. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-6.

606. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-7.

607. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-7.

608. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-8.

609. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-8.

610. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-9.

611. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-9.

612. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-10.

613. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-10.

614. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-11.

615. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-11.

616. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-12.

617. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-12.

618. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-13.

619. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-13.

620. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-14.

621. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-14.

622. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-15.

623. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-15.

624. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-16.

625. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-16.

626. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-17.

627. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-17.

628. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-18.

629. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-18.

630. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-19.

631. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-19.

632. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-20.

633. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-20.

634. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-21.

635. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-21.

636. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-22.

637. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-22.

638. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-23.

639. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-23.

640. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-24.

641. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-24.

642. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-25.

643. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-25.

644. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-26.

645. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-26.

646. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-27.

647. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-27.

648. The TBM of embodiment 593, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the binding domain designated as CD3-28.

649. The TBM of embodiment 593, wherein ABM2 comprises the VH and/or VL sequences of the binding domain designated as CD3-28.

650. The TBM of embodiment 592, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat) of any one of the binding domains designated as CD3-29 through CD3-128.

651. The TBM of embodiment 650, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat) of any one of the binding domains designated as CD3-29 through CD3-38.

652. The TBM of embodiment 650, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat) of any one of the binding domains designated as CD3-39 through CD3-48.

653. The TBM of embodiment 650, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat) of any one of the binding domains designated as CD3-49 through CD3-58.

654. The TBM of embodiment 650, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat) of any one of the binding domains designated as CD3-59 through CD3-68.

655. The TBM of embodiment 650, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat) of any one of the binding domains designated as CD3-69 through CD3-78.

656. The TBM of embodiment 650, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat) of any one of the binding domains designated as CD3-79 through CD3-88.

657. The TBM of embodiment 650, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat) of any one of the binding domains designated as CD3-89 through CD3-98.

658. The TBM of embodiment 650, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat) of any one of the binding domains designated as CD3-99 through CD3-108.

659. The TBM of embodiment 650, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat) of any one of the binding domains designated as CD3-109 through CD3-118.

660. The TBM of embodiment 650, wherein ABM2 comprises the heavy and light chain CDRs (as defined by Kabat) of any one of the binding domains designated as CD3-119 through CD3-128.

661. The TBM of any one of embodiments 1 to 589, wherein the component of a human TCR complex is the alpha subunit of the TCR.

662. The TBM of embodiment 661, wherein ABM2:

(a) an immunoglobulin scaffold-based ABM which is optionally an antibody, an antibody fragment, an scFv, a dsFv, a Fv, a Fab, an scFab, a (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain; or

(b) a non-immunoglobulin scaffold-based ABM which is optionally a Kunitz domain, an Adnexin, an Affibody, a DARPin, an Avimer, an Anticalin, a Lipocalin, a Centyrin, a Versabody, a Knottin, an Adnectin, a Pronectin, an Affitin/Nanofitin, an Affilin, an Atrimer/Tetranectin, a bicyclic peptide, a cys-knot, a Fn3 scaffold, an Obody, a Tn3, an Aan Affimer, BD, an Adhiron, a Duocalin, an Alphabody, an Armadillo Repeat Protein, a Repebody, or a Fynomer.

663. The TBM of embodiment 662, wherein ABM2 comprises CDRs corresponding to the heavy and light chain CDRs of the antibody BMA031.

664. The TBM of embodiment 662, wherein ABM2 comprises variable regions corresponding to the VH and VL of the antibody BMA031.

665. The TBM of any one of embodiments 591 to 664, wherein ABM2 is an scFv.

666. The TBM of any one of embodiments 591 to 664, wherein ABM2 is a Fab.
667. The TBM of embodiment 666, wherein the Fab is a Fab heterodimer.
668. The TBM of any one of embodiments 1 to 667, wherein the TAA is a lineage marker.
669. The TBM of any one of embodiments 1 to 667, wherein the TAA is present on normal cells.
670. The TBM of embodiment 669, wherein the TAA is upregulated on cancer cells.
671. The TBM of any one of embodiments 1 to 670, wherein ABM3 is:
- (a) an immunoglobulin scaffold-based ABM which is optionally an anti-TAA antibody, an antibody fragment, an scFv, a dsFv, a Fv, a Fab, an scFab, a (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain; or
 - (b) a non-immunoglobulin scaffold-based ABM which is optionally a Kunitz domain, an Adnexin, an Affibody, a DARPin, an Avimer, an Anticalin, a Lipocalin, a Centyrin, a Versabody, a Knottin, an Adnectin, a Pronectin, an Affitin/Nanofitin, an Affilin, an Atrimer/Tetranectin, a bicyclic peptide, a cys-knot, a Fn3 scaffold, an Obody, a Tn3, an Aan Affimer, BD, an Adhiron, a Duocalin, an Alphabody, an Armadillo Repeat Protein, a Repebody, or a Fynomer.
672. The TBM of embodiment 668, wherein the TAA is TSHR, CD171, CS-1, CLL-1, GD3, Tn Ag, FLT3, CD38, CD44v6, B7H3, KIT, IL-13Ra2, IL-11Ra, PSCA, PRSS21, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, MUC1, EGFR, NCAM, CAIX, LMP2, EphA2, fucosyl GM1, sLe, GM3, TGS5, HMWMAA, o-acetyl-GD2, GD2, folate receptor alpha, 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, TAARP, WT1, ETV6-AML, sperm protein 17, XAGE1, Tie 2, MAD-CT-1, MAD-CT-2, Fos-related antigen 1, p53 mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP-4, SSX2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3, FCRL5, IGLL1, CD19, CD20, CD30, ERBB2, ROR1, FLT3, TAAG72, CD22, CD33, GD2, BCMA, gp100Tn, FAP, tyrosinase, EPCAM, CEA, Igf-I receptor, or EphB2.
673. The TBM of embodiment 668, wherein ABM3 comprises the CDRs or variable region sequences of the antibodies set forth in Table 11.

674. The TBM of any one of embodiments 668 to 673, wherein the TAA is BCMA.

675. The TBM of embodiment 674, wherein ABM3 comprises any of the binding sequences set forth in any one of Tables 12A, 12B, 12C, 12D, 12E, 12F or 12G.

676. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-1.

677. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-1.

678. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-2.

679. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-2.

680. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-3.

681. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-3.

682. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-4.

683. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-4.

684. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-5.

685. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-5.

686. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-6.

687. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-6.

688. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-7.

689. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-7.

690. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-8.

691. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-8.

692. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-9.

693. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-9.

694. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-10.

695. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-10.

696. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-11.

697. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-11.

698. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-12.

699. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-12.

700. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-13.

701. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-13.

702. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-14.

703. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-14.

704. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-15.

705. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-15.

706. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-16.

707. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-16.

708. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-17.

709. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-17.

710. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-18.

711. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-18.

712. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-19.

713. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-19.

714. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-20.

715. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-20.

716. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-21.

717. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-21.

718. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-22.

719. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-22.

720. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-23.

721. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-23.

722. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-24.

723. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-24.

724. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-25.

725. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-25.

726. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-26.

727. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-26.

728. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-27.

729. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-27.

730. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-28.

731. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-28.

732. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-29.

733. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-29.

734. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-30.

735. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-30.

736. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-31.

737. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-31.

738. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-32.

739. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-32.

740. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-33.

741. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-33.

742. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-34.

743. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-34.

744. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-35.

745. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-35.

746. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-36.

747. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-36.

748. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-37.

749. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-37.

750. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-38.

751. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-38.

752. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-39.

753. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-39.

754. The TBM of embodiment 675, wherein ABM3 comprises the heavy and light chain CDRs (as defined by Kabat, Chothia or a combination thereof) of the antibody designated BCMA-40.

755. The TBM of embodiment 675, wherein ABM3 comprises the VH and/or VL sequences of the antibody designated as BCMA-40.

756. The TBM of any one of embodiments 668 to 673, wherein the TAA is CD19.

757. The TBM of embodiment 756, wherein ABM3 comprises any of the binding sequences set forth Table 13.

758. The TBM of embodiment 757, wherein ABM3 comprises:

- (a) a CDR-H1 having the amino acid sequence of the CDR designated as CD19-H1;
- (b) a CDR-H2 having the amino acid sequence of any one of the CDRs designated as CD19-H2A, HD19-H2B, CD19-H2C and CD19-H2D;
- (c) a CDR-H3 having the amino acid sequence of the CDR designated as CD19-H3;
- (d) a CDR-L1 having the amino acid sequence of the CDR designated as CD19-L1;
- (e) a CDR-L2 having the amino acid sequence of the CDR designated as CD19-L2; and
- (f) a CDR-L3 having the amino acid sequence of the CDR designated as CD19-L23.

759. The TBM of embodiment 757, wherein ABM3 comprises:

- (a) a VH having the amino acid sequence of any one of the VH's designated as CD19-VHA, CD19-VHB, CD19-VHC, and CD19-VHD; and
- (b) a VL having the amino acid sequence of any one of the VL's designated as CD19-VLA and CD19-VLB.

760. The TBM of any one of embodiments any one of embodiments 668 to 759, wherein ABM3 is an scFv.

761. The TBM of any one of embodiments 668 to 757, wherein ABM3 is a Fab.

762. The TBM of embodiment 761, wherein the Fab is a Fab heterodimer.

763. The TBM of any one of embodiments 1 to 762 which comprises an Fc domain.

764. The TBM of embodiment 763, wherein the Fc domain is an Fc heterodimer.

765. The TBM of embodiment 764, wherein the Fc heterodimer comprises knob-in-hole ("KIH") modifications.

766. The TBM of embodiment 765, wherein the KIH modifications are any of the KIH modifications described in Section 4.3.1.5.1 or in Table 2.

767. The TBM of embodiment 765, wherein the KIH modifications are any of the alternative KIH modifications described in Section 4.3.1.5.2 or in Table 2.

768. The TBM of any one of embodiments 764 to 767, which comprises polar bridge modifications.

769. The TBM of embodiment 768, wherein the polar bridge modification are any of the polar bridge modifications described in Section 4.3.1.5.3 or in Table 2.

770. The TBM of any one of embodiments to 764 to 769, which comprises at least one of the Fc modifications designated as Fc 1 through Fc 150.

771. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 1 through Fc 5.

772. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 6 through Fc 10.

773. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 11 through Fc 15.

774. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 16 through Fc 20.

775. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 21 through Fc 25.

776. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 26 through Fc 30.

777. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 31 through Fc 35.

778. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 36 through Fc 40.

779. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 41 through Fc 45.

780. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 46 through Fc 50.

781. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 51 through Fc 55.

782. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 56 through Fc 60.

783. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 61 through Fc 65.

784. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 66 through Fc 70.

785. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 71 through Fc 75.

786. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 76 through Fc 80.

787. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 81 through Fc 85.

788. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 86 through Fc 90.

789. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 91 through Fc 95.

790. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 96 through Fc 100.

791. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 101 through Fc 105.

792. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 106 through Fc 110.

793. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 111 through Fc 115.

794. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 116 through Fc 120.

795. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 121 through Fc 125.

796. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 126 through Fc 130.

797. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 131 through Fc 135.

798. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 136 through Fc 140.

799. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 141 through Fc 145.

800. The TBM of embodiment 770, which comprises at least one of the Fc modifications designated as Fc 146 through Fc 150.

801. The TBM of any one of embodiments 763 to 800, wherein the Fc domain has altered effector function.

802. The TBM of embodiment 801, wherein the Fc domain has altered binding to one or more Fc receptors.

803. The TBM of embodiment 802, wherein the one or more Fc receptors comprise FcRN.

804. The TBM of embodiment 802 or embodiment 803, wherein the one or more Fc receptors comprise leukocyte receptors.

805. The TBM of any one of embodiments 763 to 804, wherein the Fc has modified disulfide bond architecture.

806. The TBM of any one of embodiments 763 to 805, wherein the Fc has altered glycosylation patterns.

807. The TBM of any one of embodiments 763 to 806, wherein the Fc comprises a hinge region.

808. The TBM of embodiment 807, wherein the hinge region comprises any of the hinge regions described in Section 4.3.2.

809. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H1.

810. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H2.

811. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H3.

812. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H4.

813. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H5.

814. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H6.

815. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H7.

816. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H8.

817. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H9.

818. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H10.

819. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H11.

820. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H12.

821. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H13.

822. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H14.

823. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H15.

824. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H16.

825. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H17.

826. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H18.

827. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H19.

828. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H20.

829. The TBM of embodiment 808, wherein the hinge region comprises the amino acid sequence of the hinge region designated H21.

830. The TBM of any one of embodiments 1 to 829, which comprises at least one scFv domain.

831. The TBM of embodiment 830, wherein at least one scFv comprises a linker connecting the VH and VL domains.

832. The TBM of embodiment 831, wherein the linker is 5 to 25 amino acids in length.

833. The TBM of embodiment 832, wherein the linker is 12 to 20 amino acids in length.

834. The TBM of any one of embodiments 831 to 833, wherein the linker is a charged linker and/or a flexible linker.

835. The TBM of any one of embodiments 831 to 834, wherein the linker is selected from any one of linkers L1 through L54.

836. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L1.

837. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L2.

838. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L3.

839. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L4.

840. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L5.

841. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L6.

842. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L7.

843. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L8.

844. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L9.

845. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L10.

846. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L11.

847. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L12.

848. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L13.

849. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L14.

850. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L15.

851. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L16.

852. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L17.

853. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L18.

854. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L19.

855. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L20.

856. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L21.

857. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L22.

858. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L23.

859. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L24.

860. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L25.

861. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L26.

862. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L27.

863. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L28.

864. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L29.

865. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L30.

866. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L31.

867. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L32.

868. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L33.

869. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L34.

870. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L35.

871. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L36.

872. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L37.

873. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L38.

874. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L39.

875. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L40.

876. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L41.

877. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L42.

878. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L43.

879. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L44.

880. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L45.

881. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L46.

882. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L47.

883. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L48.

884. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L49.

885. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L50.

886. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L51.

887. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L52.

888. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L53.

889. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L54.

890. The TBM of any one of embodiments 1 to 889, which comprises at least one Fab domain.

891. The TBM of embodiment 890, wherein at least one Fab domain comprises any of the Fab heterodimerization modifications set forth in Table 1.

892. The TBM of embodiment 891, wherein at least one Fab domain comprises the Fab heterodimerization modifications designated as F1.

893. The TBM of embodiment 891, wherein at least one Fab domain comprises the Fab heterodimerization modifications designated as F2.

894. The TBM of embodiment 891, wherein at least one Fab domain comprises the Fab heterodimerization modifications designated as F3.

895. The TBM of embodiment 891, wherein at least one Fab domain comprises the Fab heterodimerization modifications designated as F4.

896. The TBM of embodiment 891, wherein at least one Fab domain comprises the Fab heterodimerization modifications designated as F5.

897. The TBM of embodiment 891, wherein at least one Fab domain comprises the Fab heterodimerization modifications designated as F6.

898. The TBM of embodiment 891, wherein at least one Fab domain comprises the Fab heterodimerization modifications designated as F7.

899. The TBM of any one of embodiments 1 to 898, which comprises at least two ABMs, an ABM and an ABM chain, or two ABM chains connected to one another via a linker.

900. The TBM of embodiment 899, wherein the linker is 5 to 25 amino acids in length.

901. The TBM of embodiment 900, wherein the linker is 12 to 20 amino acids in length.

902. The TBM of any one of embodiments 899 to 901, wherein the linker is a charged linker and/or a flexible linker.

903. The TBM of any one of embodiments 899 to 902, wherein the linker is selected from any one of linkers L1 through L54.

904. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L1.

905. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L2.

906. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L3.

907. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L4.

908. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L5.

909. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L6.

910. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L7.

911. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L8.

912. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L9.

913. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L10.

914. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L11.

915. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L12.

916. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L13.

917. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L14.

918. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L15.

919. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L16.

920. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L17.

921. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L18.

922. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L19.

923. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L20.

924. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L21.

925. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L22.

926. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L23.

927. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L24.

928. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L25.

929. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L26.

930. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L27.

931. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L28.

932. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L29.

933. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L30.

934. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L31.

935. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L32.

936. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L33.

937. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L34.

938. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L35.

939. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L36.

940. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L37.

941. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L38.

942. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L39.

943. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L40.

944. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L41.

945. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L42.

946. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L43.

947. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L44.

948. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L45.

949. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L46.

950. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L47.

951. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L48.

952. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L49.

953. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L50.

954. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L51.

955. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L52.

956. The TBM of embodiment 835, wherein the linker region comprises the amino acid sequence of the linker designated L53.

957. The TBM of embodiment 903, wherein the linker region comprises the amino acid sequence of the linker designated L54.

958. The TBM of any one of embodiments 1 to 957, which is a trivalent TBM.

959. The TBM of embodiment 958, wherein the trivalent TBM has any one of the configurations depicted in FIGS. 1B-1O and 1U-1Z.

960. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1B.

961. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1C.

962. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1D.

963. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1E.

964. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1F.

965. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1G.

966. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1H.

967. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1I.

968. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1J.

969. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1K.

970. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1L.

971. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1M.

972. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1N.

973. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1O.

974. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1V.

975. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1W.

976. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1X.

977. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1Y.

978. The TBM of embodiment 959, wherein the trivalent TBM has the configuration depicted in FIG. 1Z.

979. The TBM of any one of embodiments 959 to 978, in which the ABMs have the configuration designated as T1.

980. The TBM of any one of embodiments 959 to 978, in which the ABMs have the configuration designated as T2.

981. The TBM of any one of embodiments 959 to 978, in which the ABMs have the configuration designated as T3.

982. The TBM of any one of embodiments 959 to 978, in which the ABMs have the configuration designated as T4.

983. The TBM of any one of embodiments 959 to 978, in which the ABMs have the configuration designated as T5.

984. The TBM of any one of embodiments 959 to 978, in which the ABMs have the configuration designated as T6.

985. The TBM of any one of embodiments 1 to 957, which is a tetravalent TBM.

986. The TBM of embodiment 985, wherein the tetravalent TBM has any one of the configurations depicted in FIGS. 1P-1R.

987. The TBM of embodiment 986, wherein the tetravalent TBM has the configuration depicted in FIG. 1P.

988. The TBM of embodiment 986, wherein the tetravalent TBM has the configuration depicted in FIG. 1Q.

989. The TBM of embodiment 986, wherein the tetravalent TBM has the configuration depicted in FIG. 1R.

990. The TBM of any one of embodiments 986 to 989, in which the ABMs have any of the configurations designated Tv 1 through Tv 12.

991. The TBM of embodiment 990, in which the ABMs have the configuration designated Tv 1.

992. The TBM of embodiment 990, in which the ABMs have the configuration designated Tv 2.

993. The TBM of embodiment 990, in which the ABMs have the configuration designated Tv 3.

994. The TBM of embodiment 990, in which the ABMs have the configuration designated Tv 4.

995. The TBM of embodiment 990, in which the ABMs have the configuration designated Tv 5.

996. The TBM of embodiment 990, in which the ABMs have the configuration designated Tv 6.

997. The TBM of embodiment 990, in which the ABMs have the configuration designated Tv 7.

998. The TBM of embodiment 990, in which the ABMs have the configuration designated Tv 8.

999. The TBM of embodiment 990, in which the ABMs have the configuration designated Tv 9.

1000. The TBM of embodiment 990, in which the ABMs have the configuration designated Tv 10.

1001. The TBM of embodiment 990, in which the ABMs have the configuration designated Tv 11.

1002. The TBM of embodiment 990, in which the ABMs have the configuration designated Tv 12.

1003. The TBM of any one of embodiments 1 to 957, which is a pentavalent TBM.

1004. The TBM of embodiment 1003, wherein the pentavalent TBM has the configuration depicted in FIG. 1S.

1005. The TBM of embodiment 1004, in which the ABMs have any of the configurations designated Pv 1 through Pv 80.

1006. The TBM of embodiment 1005, in which the ABMs have a configuration selected from any one of the configurations designated Pv 1 through Pv 10.

1007. The TBM of embodiment 1005, in which the ABMs have a configuration selected from any one of the configurations designated Pv 11 through Pv 20.

1008. The TBM of embodiment 1005, in which the ABMs have a configuration selected from any one of the configurations designated Pv 21 through Pv 30.

1009. The TBM of embodiment 1005, in which the ABMs have a configuration selected from any one of the configurations designated Pv 31 through Pv 40.

1010. The TBM of embodiment 1005, in which the ABMs have a configuration selected from any one of the configurations designated Pv 41 through Pv 50.

1011. The TBM of embodiment 1005, in which the ABMs have a configuration selected from any one of the configurations designated Pv 51 through Pv 60.

1012. The TBM of embodiment 1005, in which the ABMs have a configuration selected from any one of the configurations designated Pv 61 through Pv 70.

1013. The TBM of embodiment 1005, in which the ABMs have a configuration selected from any one of the configurations designated Pv 71 through Pv 80.

1014. The TBM of any one of embodiments 1 to 957, which is a hexavalent TBM.

1015. The TBM of embodiment 1014, wherein the hexavalent TBM has the configuration depicted in FIG. 1T or FIG. 1U.

1016. The TBM of embodiment 1015, wherein the hexavalent TBM has the configuration depicted in FIG. 1T.

1017. The TBM of embodiment 1015, wherein the hexavalent TBM has the configuration depicted in FIG. 1U.

1018. The TBM of any one of embodiments 1015 to 1017, in which the ABMs have any of the configurations designated Hv 1 through Hv 240.

1019. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 1 through Hv 10.

1020. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 11 through Hv 20.

1021. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 21 through Hv 30.

1022. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 31 through Hv 40.

1023. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 41 through Hv 50.

1024. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 51 through Hv 60.

1025. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 61 through Hv 70.

1026. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 71 through Hv 80.

1027. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 81 through Hv 90.

1028. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 91 through Hv 100.

1029. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 101 through Hv 110.

1030. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 111 through Hv 120.

1031. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 121 through Hv 130.

1032. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 131 through Hv 140.

1033. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 141 through Hv 150.

1034. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 151 through Hv 160.

1035. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 161 through Hv 70.

1036. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 171 through Hv 80.

1037. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 181 through Hv 90.

1038. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 191 through Hv 200.

1039. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 201 through Hv 210.

1040. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 211 through Hv 220.

1041. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 221 through Hv 230.

1042. The TBM of embodiment 1018, in which the ABMs have a configuration selected from any one of the configurations designated Hv 231 through Hv 240.

1043. The TBM of any one of embodiments 1 to 453 and 575 to 1042, wherein any one, any two, or all three of ABM1, ABM2 and ABM3 has cross-species reactivity.

1044. The TBM of embodiment 1043, wherein ABM1 further binds specifically to CD2 in one or more non-human mammalian species.

1045. The TBM of embodiment 1043 or embodiment 1044, wherein ABM2 further binds specifically to the component of the TCR complex in one or more non-human mammalian species.

1046. The TBM of any one of embodiments 1043 to 1045, wherein ABM3 further binds specifically to the TAA in one or more non-human mammalian species.

1047. The TBM of any one of embodiments 1043 to 1046, wherein the one or more non-human mammalian species comprises one or more non-human primate species.

1048. The TBM of embodiment 1047, wherein the one or more non-human primate species comprises *Macaca fascicularis*.

1049. The TBM of embodiment 1047, wherein the one or more non-human primate species comprises *Macaca mulatta*.

1050. The TBM of embodiment 1047, wherein the one or more non-human primate species comprises *Macaca nemestrina*.

1051. The TBM of any one of embodiments 1043 to 1046, wherein the one or more non-human mammalian species comprises *Mus musculus*.

1052. The TBM of any one of embodiments 1 to 468 and 575 to 1051, wherein any one, any two, or all three of ABM1, ABM2 and ABM3 does not have cross-species reactivity.

1053. The TBM of any one of embodiments 575 to 1052, which has been recombinantly produced, optionally in a mammalian host cell, which is optionally selected from Vero cells, HeLa cells, COS cells, CHO cells, HEK293 cells, BHK cells and MDCKII cells.

1054. A conjugate comprising the TBM of any one of embodiments 1 to 468 or 575 to 1053 and an agent, optionally a therapeutic agent, a diagnostic agent, a masking moiety, a cleavable moiety, or any combination thereof.

1055. The conjugate of embodiment 1054, wherein the agent is a cytotoxic or cytostatic agent.

1056. The conjugate of embodiment 1055, wherein the agent is any of the agents described in Section 4.9.

1057. The conjugate of embodiment 1055 or 1056, wherein the agent is any of the agents described in Section 4.9.1.

1058. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a radionuclide.

1059. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to an alkylating agent.

1060. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a topoisomerase inhibitor, which is optionally a topoisomerase I inhibitor or a topoisomerase II inhibitor.

1061. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a DNA damaging agent.

1062. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a DNA intercalating agent, optionally a groove binding agent such as a minor groove binding agent.

1063. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a RNA/DNA antimetabolite.

1064. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a kinase inhibitor.

1065. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a protein synthesis inhibitor.

1066. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a histone deacetylase (HDAC) inhibitor.

1067. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a mitochondrial inhibitor, which is optionally an inhibitor of a phosphoryl transfer reaction in mitochondria.

1068. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to an antimitotic agent.

1069. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a maytansinoid.

1070. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a kinesin inhibitor.

1071. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a kinesin-like protein KIF11 inhibitor.

1072. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a V-ATPase (vacuolar-type H⁺-ATPase) inhibitor.

1073. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a pro-apoptotic agent.

1074. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a Bcl2 (B-cell lymphoma 2) inhibitor.

1075. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to an MCL1 (myeloid cell leukemia 1) inhibitor.

1076. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a HSP90 (heat shock protein 90) inhibitor.

1077. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to an IAP (inhibitor of apoptosis) inhibitor.

1078. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to an mTOR (mechanistic target of rapamycin) inhibitor.

1079. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a microtubule stabilizer.

1080. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a microtubule destabilizer.

1081. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to an auristatin.

1082. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a dolastatin.

1083. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a MetAP (methionine aminopeptidase).

1084. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a CRM1 (chromosomal maintenance 1) inhibitor.

1085. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a DPPIV (dipeptidyl peptidase IV) inhibitor.

1086. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a proteasome inhibitor.

1087. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a protein synthesis inhibitor.

1088. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a CDK2 (cyclin-dependent kinase 2) inhibitor.

1089. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a CDK9 (cyclin-dependent kinase 9) inhibitor.

1090. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a RNA polymerase inhibitor.

1091. The conjugate of any one of embodiments 1054 to 1057, wherein the TBM is conjugated to a DHFR (dihydrofolate reductase) inhibitor.

1092. The conjugate of any one of embodiments 1054 to 1057, wherein the agent is attached to the TBM with a linker, which is optionally a cleavable linker or a non-cleavable linker, e.g.

1093. The conjugate of any one of embodiments 1054 to 1092, wherein the cytotoxic or cytostatic agent is conjugated to the TBM via a linker as described in Section 4.9.2.

1094. A preparation of TBMs comprising a plurality of TBM molecules according to any one of embodiments 575 to 1053 or a plurality of conjugate molecules according to any one of embodiments 1054 to 1093, optionally wherein the plurality comprises at least 100, at least 1,000, at least 10,000, or at least 100,000 TBM molecules or conjugate molecules.

1095. The preparation of embodiment 1094, wherein at least 50% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1096. The preparation of embodiment 1094, wherein at least 60% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1097. The preparation of embodiment 1094, wherein at least 70% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1098. The preparation of embodiment 1094, wherein at least 80% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1099. The preparation of embodiment 1094, wherein at least 90% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1100. The preparation of embodiment 1094, wherein at least 95% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1101. The preparation of embodiment 1094, wherein at least 97% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1102. The preparation of embodiment 1094, wherein at least 98% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1103. The preparation of embodiment 1094, wherein at least 99% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1104. The preparation of embodiment 1094, wherein 50% to 95% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1105. The preparation of embodiment 1094, wherein 50% to 80% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1106. The preparation of embodiment 1094, wherein 50% to 70% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1107. The preparation of embodiment 1094, wherein 60% to 95% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1108. The preparation of embodiment 1094, wherein 60% to 80% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1109. The preparation of embodiment 1094, wherein 60% to 70% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1110. The preparation of embodiment 1094, wherein 70% to 95% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1111. The preparation of embodiment 1094, wherein 70% to 80% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1112. The preparation of embodiment 1094, wherein 80% to 95% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1113. The preparation of embodiment 1094, wherein 95% to 99% of the trispecific molecules in the preparation have the same primary amino acid sequence.

1114. The preparation of any one of embodiments 1094 to 1113, wherein at least 50% of the trispecific molecules in the preparation have the same interchain crosslinks.

1115. The preparation of any one of embodiments 1094 to 1113, wherein at least 60% of the trispecific molecules in the preparation have the same interchain crosslinks.

1116. The preparation of any one of embodiments 1094 to 1113, wherein at least 70% of the trispecific molecules in the preparation have the same interchain crosslinks.

1117. The preparation of any one of embodiments 1094 to 1113, wherein at least 80% of the trispecific molecules in the preparation have the same interchain crosslinks.

1118. The preparation of any one of embodiments 1094 to 1113, wherein at least 90% of the trispecific molecules in the preparation have the same interchain crosslinks.

1119. The preparation of any one of embodiments 1094 to 1113, wherein at least 95% of the trispecific molecules in the preparation have the same interchain crosslinks.

1120. The preparation of any one of embodiments 1094 to 1113, wherein at least 97% of the trispecific molecules in the preparation have the same interchain crosslinks.

1121. The preparation of any one of embodiments 1094 to 1113, wherein at least 98% of the trispecific molecules in the preparation have the same interchain crosslinks.

1122. The preparation of any one of embodiments 1094 to 1113, wherein at least 99% of the trispecific molecules in the preparation have the same interchain crosslinks.

1123. The preparation of any one of embodiments 1094 to 1113, wherein 50% to 95% of the trispecific molecules in the preparation have the same interchain crosslinks.

1124. The preparation of any one of embodiments 1094 to 1113, wherein 50% to 80% of the trispecific molecules in the preparation have the same interchain crosslinks.

1125. The preparation of any one of embodiments 1094 to 1113, wherein 50% to 70% of the trispecific molecules in the preparation have the same interchain crosslinks.

1126. The preparation of any one of embodiments 1094 to 1113, wherein 60% to 95% of the trispecific molecules in the preparation have the same interchain crosslinks.

1127. The preparation of any one of embodiments 1094 to 1113, wherein 60% to 80% of the trispecific molecules in the preparation have the same interchain crosslinks.

1128. The preparation of any one of embodiments 1094 to 1113, wherein 60% to 70% of the trispecific molecules in the preparation have the same interchain crosslinks.

1129. The preparation of any one of embodiments 1094 to 1113, wherein 70% to 95% of the trispecific molecules in the preparation have the same interchain crosslinks.

1130. The preparation of any one of embodiments 1094 to 1113, wherein 70% to 80% of the trispecific molecules in the preparation have the same interchain crosslinks.

1131. The preparation of any one of embodiments 1094 to 1113, wherein 80% to 95% of the trispecific molecules in the preparation have the same interchain crosslinks.

1132. The preparation of any one of embodiments 1094 to 1113, wherein 95% to 99% of the trispecific molecules in the preparation have the same interchain crosslinks.

1133. The preparation of any one of embodiments 1094 to 1132, wherein at least 50% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1134. The preparation of any one of embodiments 1094 to 1132, wherein at least 60% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1135. The preparation of any one of embodiments 1094 to 1132, wherein at least 70% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1136. The preparation of any one of embodiments 1094 to 1132, wherein at least 80% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1137. The preparation of any one of embodiments 1094 to 1132, wherein at least 90% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1138. The preparation of any one of embodiments 1094 to 1132, wherein at least 95% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1139. The preparation of any one of embodiments 1094 to 1132, wherein at least 97% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1140. The preparation of any one of embodiments 1094 to 1132, wherein at least 98% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1141. The preparation of any one of embodiments 1094 to 1132, wherein at least 99% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1142. The preparation of any one of embodiments 1094 to 1132, wherein 50% to 95% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1143. The preparation of any one of embodiments 1094 to 1132, wherein 50% to 80% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1144. The preparation of any one of embodiments 1094 to 1132, wherein 50% to 70% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1145. The preparation of any one of embodiments 1094 to 1132, wherein 60% to 95% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1146. The preparation of any one of embodiments 1094 to 1132, wherein 60% to 80% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1147. The preparation of any one of embodiments 1094 to 1132, wherein 60% to 70% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1148. The preparation of any one of embodiments 1094 to 1132, wherein 70% to 95% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1149. The preparation of any one of embodiments 1094 to 1132, wherein 70% to 80% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1150. The preparation of any one of embodiments 1094 to 1132, wherein 80% to 95% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1151. The preparation of any one of embodiments 1094 to 1132, wherein 95% to 99% of the trispecific molecules in the preparation have the same ABM1:ABM2:ABM3 ratio.

1152. A pharmaceutical composition comprising the TBM of any one of embodiments 1 to 468 or 575 to 1053, the conjugate of any one of embodiments 1054 to 1093, or the preparation of any one of embodiments 1094 to 1151, and an excipient.

1153. A method of treating a subject with cancer, comprising administering to a subject suffering from cancer an effective amount of the TBM of any one of embodiments 1 to 468 or 575 to 1053, the conjugate of any one of embodiments 1054 to 1093, the preparation of any one of embodiments 1094 to 1151, or the pharmaceutical composition of embodiment 1152.

1154. The method of embodiment 1153, wherein the cancer is selected from HER2+ cancer, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), adrenocortical carcinoma, anal cancer, appendix cancer, astrocytoma, basal cell carcinoma, brain tumor, bile duct cancer, bladder cancer, bone cancer, breast cancer, bronchial tumor, Burkitt Lymphoma, carcinoma of unknown primary origin, cardiac tumor, cervical cancer, chordoma, chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), chronic myeloproliferative neoplasm, colon cancer, colorectal cancer, craniopharyngioma, cutaneous T-cell lymphoma, ductal carcinoma, embryonal tumor, endometrial cancer, ependymoma, esophageal cancer, esthesioneuroblastoma, fibrous histiocytoma, Ewing sarcoma, eye cancer, germ cell tumor, gallbladder cancer, gastric cancer, gastrointestinal carcinoid tumor, gastrointestinal stromal tumor, gestational trophoblastic disease, glioma, head and neck cancer, hairy cell leukemia, hepatocellular cancer, histiocytosis, Hodgkin lymphoma, hypopharyngeal cancer, intraocular melanoma, islet cell tumor, Kaposi sarcoma, kidney cancer, Langerhans cell histiocytosis,

laryngeal cancer, leukemia, lip and oral cavity cancer, liver cancer, lobular carcinoma in situ, lung cancer, lymphoma, macroglobulinemia, malignant fibrous histiocytoma, melanoma, Merkel cell carcinoma, mesothelioma, metastatic squamous neck cancer with occult primary, midline tract carcinoma involving NUT gene, mouth cancer, multiple endocrine neoplasia syndrome, multiple myeloma, mycosis fungoides, myelodysplastic syndrome, myelodysplastic/myeloproliferative neoplasm, nasal cavity and para-nasal sinus cancer, nasopharyngeal cancer, neuroblastoma, non-Hodgkin lymphoma, non-small cell lung cancer, oropharyngeal cancer, osteosarcoma, ovarian cancer, pancreatic cancer, papillomatosis, paraganglioma, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytomas, pituitary tumor, pleuropulmonary blastoma, primary central nervous system lymphoma, prostate cancer, rectal cancer, renal cell cancer, renal pelvis and ureter cancer, retinoblastoma, rhabdoid tumor, salivary gland cancer, Sezary syndrome, skin cancer, small cell lung cancer, small intestine cancer, soft tissue sarcoma, spinal cord tumor, stomach cancer, T-cell lymphoma, teratoid tumor, testicular cancer, throat cancer, thymoma and thymic carcinoma, thyroid cancer, urethral cancer, uterine cancer, vaginal cancer, vulvar cancer, and Wilms tumor.

1155. The method of any of embodiment 1153 or embodiment 1154, wherein the TAA and indication are any of the TAA-indication combinations set forth in Table 14.

1156. The method of any one of embodiments 1153 to 1155, further comprising administering at least one additional agent to the subject.

1157. The method of embodiment 1156, wherein the additional agent is a chemotherapeutic agent.

1158. The method of embodiment 1156 or embodiment 1157, wherein the additional agent is an anthracycline.

1159. The method of embodiment 1156 or embodiment 1157, wherein the additional agent is a vinca alkaloid.

1160. The method of embodiment 1156 or embodiment 1157, wherein the additional agent is an alkylating agent.

1161. The method of embodiment 1156 or embodiment 1157, wherein the additional agent is an immune cell antibody.

1162. The method of embodiment 1156 or embodiment 1157, wherein the additional agent is an antimetabolite.

1163. The method of embodiment 1156 or embodiment 1157, wherein the additional agent is an adenosine deaminase inhibitor

1164. The method of embodiment 1156 or embodiment 1157, wherein the additional agent is an mTOR inhibitor.

1165. The method of embodiment 1156 or embodiment 1157, wherein the additional agent is a TNFR glucocorticoid induced TNFR related protein (GITR) agonist.

1166. The method of embodiment 1156 or embodiment 1157, wherein the additional agent is a proteasome inhibitor.

1167. The method of embodiment 1156 or embodiment 1157, wherein the additional agent is an immunomodulatory.

1168. The method of embodiment 1156 or embodiment 1157, wherein the additional agent is a thalidomide derivative.

1169. A nucleic acid or plurality of nucleic acids encoding the TBM of any one of embodiments 1 to 468 and 575 to 1053.

1170. The nucleic acid or plurality of nucleic acids of embodiment 1169 which is a DNA (are DNAs).

1171. The nucleic acid or plurality of nucleic acids of embodiment 1170 which are in the form of one or more vectors, optionally expression vectors.

1172. The nucleic acid or plurality of nucleic acids of embodiment 1169 which is a mRNA (are mRNAs).

1173. A cell engineered to express the TBM of any one of embodiments 1 to 468 and 575 to 1053.

1174. A cell transfected with one or more expression vectors comprising one or more nucleic acid sequences encoding the TBM of any one of embodiments 1 to 468 and 575 to 1053 under the control of one or more promoters.

1175. The cell of embodiment 1173 or embodiment 1174, wherein expression of the TBM is under the control of one or more inducible promoters.

1176. The cell of any one of embodiments 1173 to 1175, wherein the TBM is produced in secretable form.

1177. A method of producing a TBM, comprising:

(a) culturing the cell of any one of embodiments 1173 to 1177 in conditions under which the TBM is expressed; and

(b) recovering the TBM from the cell culture.

1178. An anti-CD3 antibody or antigen-binding fragment thereof, comprising the CDR sequences of CD3-21.

1179. The anti-CD3 antibody or antigen-binding fragment thereof of embodiment 1178, wherein the CDRs are defined by Kabat numbering, as set forth in Table 7B.

1180. The anti-CD3 antibody or antigen-binding fragment thereof of embodiment 1178, wherein the CDRs are defined by Chothia numbering, as set forth in Table 7C.

1181. The anti-CD3 antibody or antigen-binding fragment thereof of embodiment 1178, which comprises the heavy and light chain variable sequences of CD3-21 as set forth in Table 7A.

1182. The anti-CD3 antibody or antigen-binding fragment thereof of any one of embodiments 1178 to 1181, which is in the form of an antibody.

1183. The anti-CD3 antibody or antigen-binding fragment thereof of any one of embodiment 1182, which is in the form of a monospecific antibody.

1184. The anti-CD3 antibody or antigen-binding fragment thereof of any one of embodiment 1182, which is in the form of a multispecific antibody.

1185. The anti-CD3 antibody or antigen-binding fragment thereof of any one of embodiment 1182, which is in the form of a trispecific antibody.

1186. The anti-CD3 antibody or antigen-binding fragment thereof of any one of embodiments 1178 to 1181, which is in the form of an antibody fragment.

1187. The anti-CD3 antibody or antigen-binding fragment thereof of embodiment 1186, which is in the form of a scFv.

1188. The anti-CD3 antibody or antigen-binding fragment thereof of embodiment 1187, comprising the CD3-21 scFv sequence set forth in Table 7A.

[0604] All publications, patents, patent applications and other documents cited in this application are hereby incorporated by reference in their entireties for all purposes to the same extent as if each individual publication, patent, patent application or other document were individually indicated to be incorporated by reference for all purposes. In the event that there is an inconsistency between the teachings of one or more of the references incorporated herein and the present disclosure, the teachings of the present specification are intended.

WHAT IS CLAIMED IS:

1. A trispecific binding molecule (TBM), comprising:
 - (a) an antigen-binding module 1 (ABM1) that binds specifically to human CD2;
 - (b) an antigen-binding module 2 (ABM2) that binds specifically to a component of a human T-cell receptor (TCR) complex; and
 - (c) an antigen-binding module 3 (ABM3) that binds specifically to a human tumor-associated antigen (TAA),
2. The TBM of claim 1, wherein each antigen-binding module is capable of binding its respective target at the same time as each of the other antigen-binding modules is bound to its respective target.
3. The TBM of claim 1, wherein ABM1 is:
 - (a) an immunoglobulin scaffold-based ABM which is optionally an anti-CD2 antibody, an antibody fragment, an scFv, a dsFv, a Fv, a Fab, an scFab, a (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain; or
 - (b) a non-immunoglobulin scaffold-based ABM which is optionally a Kunitz domain, an Adnexin, an Affibody, a DARPin, an Avimer, an Anticalin, a Lipocalin, a Centyrin, a Versabody, a Knottin, an Adnectin, a Pronectin, an Affitin/Nanofitin, an Affilin, an Atrimer/Tetranectin, a bicyclic peptide, a cys-knot, a Fn3 scaffold, an Obody, a Tn3, an Aan Affimer, BD, an Adhiron, a Duocalin, an Alphabody, an Armadillo Repeat Protein, a Repebody, or a Fynomer.
4. The TBM of claim 3, wherein ABM1 is an scFv or a Fab.
5. The TBM of claim 3, wherein ABM1 comprises any of the binding sequences set forth in Table 9.
6. The TBM of claim 1, wherein ABM1 comprises a receptor binding domain of a CD2 ligand.
7. The TBM of claim 1, wherein ABM1 is a CD58 moiety.
8. The TBM of claim 7, wherein ABM1 comprises amino acids 1-94 of CD58-2.
9. The TBM of claim 1, wherein ABM1 is a CD48 moiety.

10. The TBM of claim 1, wherein the component of a human TCR complex is CD3.
11. The TBM of claim 10, wherein ABM2 is:
 - (a) an immunoglobulin scaffold-based ABM which is optionally an anti-CD3 antibody, an antibody fragment, an scFv, a dsFv, a Fv, a Fab, an scFab, a (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain; or
 - (b) a non-immunoglobulin scaffold-based ABM which is optionally a Kunitz domain, an Adnexin, an Affibody, a DARPin, an Avimer, an Anticalin, a Lipocalin, a Centyrin, a Versabody, a Knottin, an Adnectin, a Pronectin, an Affitin/Nanofitin, an Affilin, an Atrimer/Tetranectin, a bicyclic peptide, a cys-knot, a Fn3 scaffold, an Obody, a Tn3, an Aan Affimer, BD, an Adhiron, a Duocalin, an Alphabody, an Armadillo Repeat Protein, a Repebody, or a Fynomer.
12. The TBM of claim 11, wherein ABM2 is an scFv or Fab.
13. The TBM of claim 11, wherein ABM2 comprises any of the binding sequences set forth in any one of Tables 7A through 7D.
14. The TBM of claim 13, wherein ABM2 comprises the VH and VL sequences of CD3-21 as set forth in Table 7A.
15. The TBM of claim 1, wherein the component of a human TCR complex is the alpha subunit of the TCR.
16. The TBM of claim 15, wherein ABM2 is an anti-CD3 antibody, an antibody fragment, an scFv, a Fv, a dsFv, a Fab, an scFab, a (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, a camelid VHH domain, a DARPin, an Avimer, an Anticalin/Lipocalin, a Centyrin, a Versabody, a Duocalin or a Fynomer.
17. The TBM of claim 1, wherein if TAA is a receptor, ABM3 comprises a receptor binding domain of a ligand of the receptor, and if TAA is a ligand, ABM3 comprises a ligand binding domain of a receptor of the ligand.
18. The TBM of claim 1, wherein ABM3 is:
 - (a) an immunoglobulin scaffold-based ABM which is optionally an anti-TAA antibody, an antibody fragment, an scFv, a dsFv, a Fv, a Fab, an scFab, a (Fab')₂, a single domain antibody (SDAB), a VH or VL domain, or a camelid VHH domain; or

(b) a non-immunoglobulin scaffold-based ABM which is optionally a Kunitz domain, an Adnexin, an Affibody, a DARPin, an Avimer, an Anticalin, a Lipocalin, a Centyrin, a Versabody, a Knottin, an Adnectin, a Pronectin, an Affitin/Nanofitin, an Affilin, an Atrimer/Tetranectin, a bicyclic peptide, a cys-knot, a Fn3 scaffold, an Obody, a Tn3, an Aan Affimer, BD, an Adhiron, a Duocalin, an Alphabody, an Armadillo Repeat Protein, a Repebody, or a Fynomer.

19. The TBM of claim 18, wherein the TAA is TSHR, CD171, CS-1, CLL-1, GD3, Tn Ag, FLT3, CD38, CD44v6, B7H3, KIT, IL-13Ra2, IL-11Ra, PSCA, PRSS21, VEGFR2, LewisY, CD24, PDGFR-beta, SSEA-4, MUC1, EGFR, EGFRvIII, NCAM, CAIX, LMP2, EphA2, fucosyl GM1, sLe, GM3, TGS5, HMWMAA, o-acetyl-GD2, GD2, folate receptor alpha, 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, TAARP, WT1, ETV6-AML, sperm protein 17, XAGE1, Tie 2, MAD-CT-1, MAD-CT-2, Fos-related antigen 1, p53 mutant, hTERT, sarcoma translocation breakpoints, ML-IAP, ERG (TMPRSS2 ETS fusion gene), NA17, PAX3, Androgen receptor, Cyclin B1, MYCN, RhoC, CYP1B1, BORIS, SART3, PAX5, OY-TES1, LCK, AKAP-4, SSX2, CD79a, CD79b, CD72, LAIR1, FCAR, LILRA2, CD300LF, CLEC12A, BST2, EMR2, LY75, GPC3, FCRL5, IGLL1, CD19, CD20, CD30, ERBB2, ROR1, FLT3, TAAG72, CD22, CD33, GD2, BCMA, gp100Tn, FAP, tyrosinase, EPCAM, CEA, Igf-I receptor, Cadherin17, CD32b, GPNMB, GPR64, HER3, LRP6, LYPD8, NKG2D, SLC34A2, SLC39A6, SLITRK6, TACSTD2, or EphB2.

20. The TBM of claim 18, wherein the TAA is BCMA.

21. The TBM of claim 20, wherein ABM3 comprises any of the binding sequences set forth in any one of Tables 12A, 12B, 12C, 12D, 12E, or 12F.

22. The TBM of claim 18, wherein the TAA is CD19.

23. The TBM of claim 22, wherein ABM3 comprises any of the binding sequences set forth Table 13.

24. The TBM of claim 18, wherein the TAA is Her2.

25. The TBM of claim 18, wherein the TAA is mesothelin.

26. The TBM of claim 18, wherein ABM3 is an scFv or a Fab.

27. The TBM of claim 1, which is a trivalent TBM.

28. The TBM of claim 27, wherein the trivalent TBM has any one of the configurations depicted in FIGS. 1B-1U and 1V-1Z.
29. The TBM of claim 28, which has the configuration depicted in FIG. 1I.
30. The TBM of claim 29, in which the ABMs have the configuration designated as T6.
31. The TBM of claim 1, which is a tetravalent TBM.
32. The TBM of claim 1, which is a pentavalent TBM.
33. The TBM of claim 1, which is a hexavalent TBM.
34. A conjugate comprising the TBM of any one of claims 1 to 33 and a cytotoxic or cytostatic agent.
35. A pharmaceutical composition comprising the TBM of any one of claims 1 to 33 and an excipient.
36. A method of treating a subject with cancer, comprising administering to a subject suffering from cancer an effective amount of the TBM of any one of claims 1 to 33.
37. The method of claim 36, wherein the cancer is selected from HER2+ cancer, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), adrenocortical carcinoma, anal cancer, appendix cancer, astrocytoma, basal cell carcinoma, brain tumor, bile duct cancer, bladder cancer, bone cancer, breast cancer, bronchial tumor, Burkitt Lymphoma, carcinoma of unknown primary origin, cardiac tumor, cervical cancer, chordoma, chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), chronic myeloproliferative neoplasm, colon cancer, colorectal cancer, craniopharyngioma, cutaneous T-cell lymphoma, ductal carcinoma, embryonal tumor, endometrial cancer, ependymoma, esophageal cancer, esthesioneuroblastoma, fibrous histiocytoma, Ewing sarcoma, eye cancer, germ cell tumor, gallbladder cancer, gastric cancer, gastrointestinal carcinoid tumor, gastrointestinal stromal tumor, gestational trophoblastic disease, glioma, head and neck cancer, hairy cell leukemia, hepatocellular cancer, histiocytosis, Hodgkin lymphoma, hypopharyngeal cancer, intraocular melanoma, islet cell tumor, Kaposi sarcoma, kidney cancer, Langerhans cell histiocytosis, laryngeal cancer, leukemia, lip and oral cavity cancer, liver cancer, lobular carcinoma in situ, lung cancer, lymphoma, macroglobulinemia, malignant fibrous histiocytoma, melanoma, Merkel cell carcinoma, mesothelioma, metastatic squamous neck cancer with occult primary, midline tract carcinoma involving NUT gene, mouth cancer, multiple endocrine neoplasia syndrome, multiple myeloma, mycosis fungoides, myelodysplastic syndrome,

myelodysplastic/myeloproliferative neoplasm, nasal cavity and para-nasal sinus cancer, nasopharyngeal cancer, neuroblastoma, non-Hodgkin lymphoma, non-small cell lung cancer, oropharyngeal cancer, osteosarcoma, ovarian cancer, pancreatic cancer, papillomatosis, paraganglioma, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytomas, pituitary tumor, pleuropulmonary blastoma, primary central nervous system lymphoma, prostate cancer, rectal cancer, renal cell cancer, renal pelvis and ureter cancer, retinoblastoma, rhabdoid tumor, salivary gland cancer, Sezary syndrome, skin cancer, small cell lung cancer, small intestine cancer, soft tissue sarcoma, spinal cord tumor, stomach cancer, T-cell lymphoma, teratoid tumor, testicular cancer, throat cancer, thymoma and thymic carcinoma, thyroid cancer, urethral cancer, uterine cancer, vaginal cancer, vulvar cancer, and Wilms tumor.

38. A nucleic acid or plurality of nucleic acids encoding the TBM of any one of claims 1 to 33.

39. A cell engineered to express the TBM of any one of claims 1 to 33.

40. A cell transfected with one or more expression vectors comprising one or more nucleic acid sequences encoding the TBM of any one of claims 1 to 33 under the control of one or more promoters.

41. A method of producing a TBM, comprising:

- (a) culturing the cell of claim 40 in conditions under which the TBM is expressed; and
- (b) recovering the TBM from the cell culture.

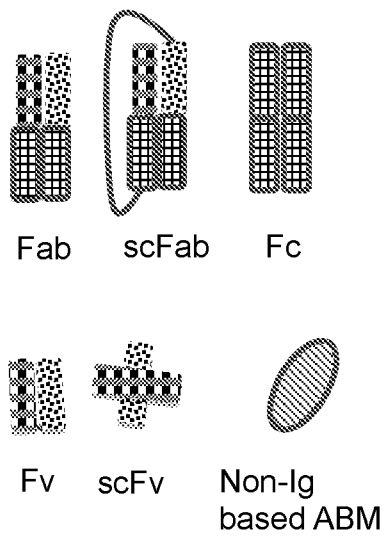


FIG. 1A

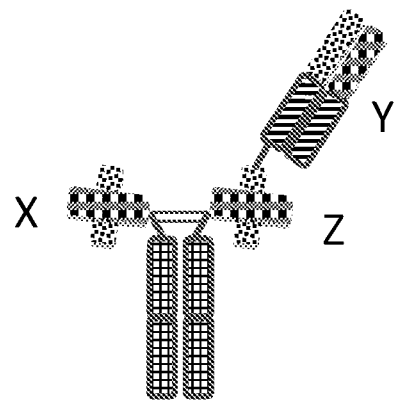


FIG. 1B

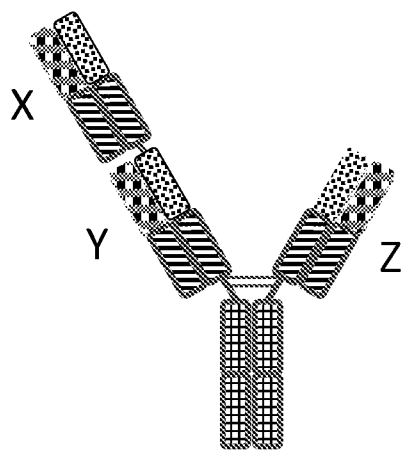


FIG. 1C

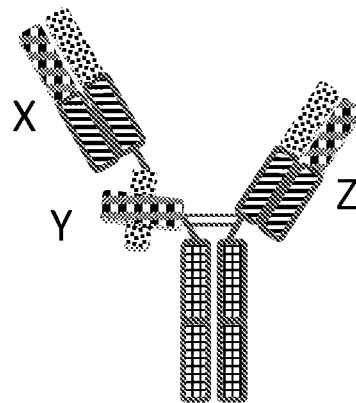


FIG. 1D

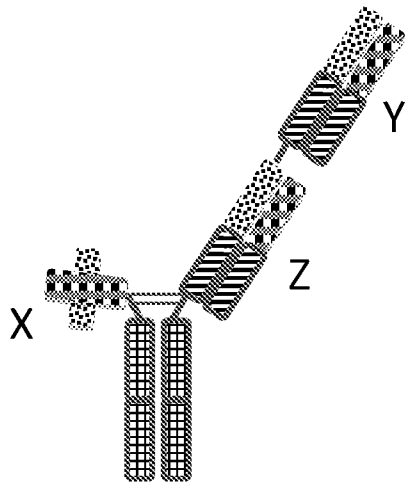


FIG. 1E

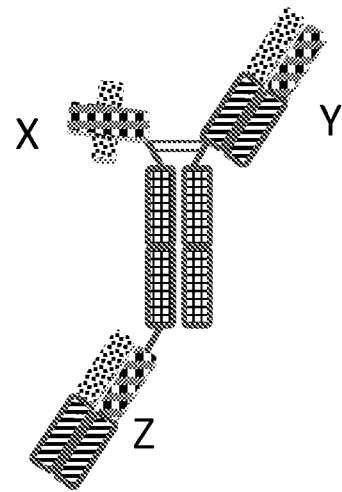


FIG. 1F

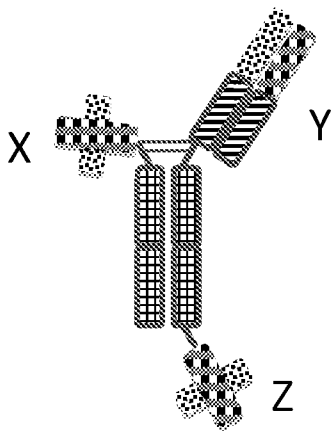


FIG. 1G

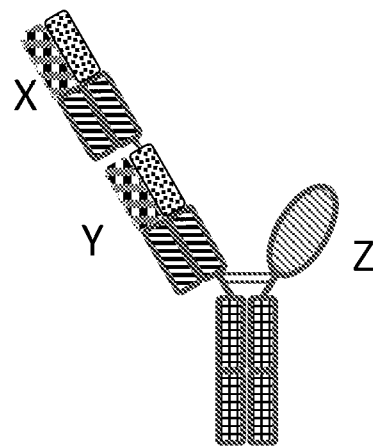


FIG. 1H

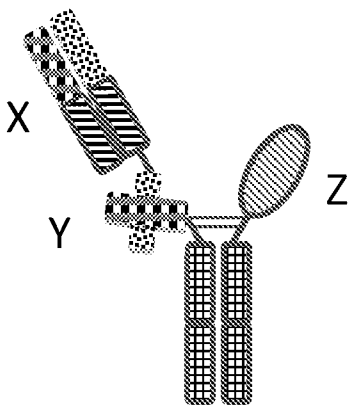


FIG. 1I

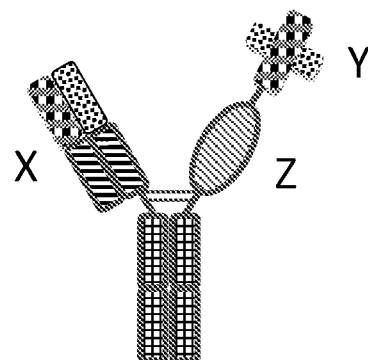


FIG. 1J

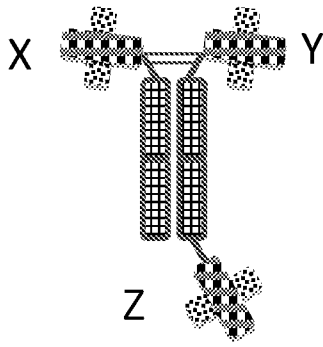


FIG. 1K

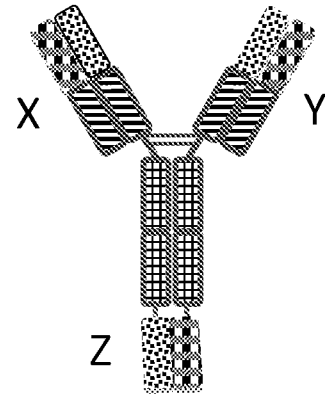


FIG. 1L

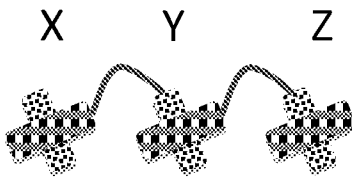


FIG. 1M

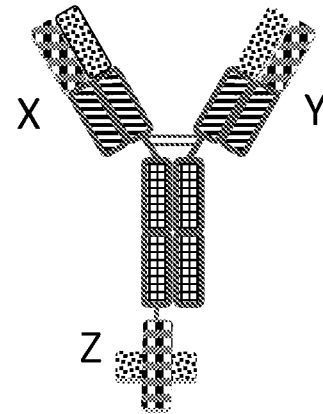


FIG. 1N

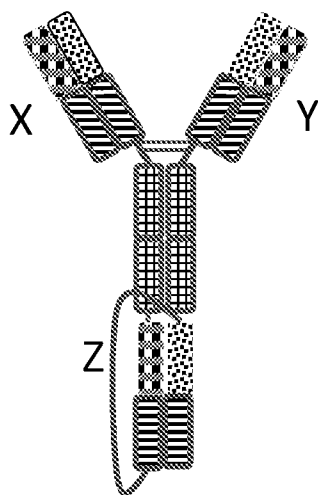


FIG. 1O

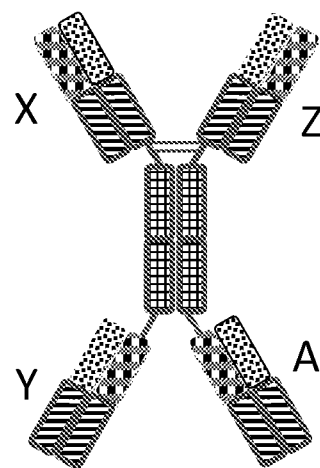


FIG. 1P

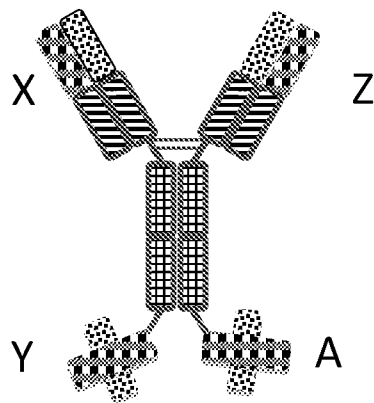


FIG. 1Q

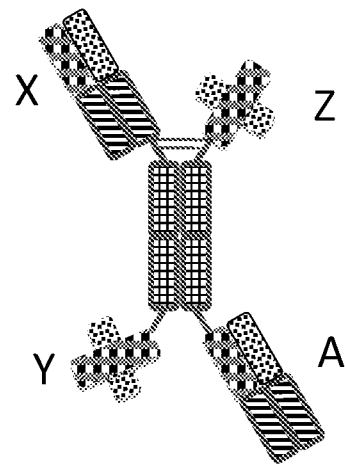


FIG. 1R

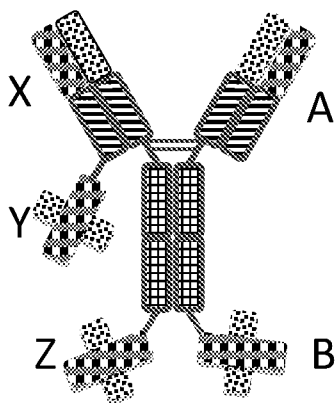


FIG. 1S

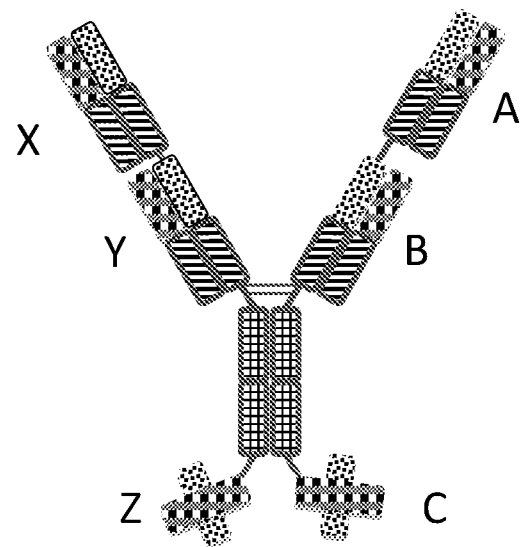


FIG. 1T

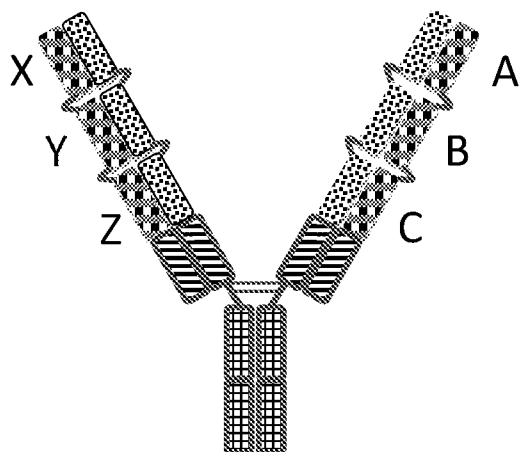


FIG. 1U

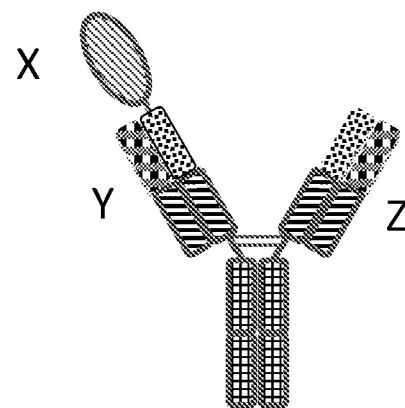


FIG. 1V

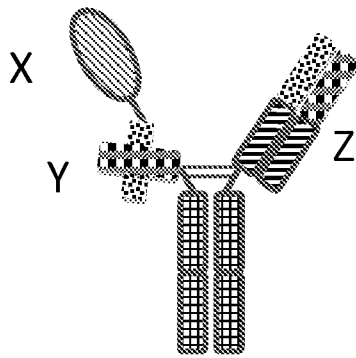


FIG. 1W

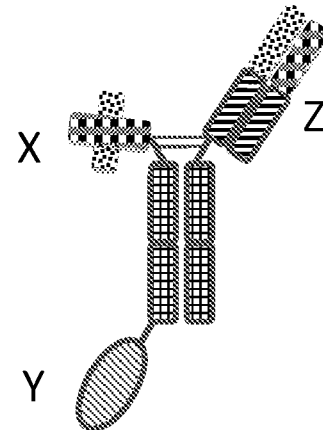


FIG. 1X

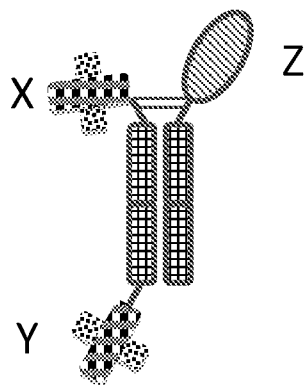


FIG. 1Y

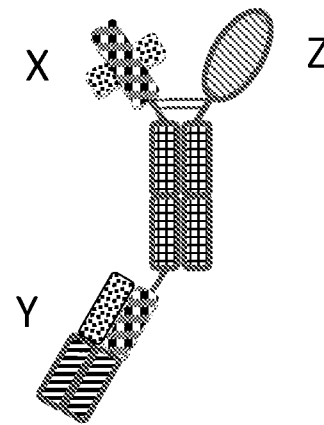


FIG. 1Z

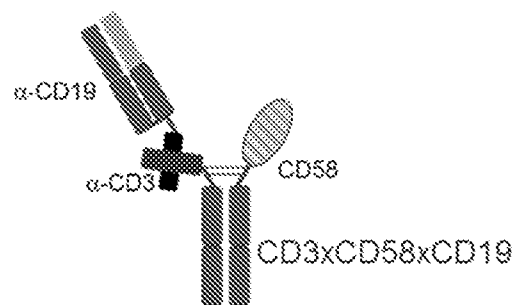
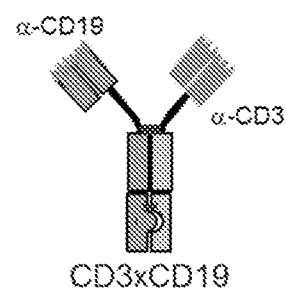
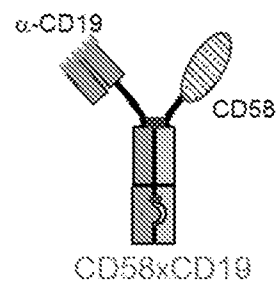


FIG. 2

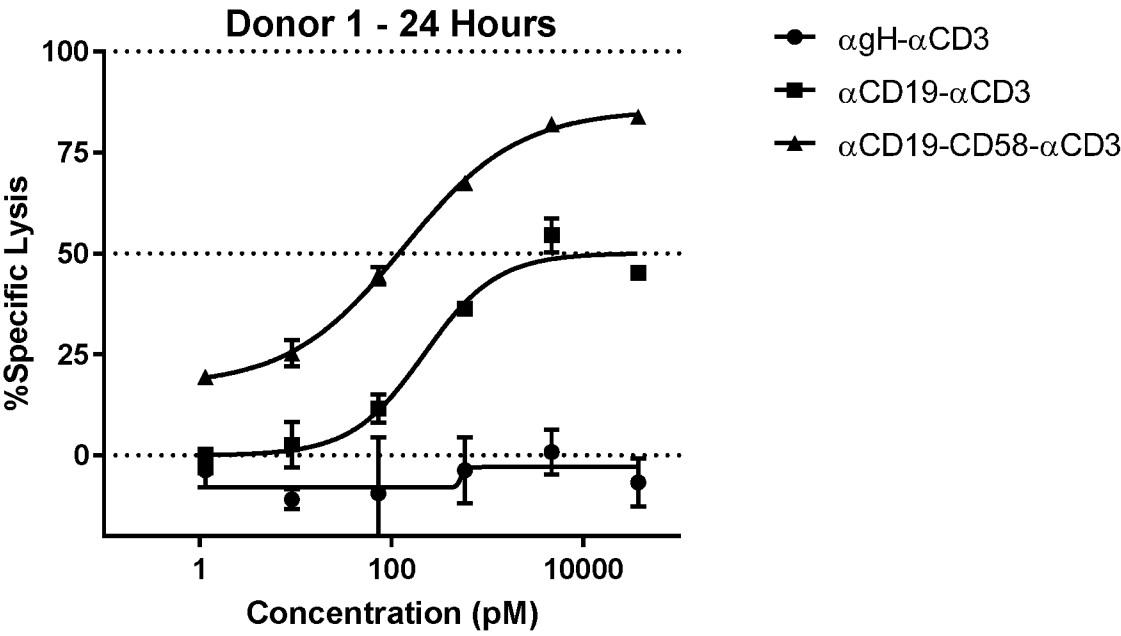


FIG. 3A

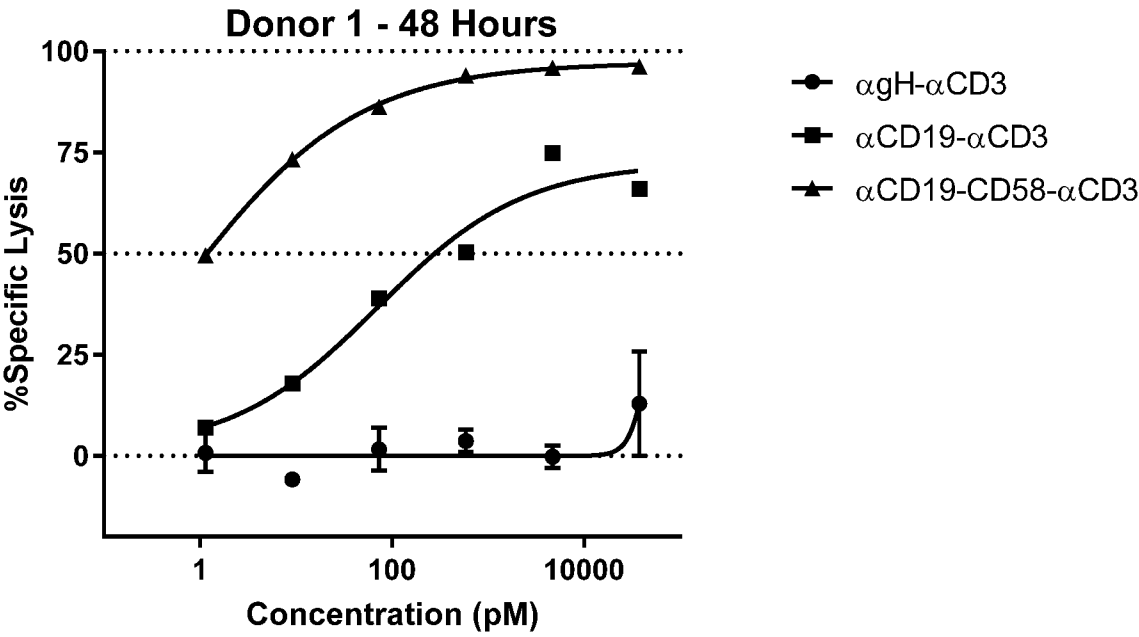


FIG. 3B

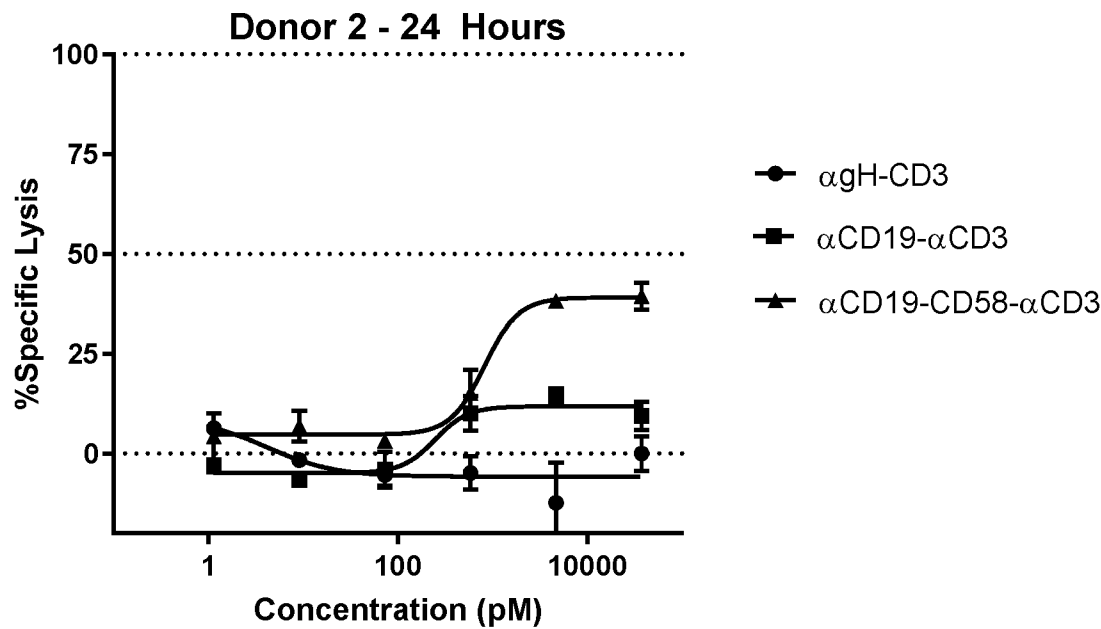


FIG. 3C

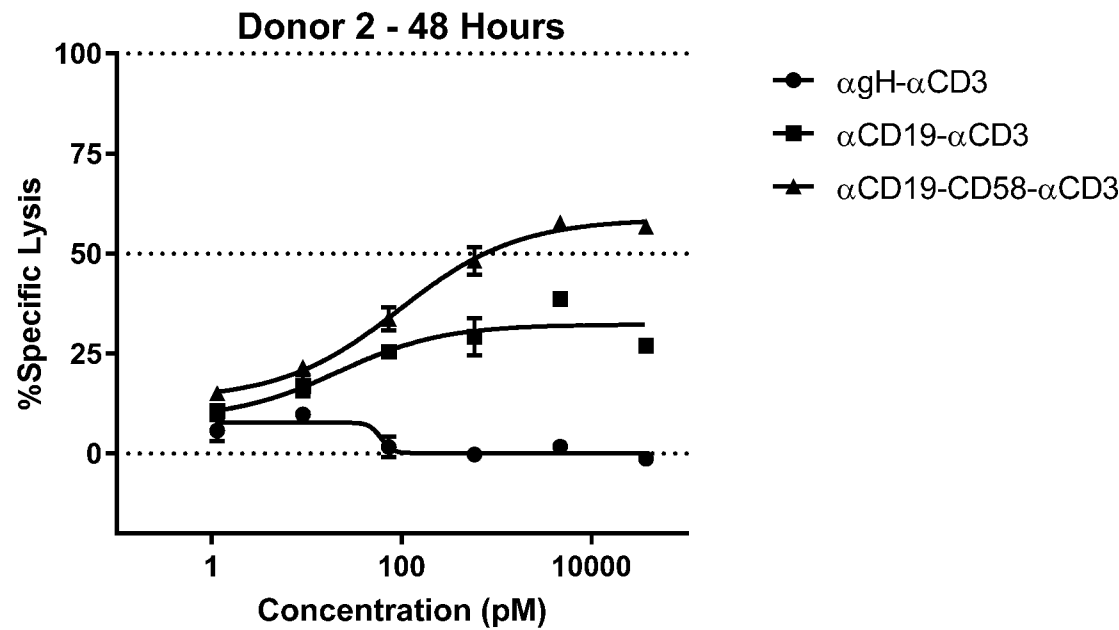


FIG. 3D

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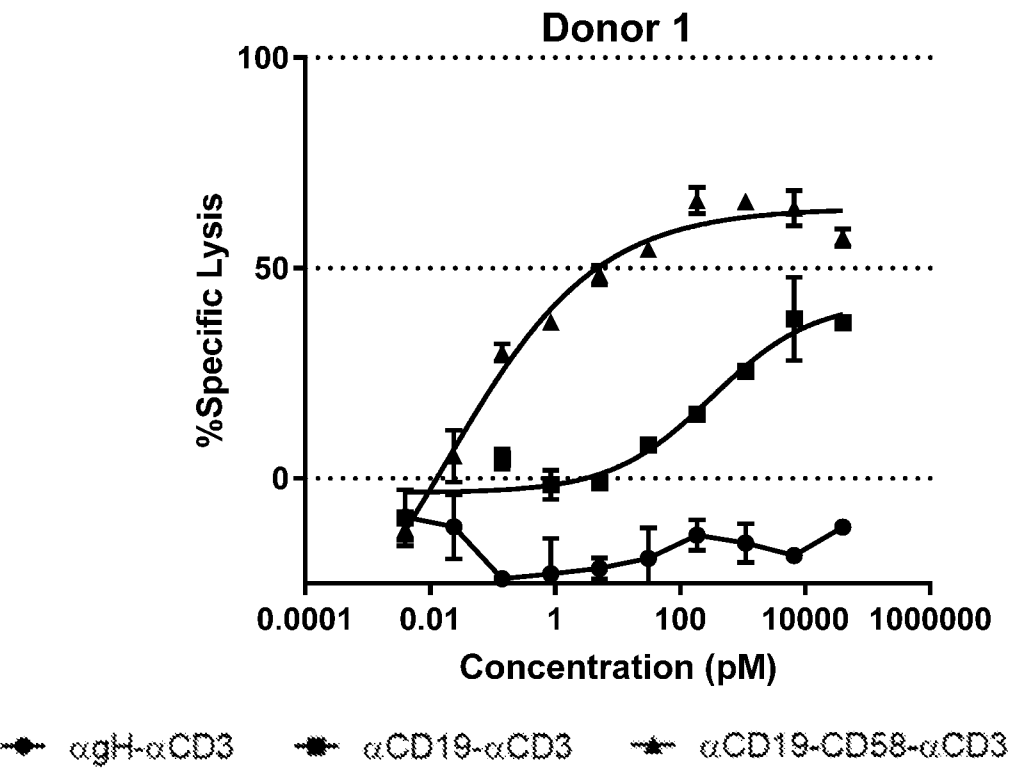


FIG. 4A

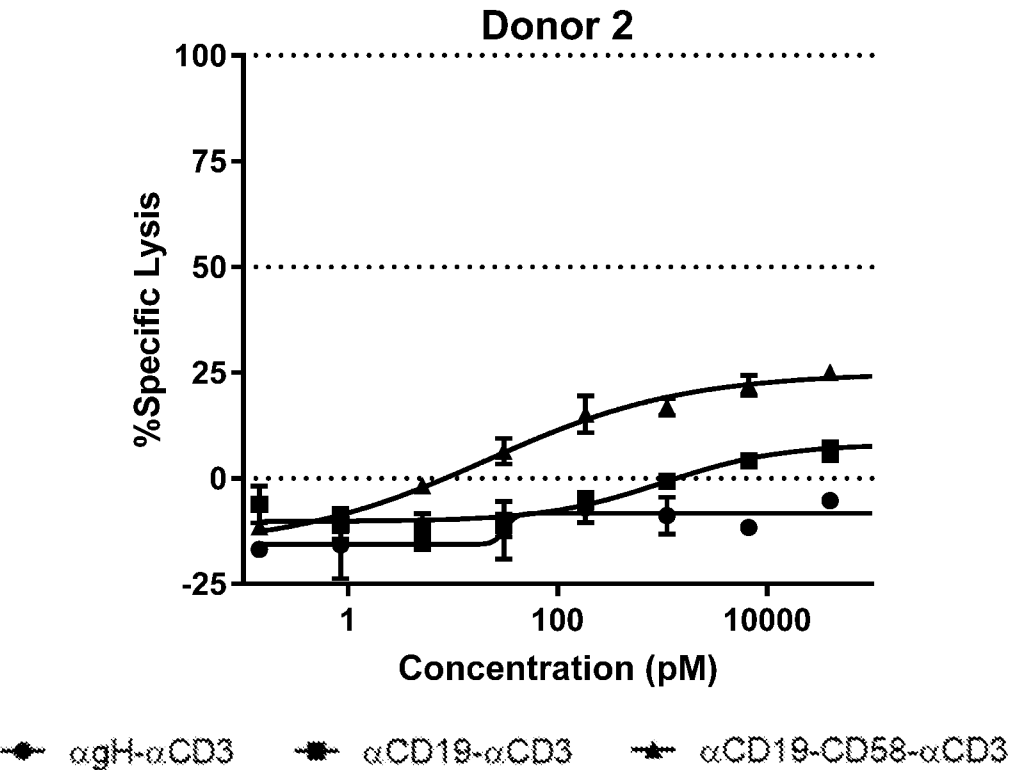


FIG. 4B

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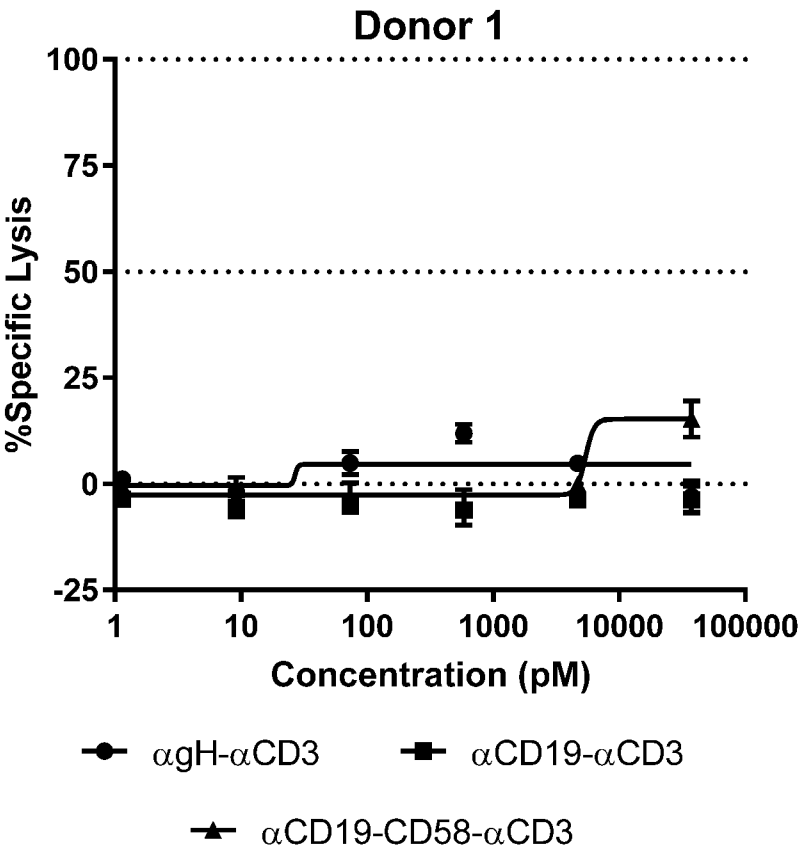


FIG. 5

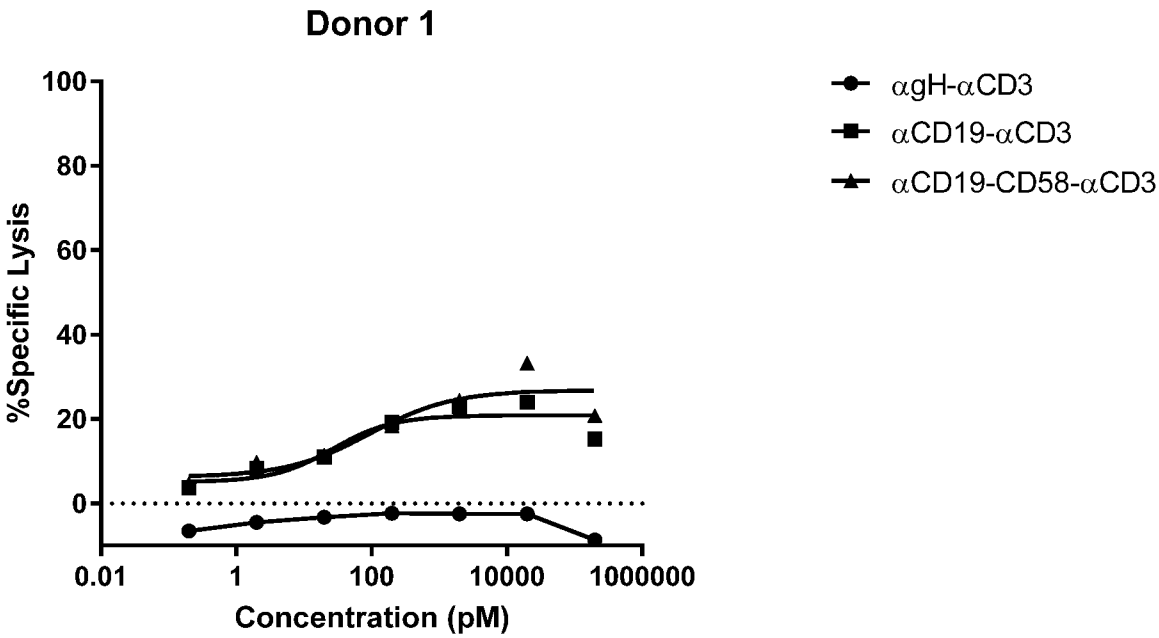


FIG. 6A

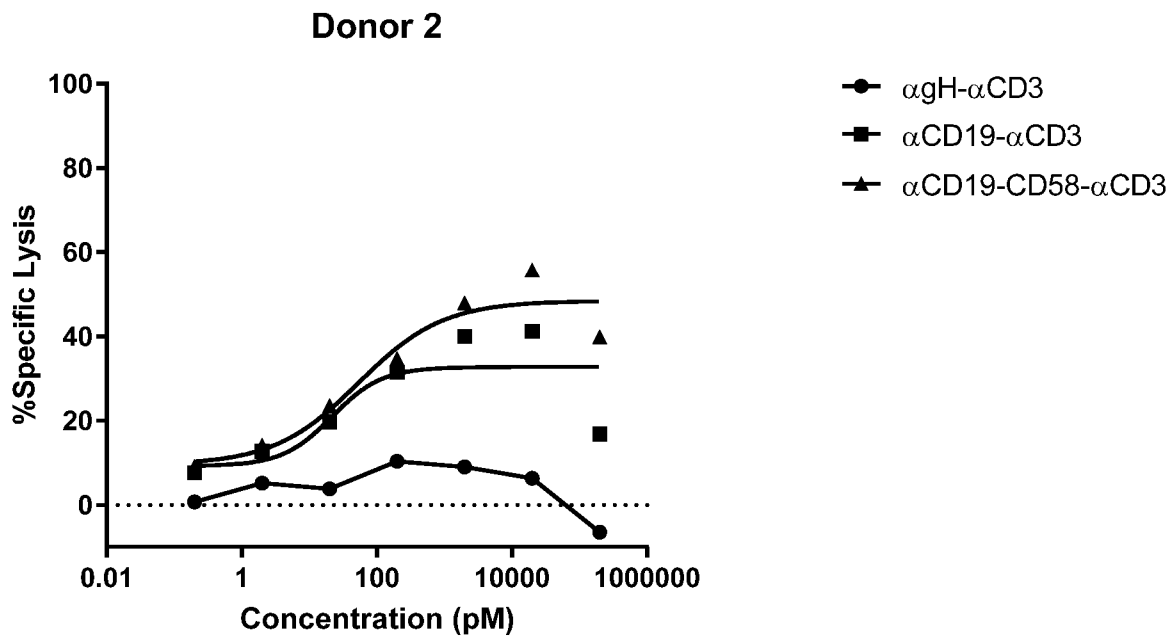


FIG. 6B

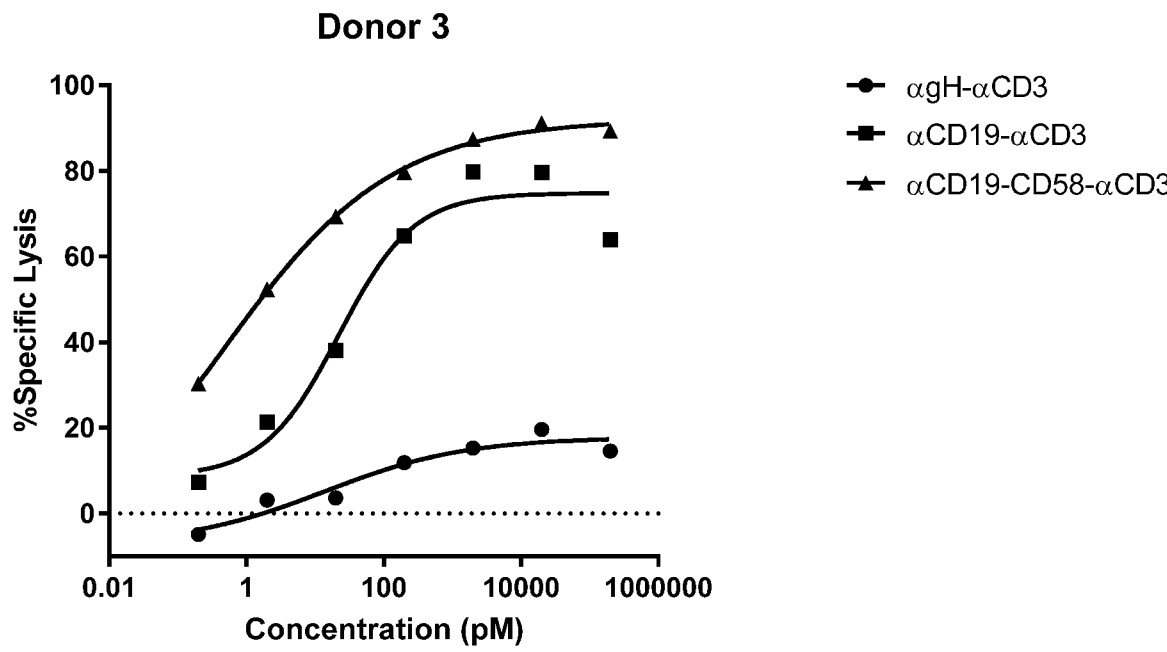


FIG. 6C

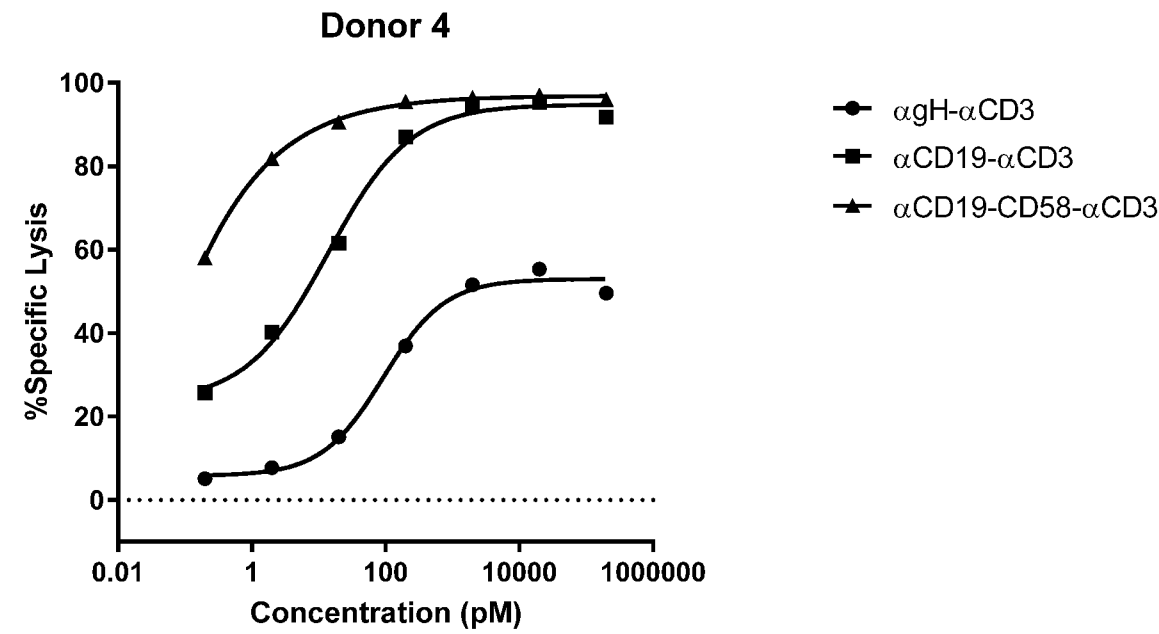


FIG. 6D

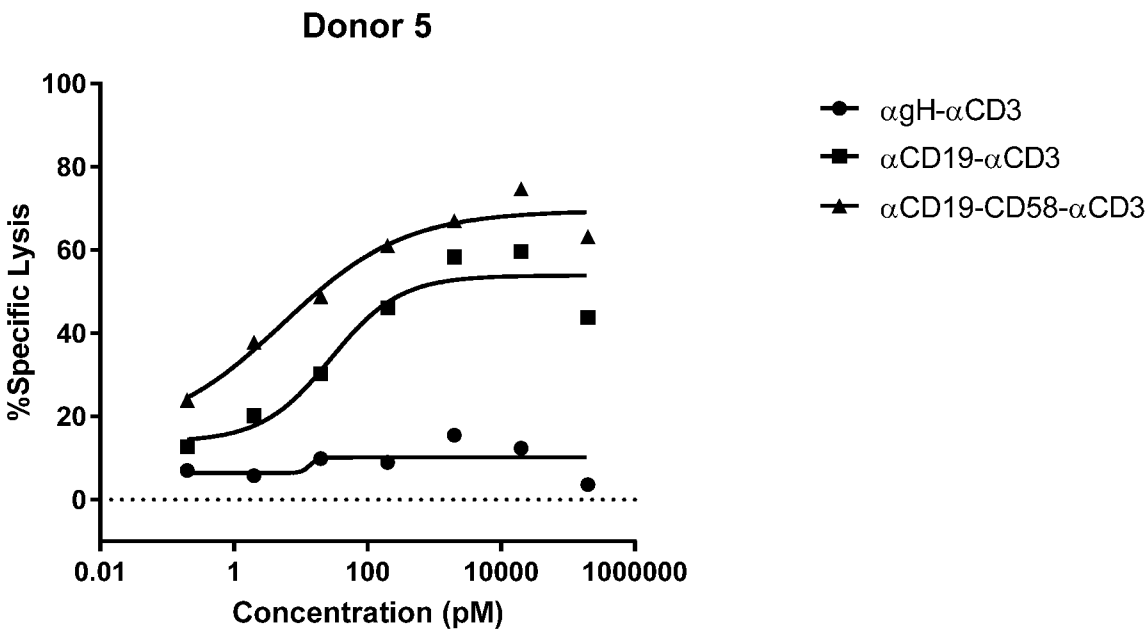


FIG. 6E

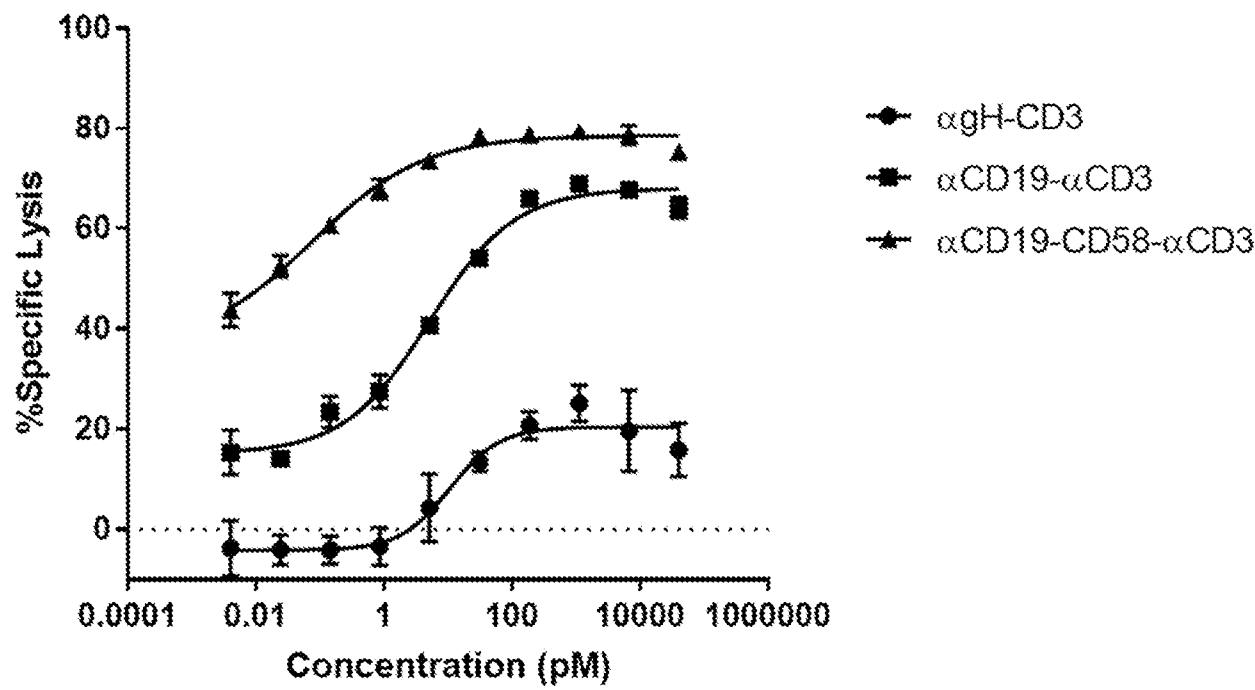


FIG. 7

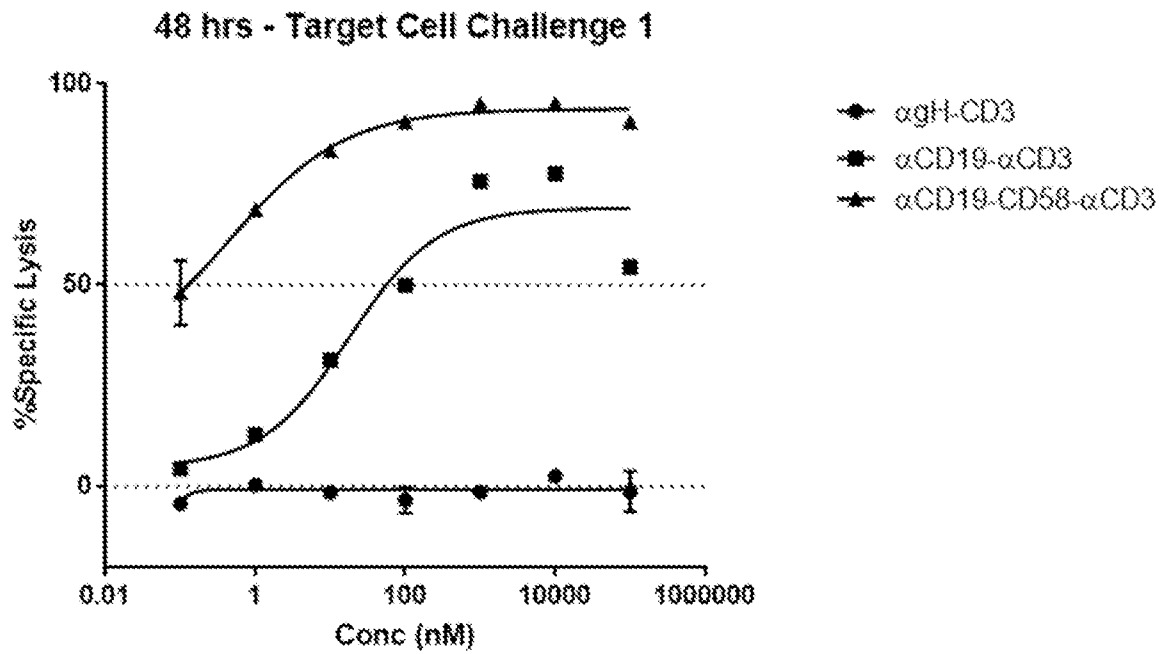


FIG. 8A

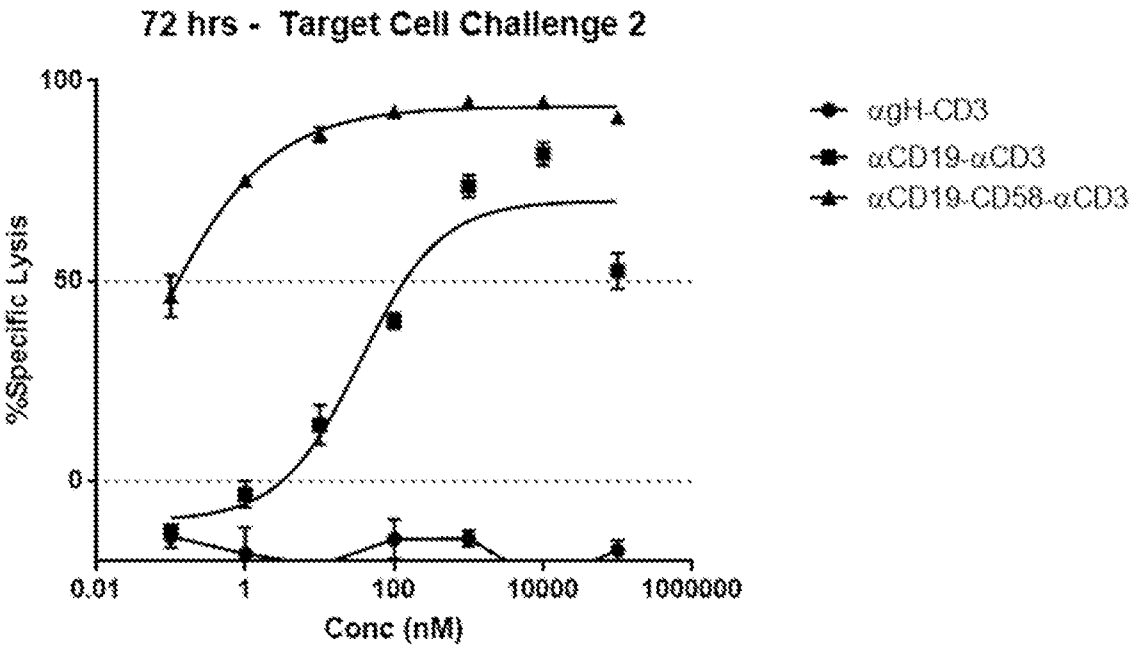


FIG. 8B

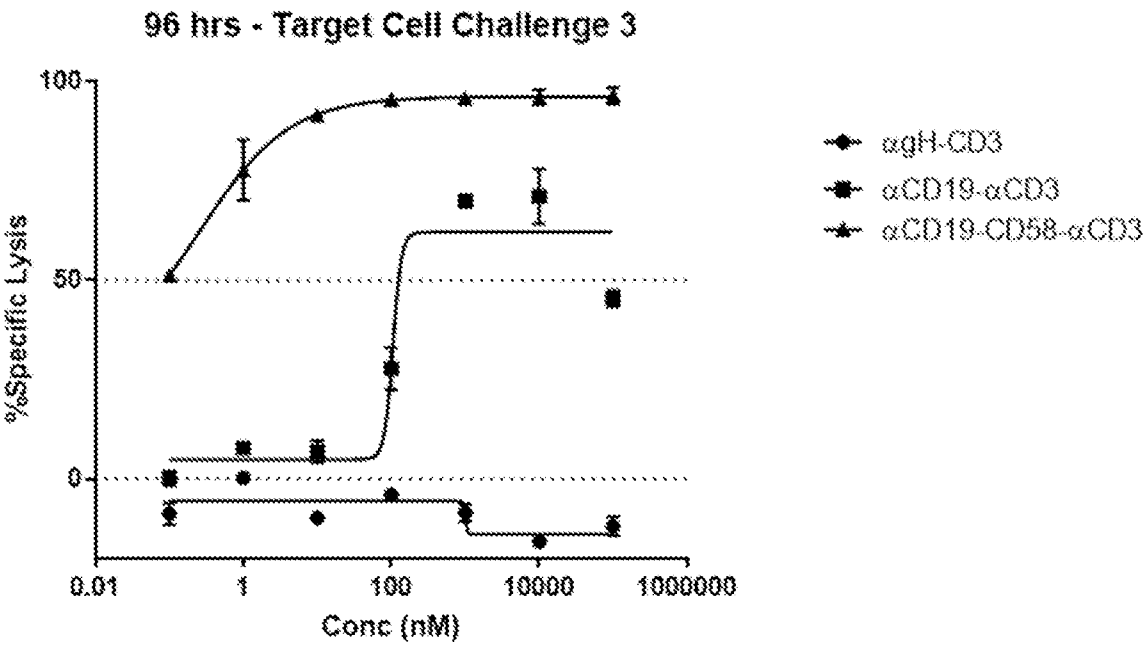


FIG. 8C

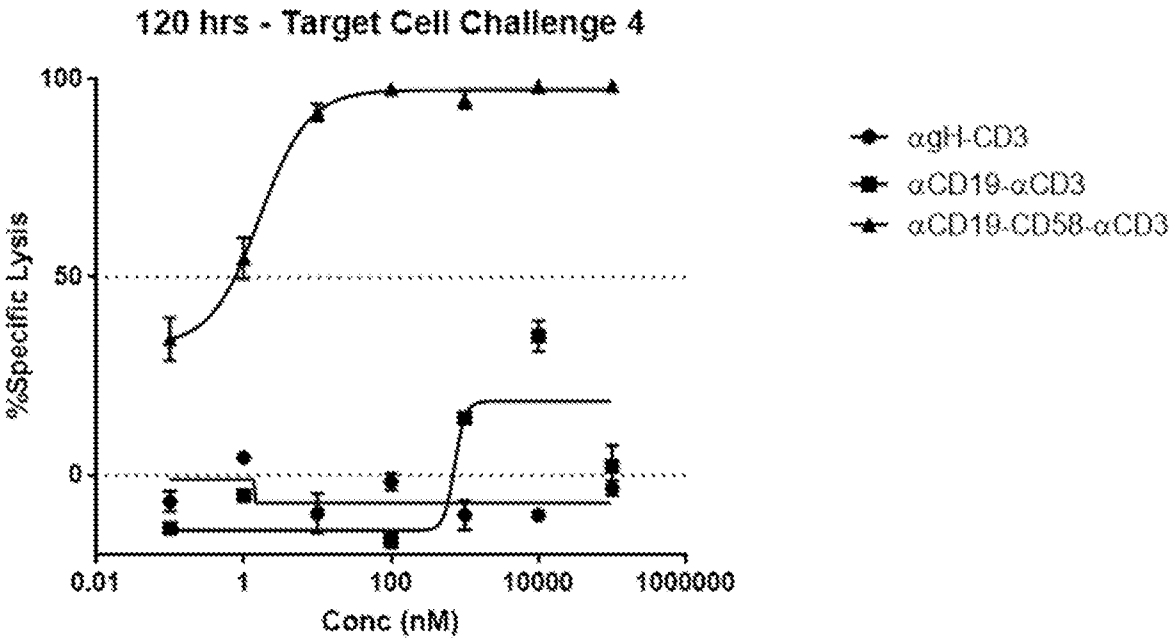


FIG. 8D

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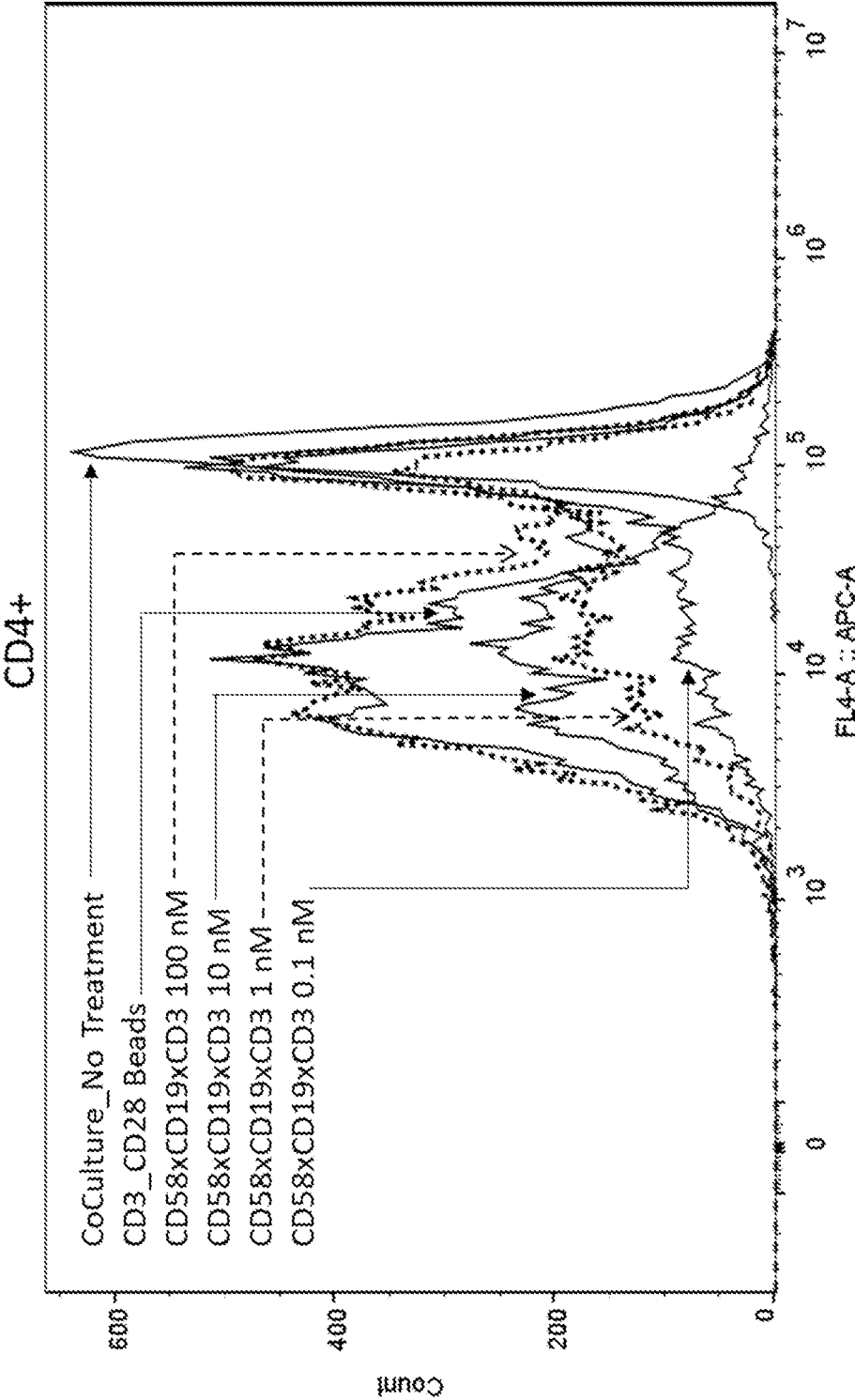


FIG. 9A

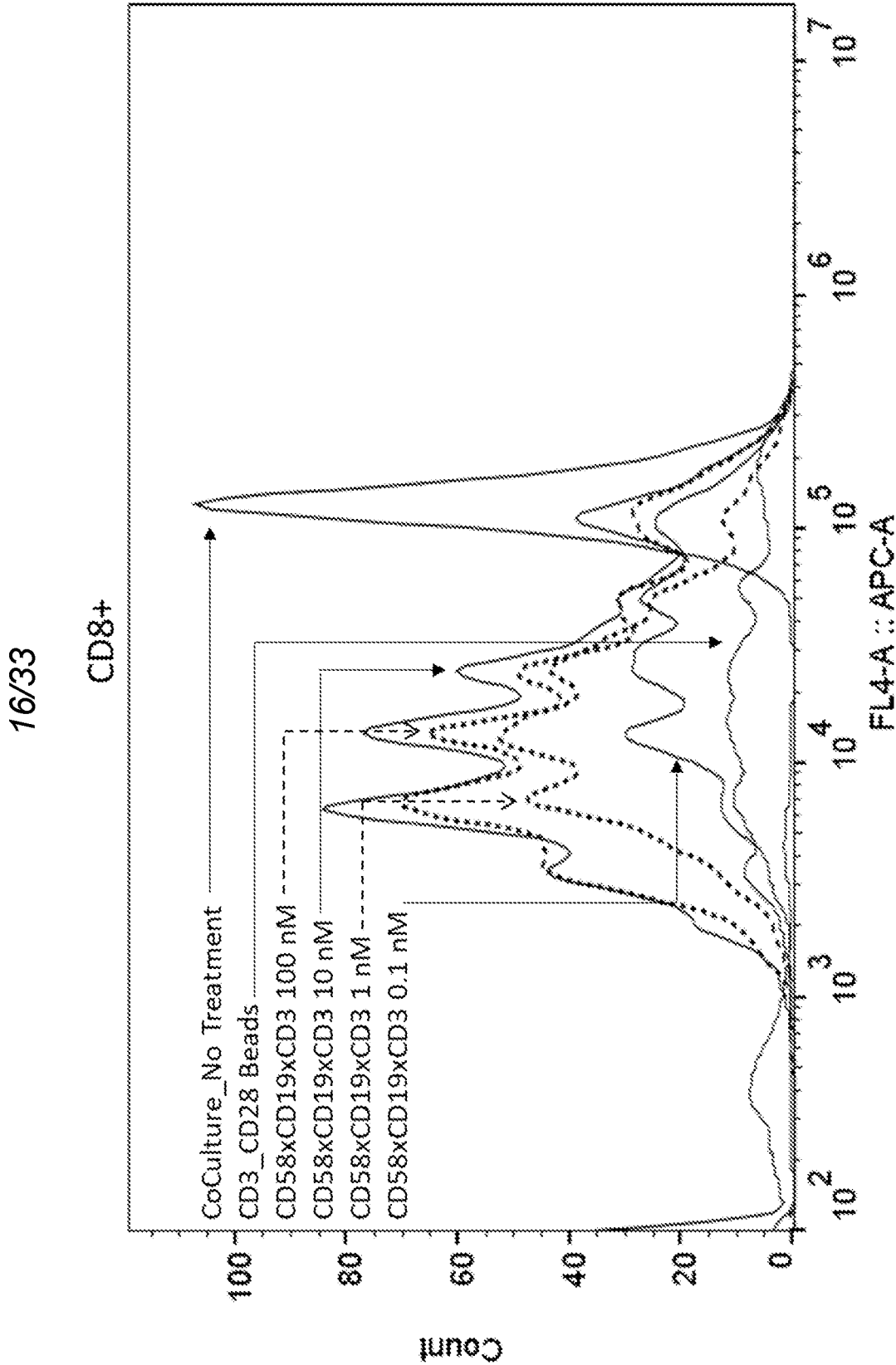


FIG. 9B

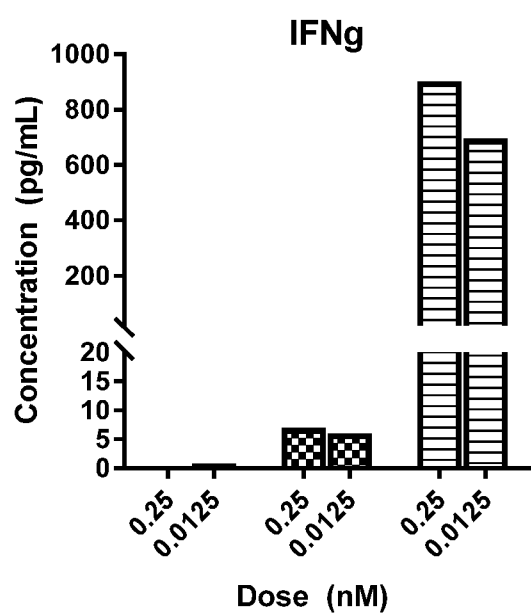


FIG. 10A

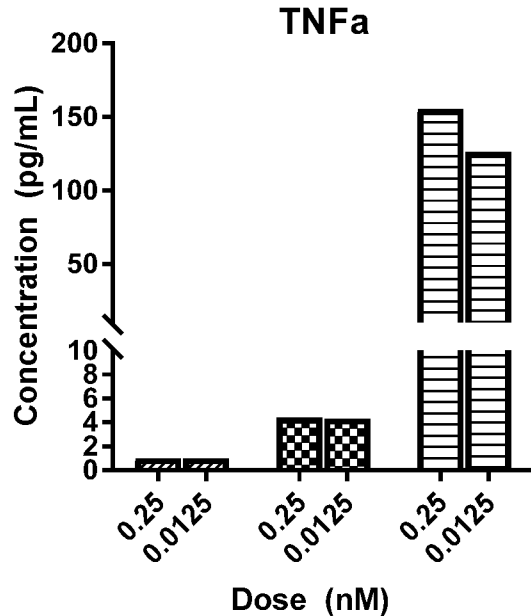


FIG. 10B

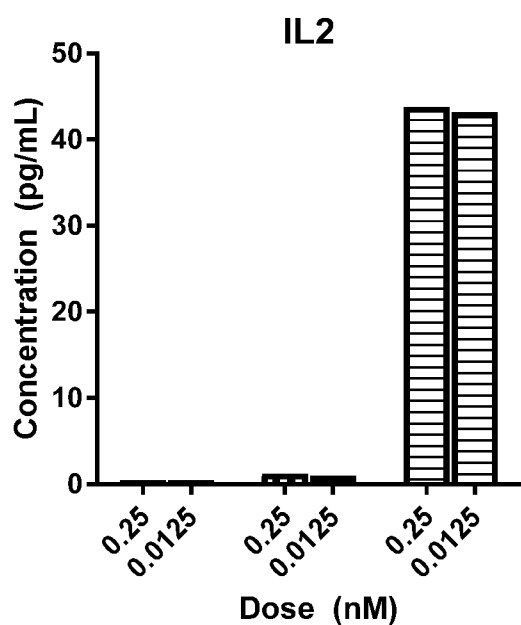


FIG. 10C

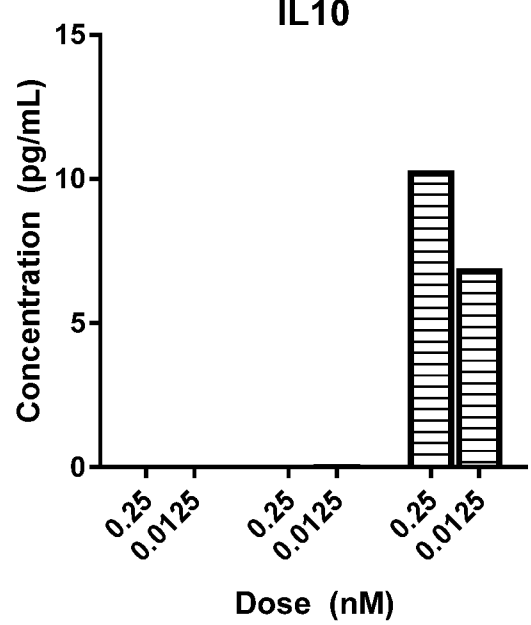


FIG. 10D

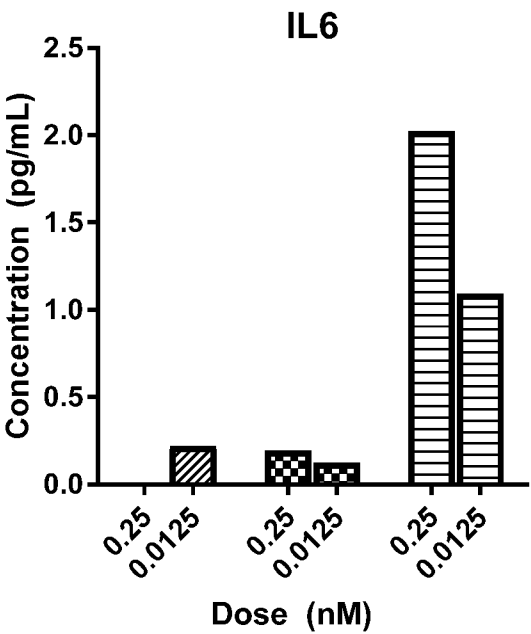


FIG. 10E

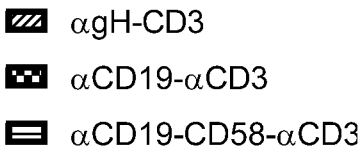


FIG. 10F

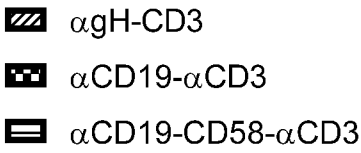
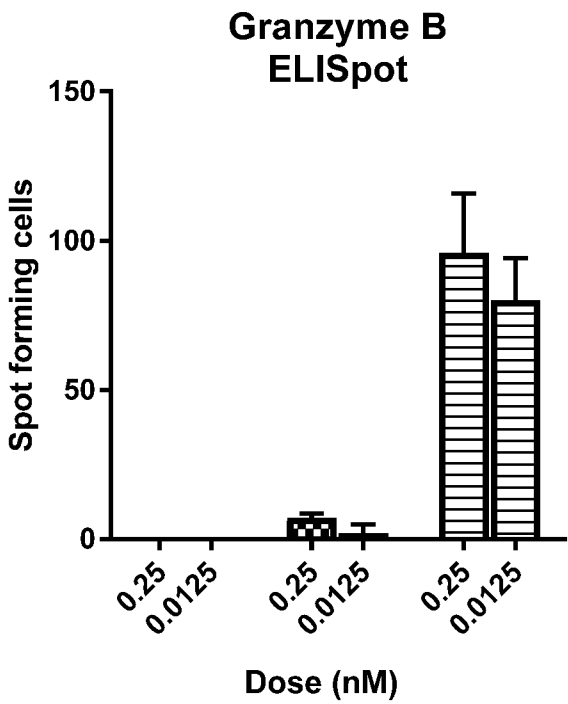


FIG. 11

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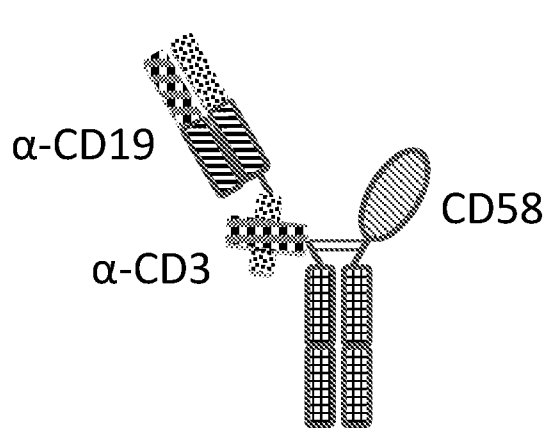


FIG. 12A

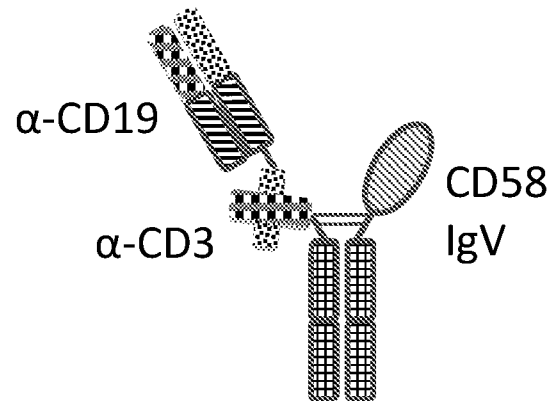


FIG. 12B

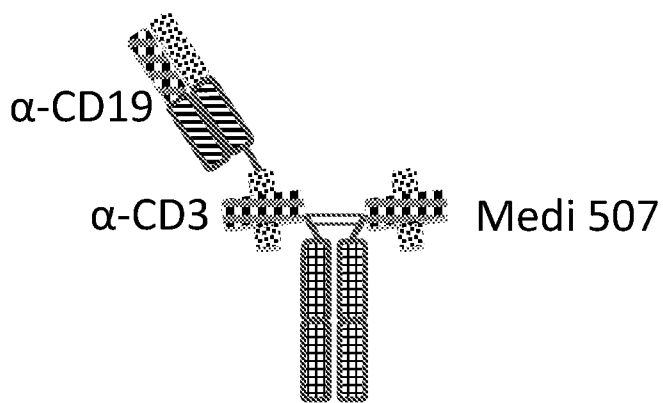


FIG. 12C

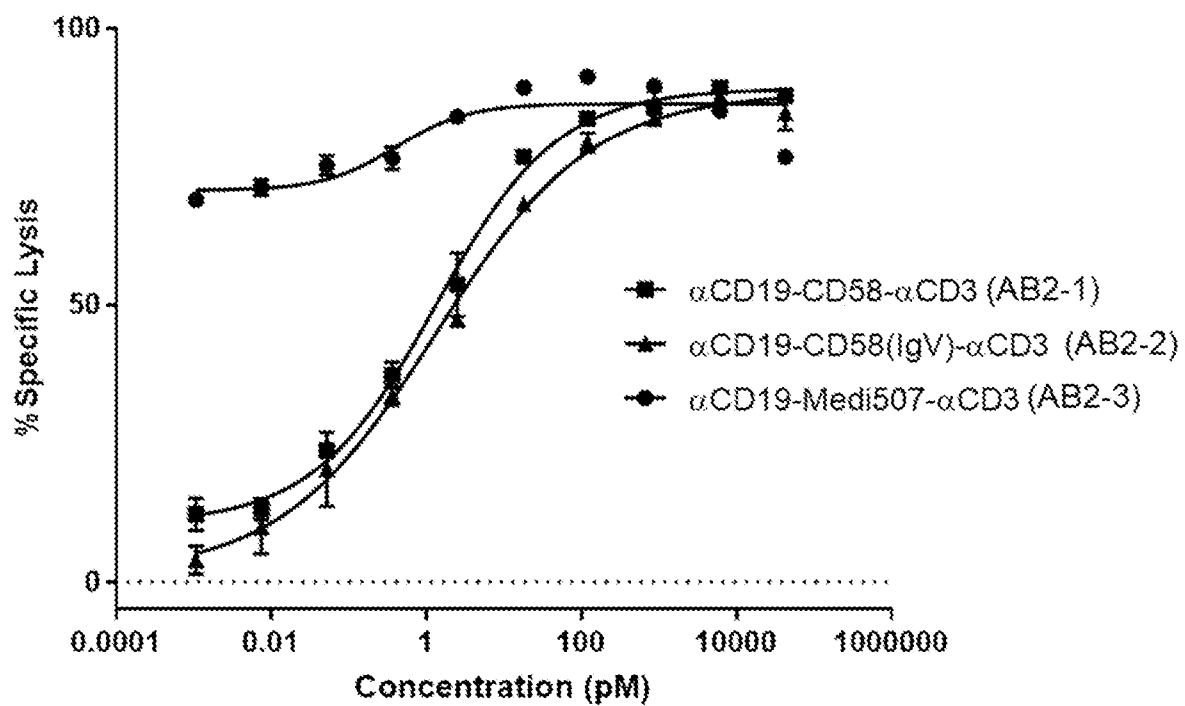


FIG. 13

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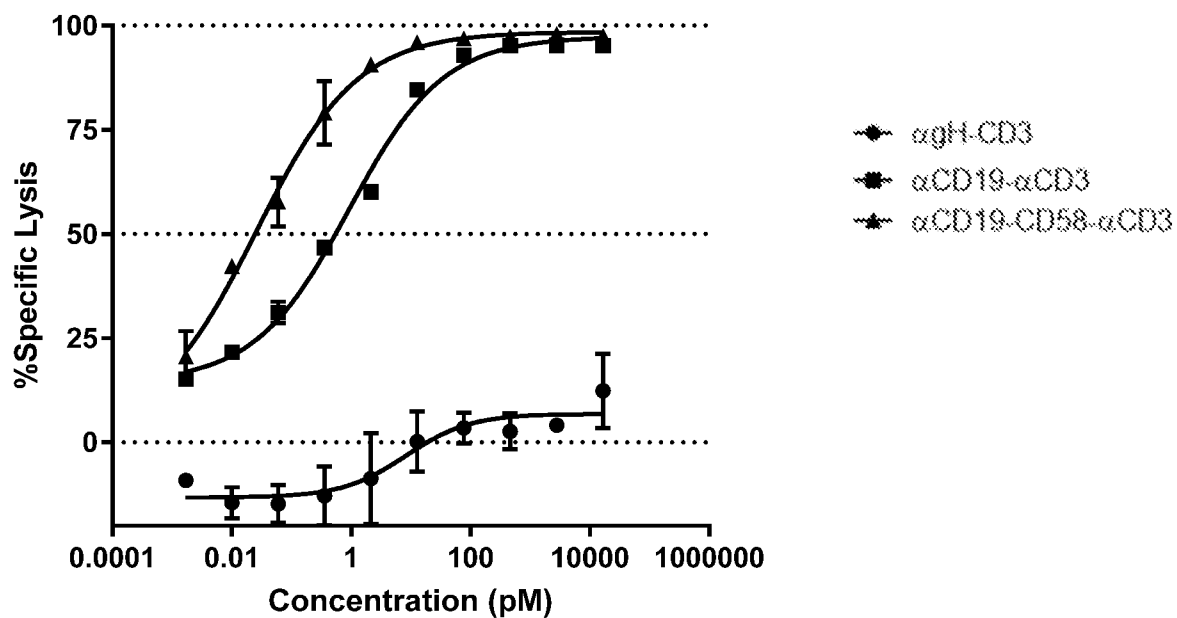


FIG. 14

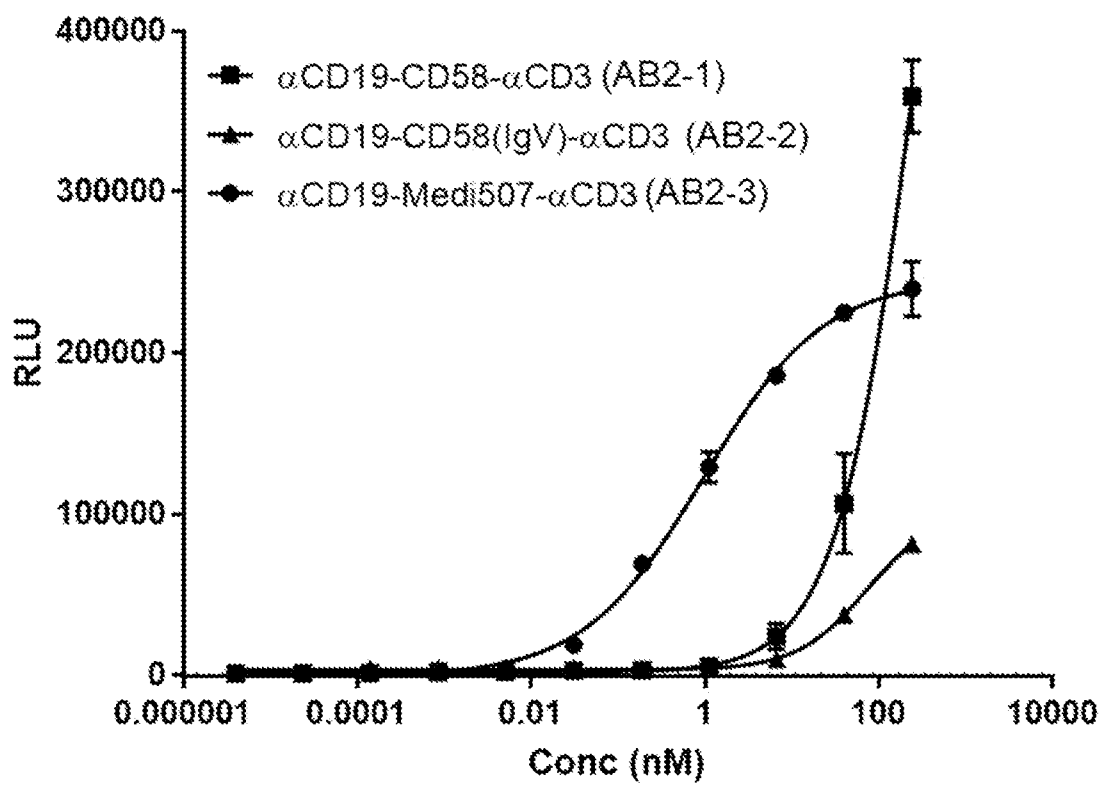


FIG. 15

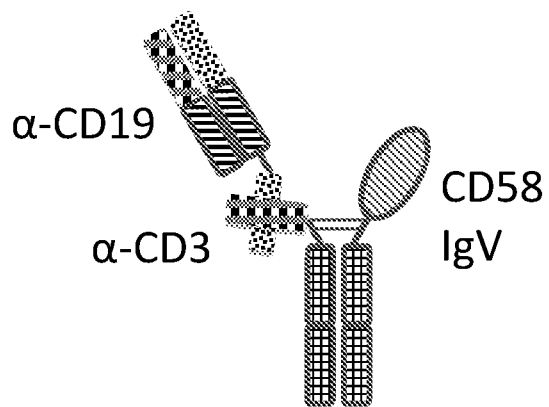


FIG. 16A

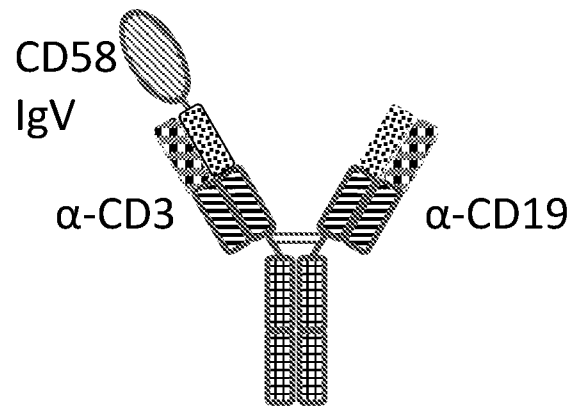


FIG. 16B

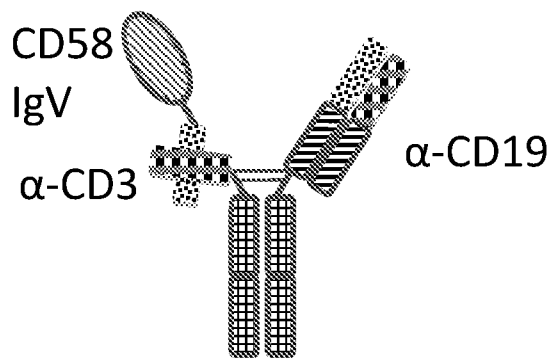


FIG. 16C

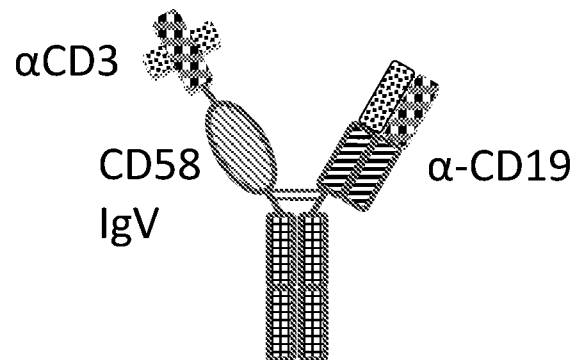


FIG. 16D

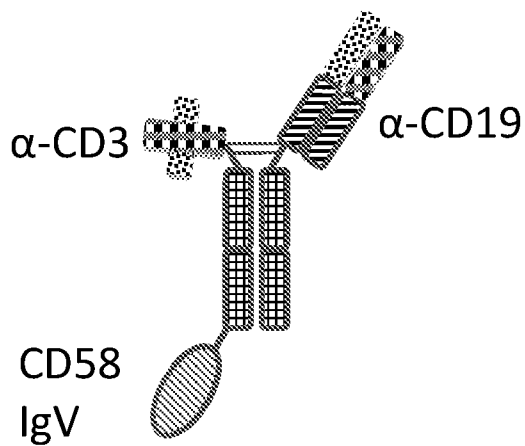


FIG. 16E

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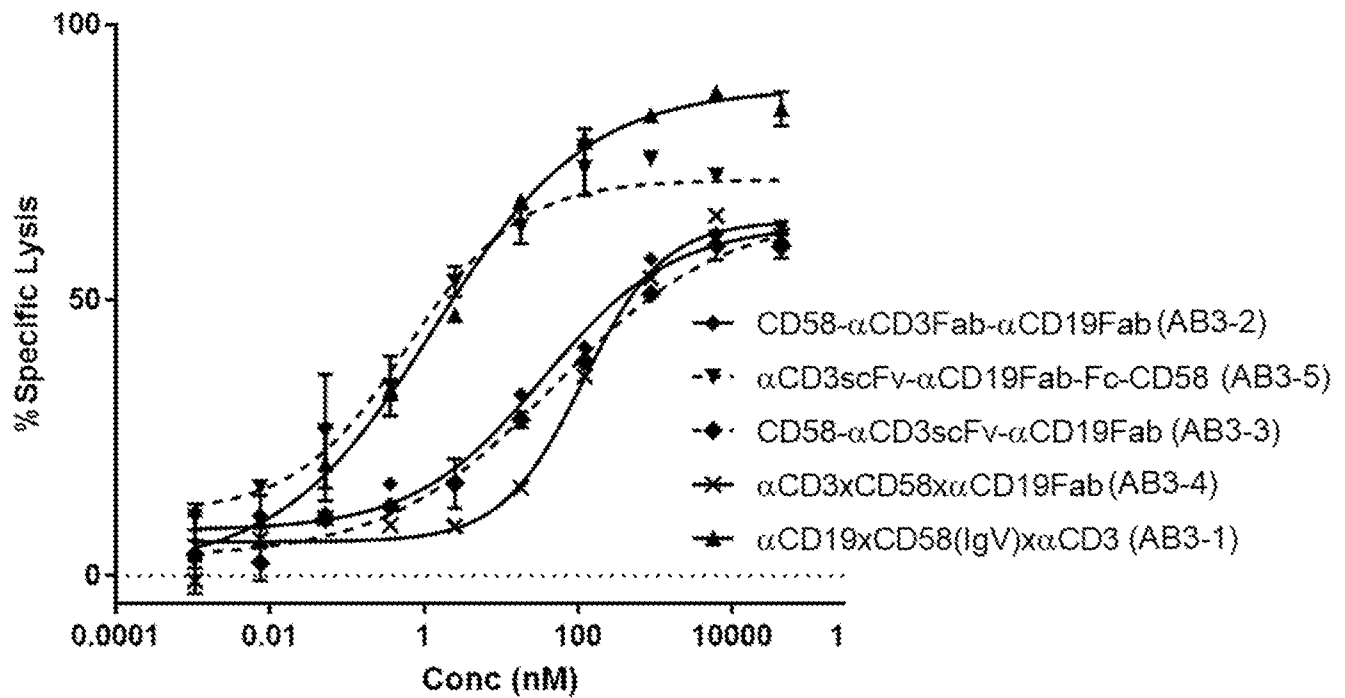


FIG. 17

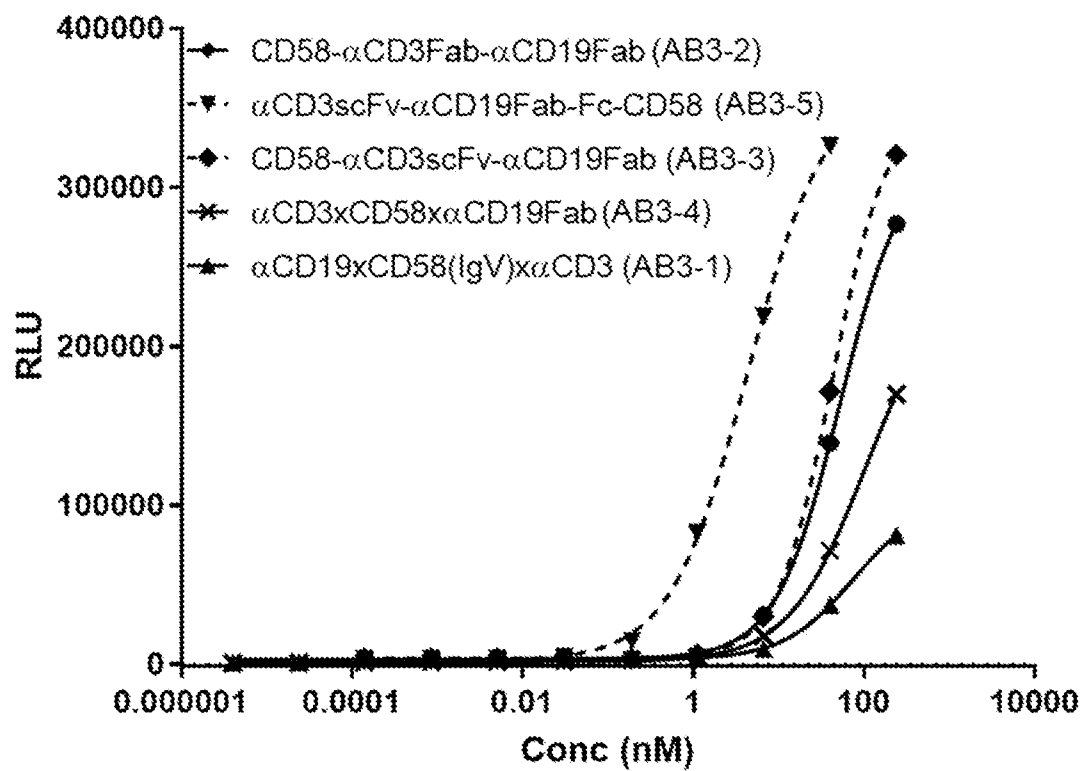


FIG. 18

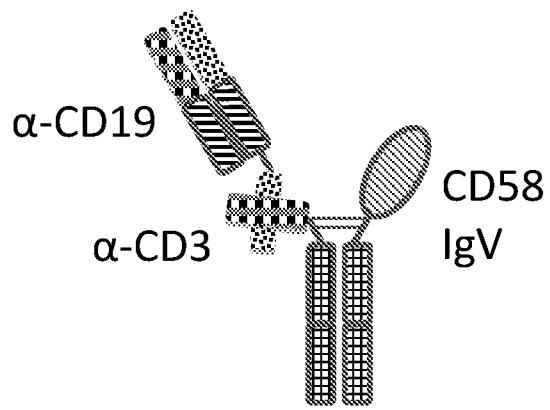


FIG. 19A

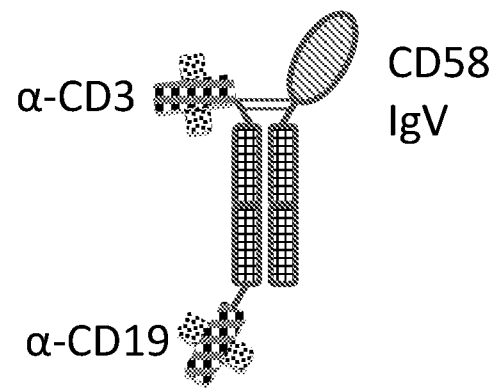


FIG. 19B

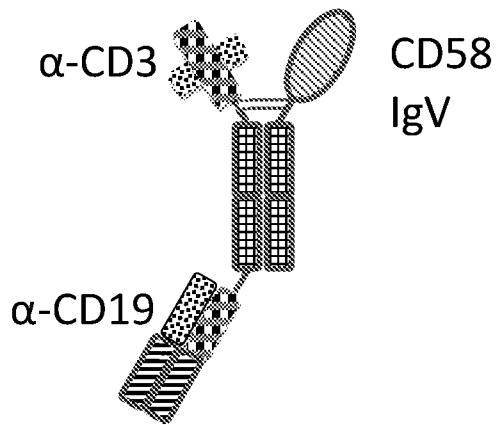


FIG. 19C

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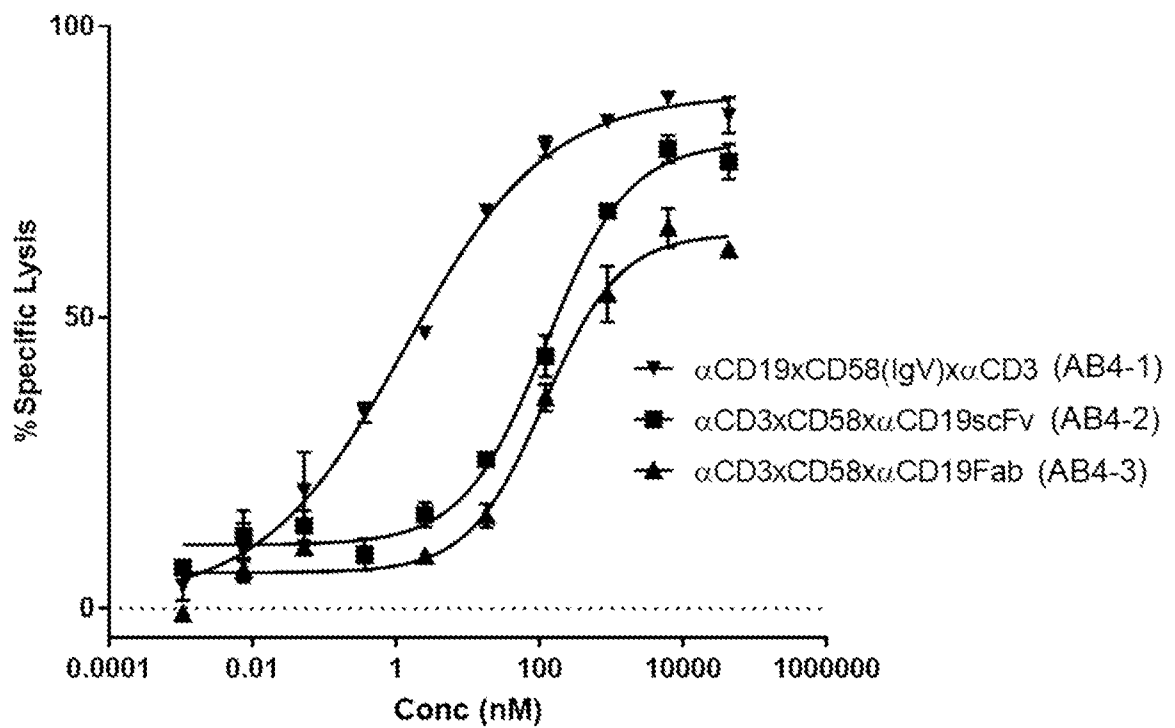


FIG. 20

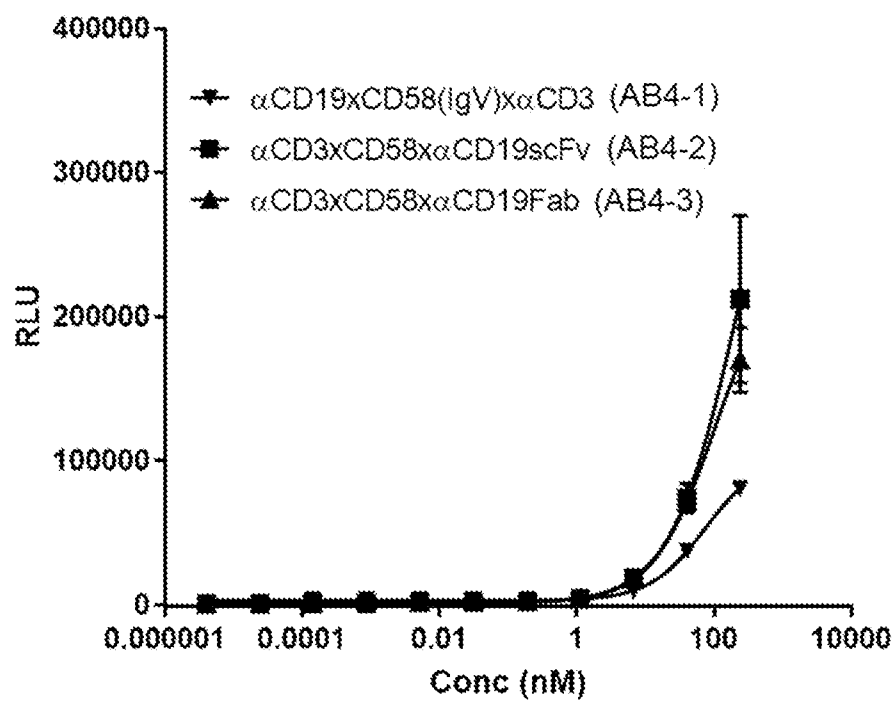


FIG. 21

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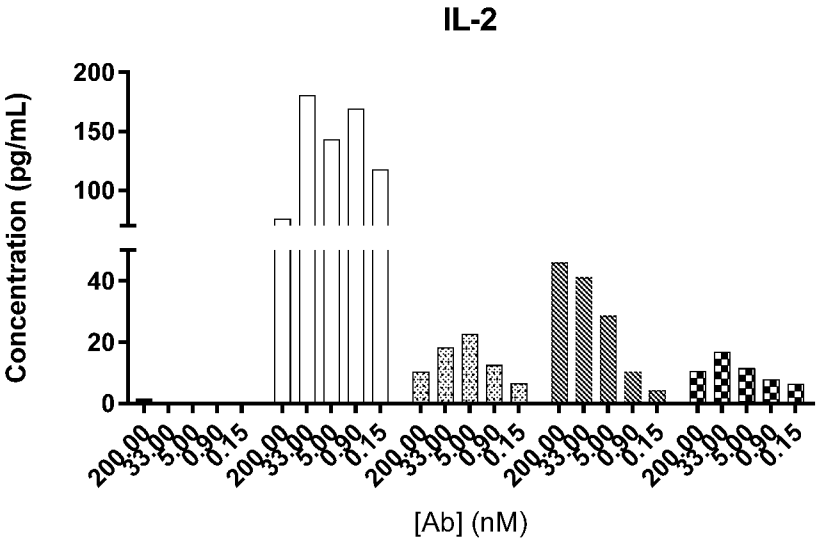


FIG. 22A

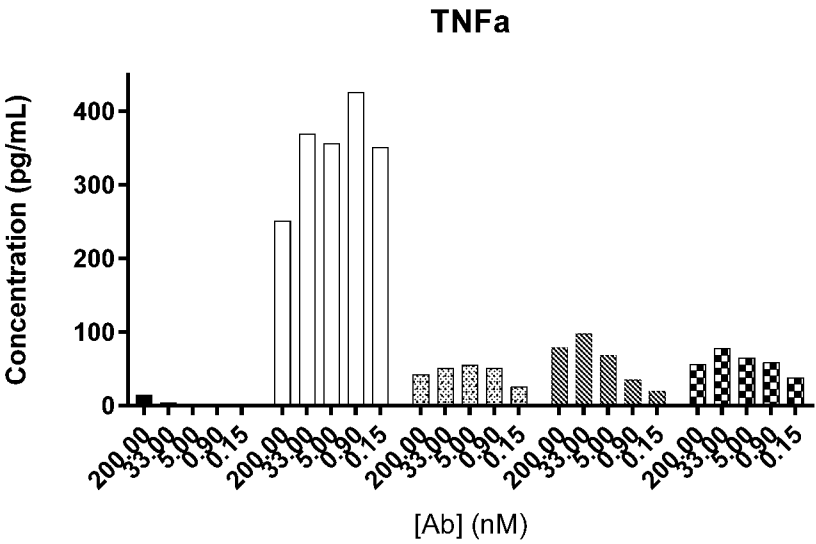


FIG. 22B

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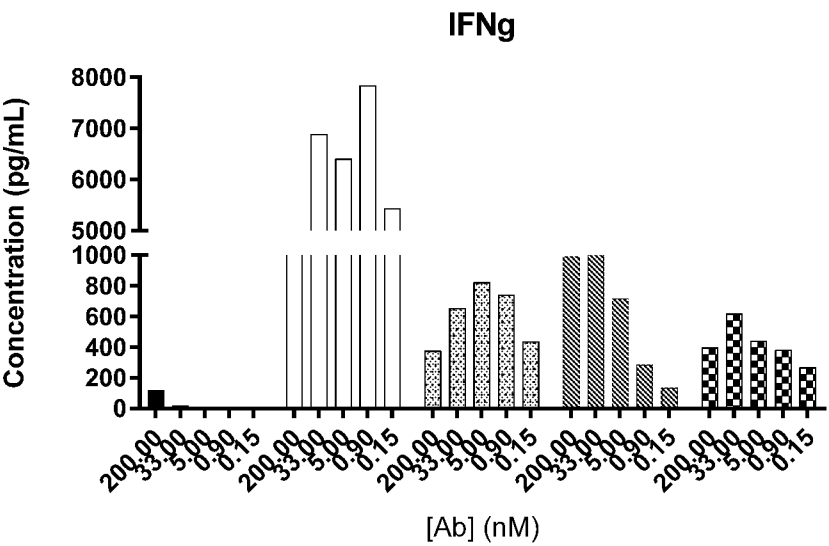


FIG. 22C

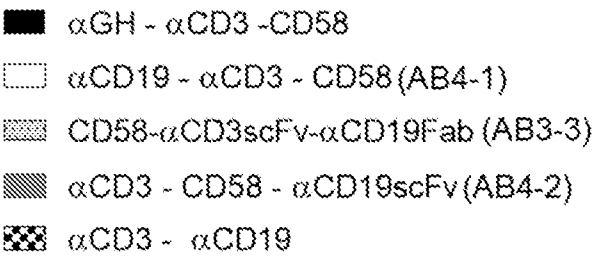


FIG. 22D

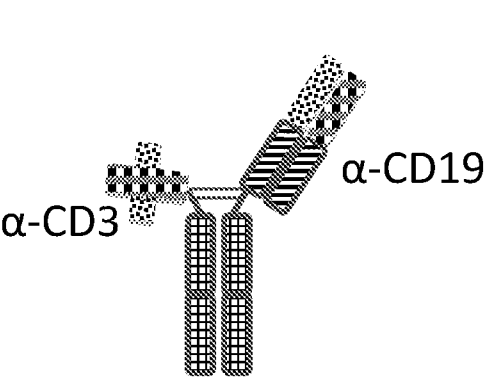


FIG. 23A

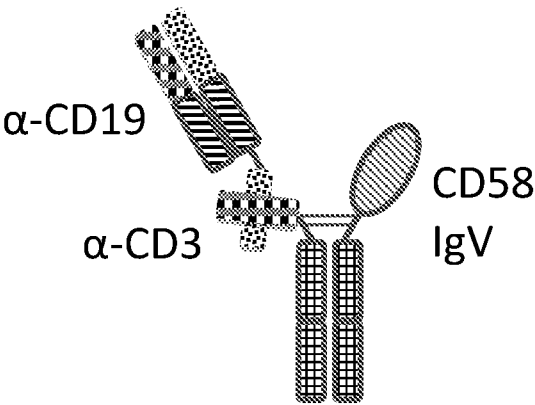


FIG. 23B

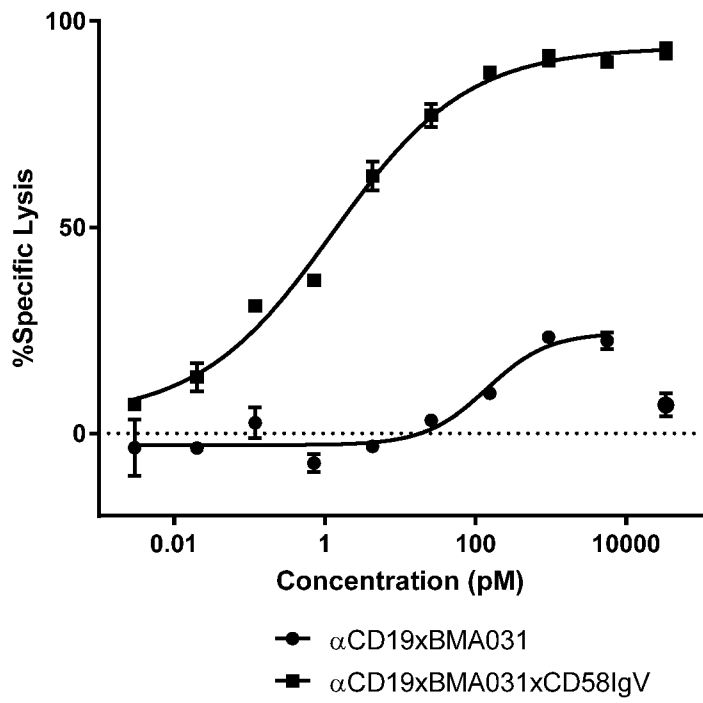


FIG. 24A

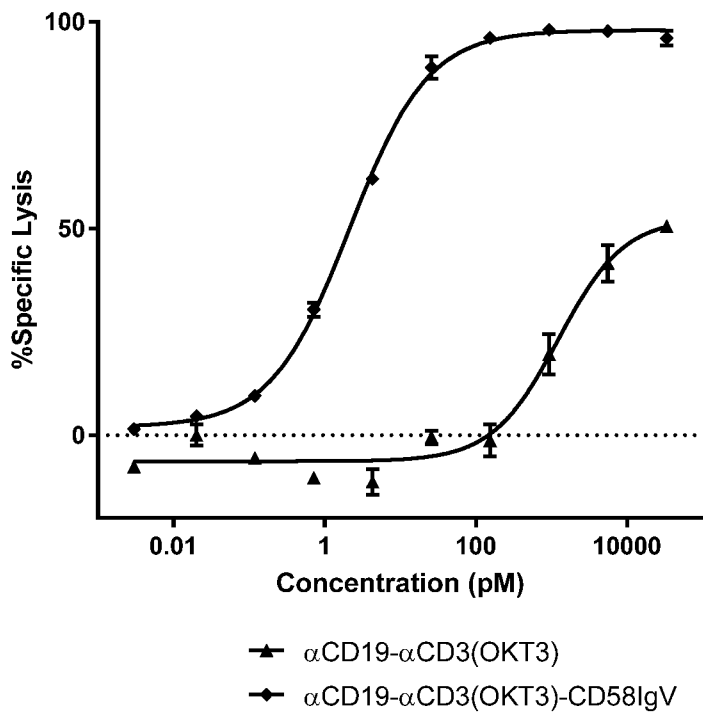


FIG. 24B

IL-2

[Ab] (mM)	Concentration (pg/mL)
200.00	~30
33.00	~35
5.00	~60
0.90	~45
0.15	~55
3.00	~5
0.50	~5
0.15	~5

IFN-g

[Ab] (mM)	Concentration (pg/mL)
200.00	~1000
33.00	~1100
5.00	~1600
0.90	~1500
0.15	~1800
3.00	~50
0.50	~50
0.15	~50

TNFa

[Ab] (mM)	Concentration (pg/mL)
200.00	~110
33.00	~120
5.00	~130
0.90	~135
0.15	~140
3.00	~10
0.50	~10
0.15	~10

FIG. 25A

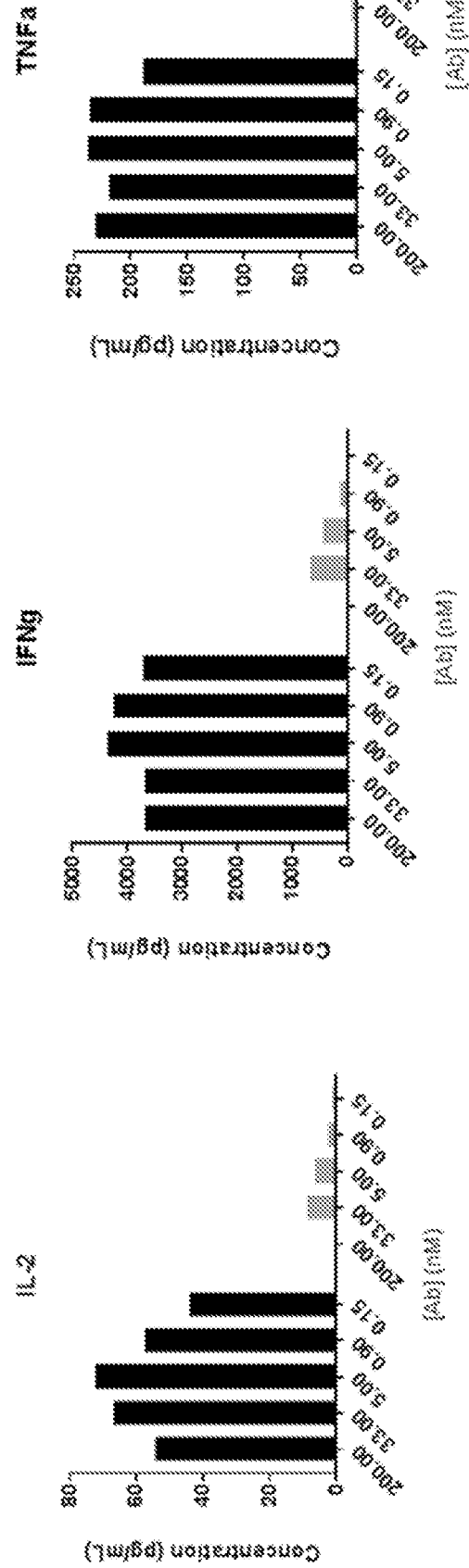
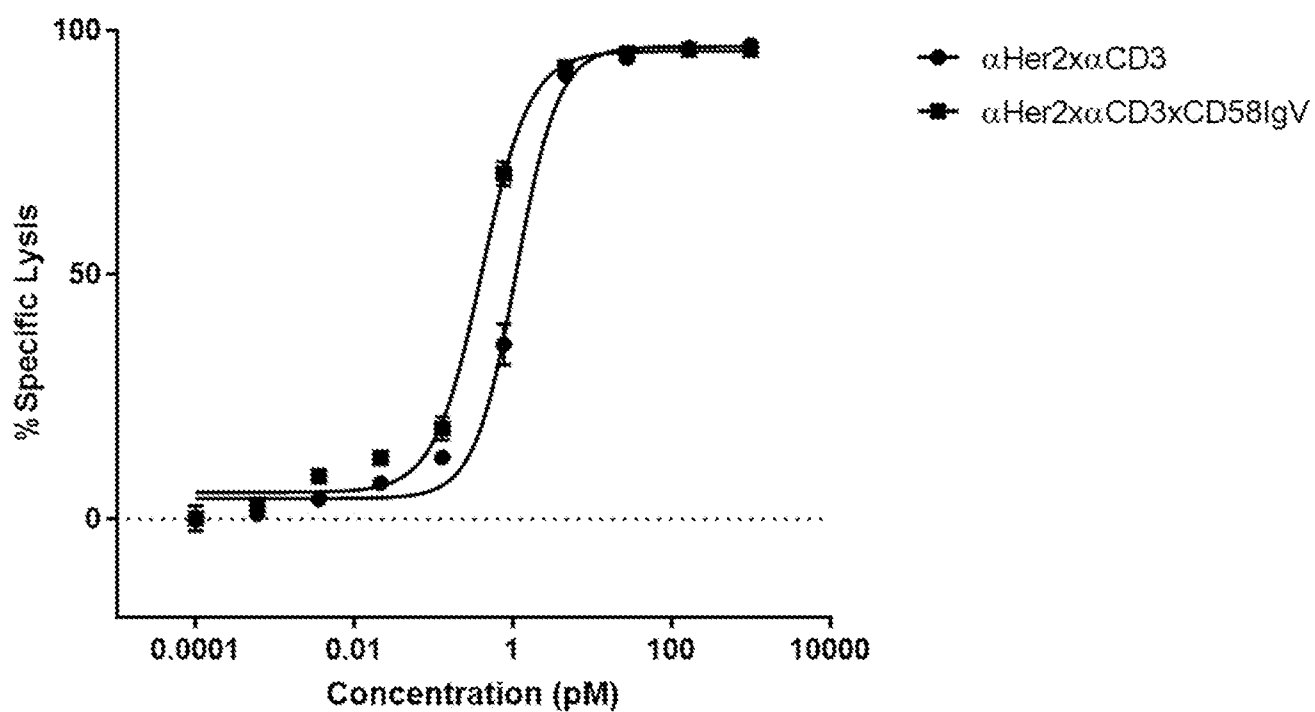
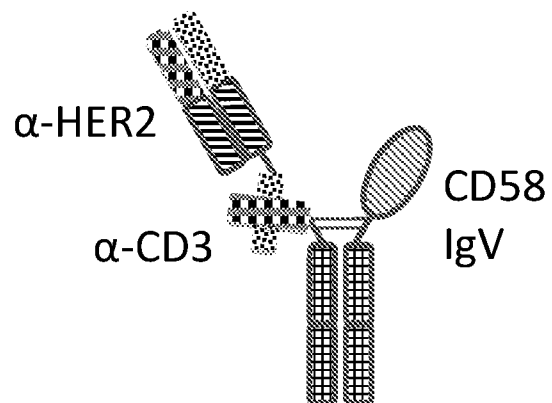
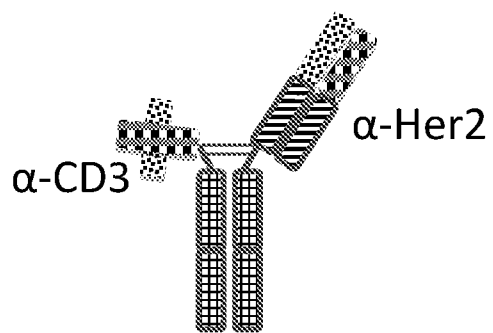


FIG. 25B

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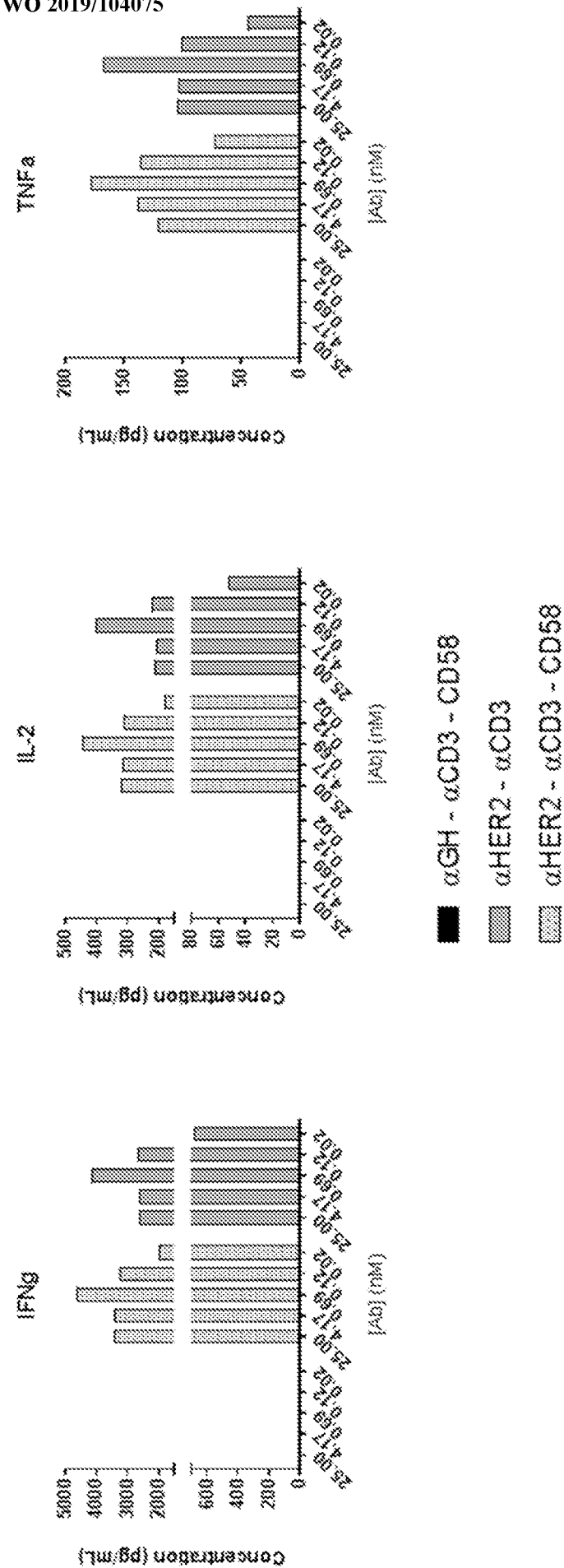


FIG. 28

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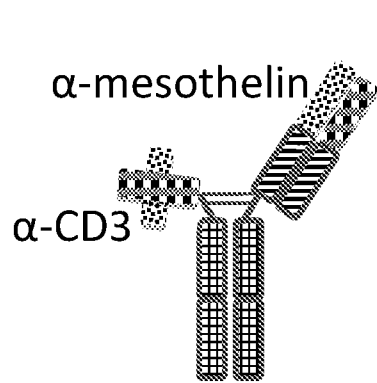


FIG. 29A

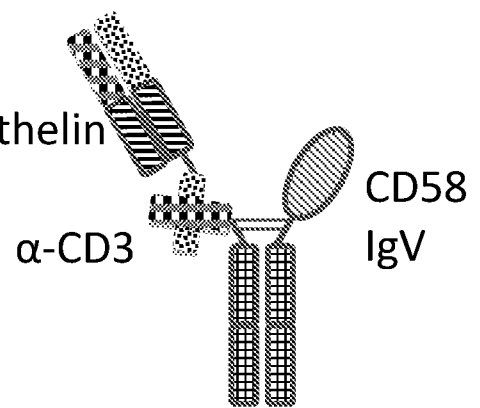


FIG. 29B

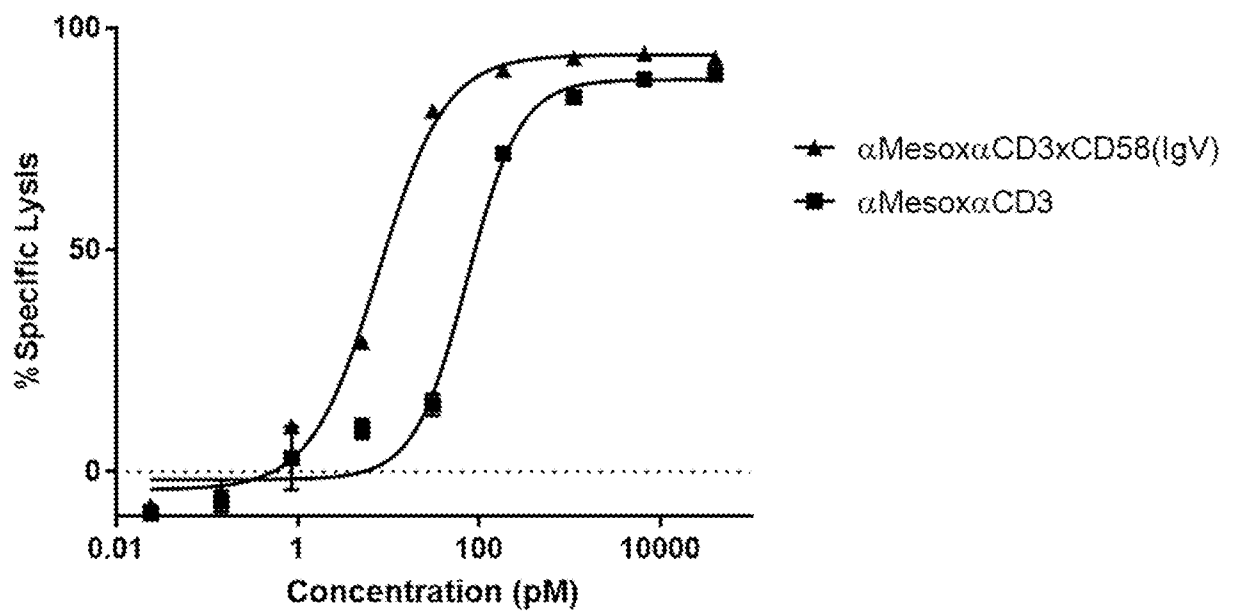


FIG. 30

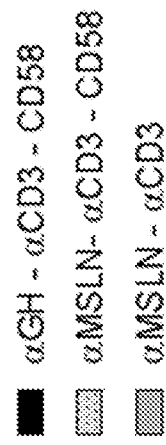


FIG. 31

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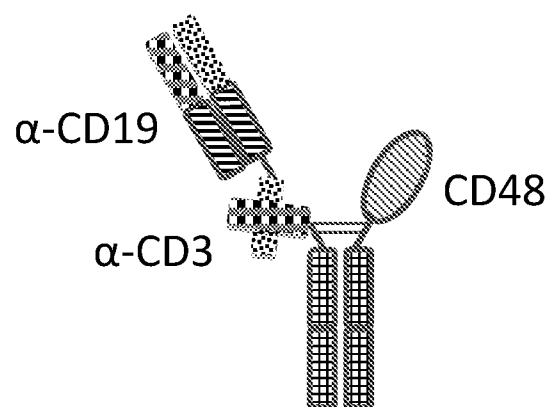


FIG. 32

NOV-001WO_SL.txt
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GRANDA, Brian
HONG, Connie
RAMONES, Melissa
SKEGRO, Darko

<120> TRISPECIFIC BINDING MOLECULES AGAINST TUMOR-ASSOCIATED ANTIGENS
AND USES THEREOF

<130> NOV-001WO

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<150> 62/589,331

<151> 2017-11-21

<160> 816

<170> PatentIn version 3.5

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peptide

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Cys Pro Pro Cys

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 1 5 10 15

Ser Pro Ser

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Asn Thr Gly Arg Gly Gly Glu Glu Lys Lys Lys Glu Lys Glu Lys Glu
 35 40 45

Glu Gln Glu Glu Arg Glu Thr Lys Thr Pro
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<210> 9
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Pro Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro
 20 25 30

NOV-001WO_SL.txt

Glu Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro Glu
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Pro Lys Ser Cys Asp Thr Pro Pro Pro Cys Pro Arg Cys Pro
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1 5 10

<210> 11
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Cys Pro Arg Cys

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Ser Pro Pro Cys

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<210> 15

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Cys Pro Pro Ser

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<210> 17
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 1 5 10 15

Pro Ala

<210> 19
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Pro Ala Thr Cys Pro Pro Cys Pro Ala
20 25

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1 5 10 15

Tyr Asn Ser Leu Val Met Ser Asp Thr Ala Gly Thr Cys Tyr
20 25 30

<210> 21
<211> 31
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<213> Artificial Sequence

<220>
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polypeptide

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peptide

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<220>

<223> Description of Artificial Sequence: Synthetic
peptide

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Asp Lys Thr His Thr Cys Pro Arg Cys Pro Glu Pro Lys Ser Cys Asp
1 5 10 15

Thr Pro Pro Pro Cys Pro Arg Cys Pro Ala
20 25

<210> 24

<211> 11

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<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 24

Asp Lys Thr His Thr Cys Pro Ser Cys Pro Ala
1 5 10

<210> 25

<211> 5

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<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

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1 5

<210> 26

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 26

Ala Asp Ala Ala Pro
1 5

<210> 27

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<220>

<223> Description of Artificial Sequence: Synthetic
peptide

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1 5 10

<210> 28

<211> 12

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<223> Description of Artificial Sequence: Synthetic
peptide

<400> 28

Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro
1 5 10

<210> 29

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<212> PRT

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<400> 29

Ala Lys Thr Thr Ala Pro
1 5

<210> 30

<211> 13

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<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 30

Ala Lys Thr Thr Ala Pro Ser Val Tyr Pro Leu Ala Pro
1 5 10

<210> 31

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<212> PRT

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<223> Description of Artificial Sequence: Synthetic peptide

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

Val

<210> 32

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<400> 33

Ala Lys Thr Thr Pro Pro
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Ala Lys Thr Thr Pro Pro Ser Val Thr Pro Leu Ala Pro
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<210> 35

<211> 6

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<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

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Ala Ser Thr Lys Gly Pro
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<210> 36

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<220>

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peptide

<400> 36

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
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<223> Description of Artificial Sequence: Synthetic
peptide

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

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
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<210> 38

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peptide

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5

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peptide

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1 5 10 15

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peptide

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1 5 10 15Glu Gly Glu Ser
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peptide

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<211> 15

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<210> 43

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<210> 44

<211> 15

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<223> Description of Artificial Sequence: Synthetic peptide

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<210> 45

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<223> This sequence may encompass 1-10 "Gly Gly Gly Gly Ser" repeating units

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1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
20 25 30

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
35 40 45

Gly Ser
50

<210> 47

<211> 10

<212> PRT

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1 5 10

<210> 48

<211> 20

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<223> Description of Artificial Sequence: Synthetic peptide

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1 5 10 15

Gly Gly Gly Ser
20

<210> 49

<211> 15

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<223> Description of Artificial Sequence: Synthetic peptide

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Gly Gly Gly Lys Ser Gly Gly Gly Lys Ser Gly Gly Gly Lys Ser
1 5 10 15

<210> 50

<211> 15

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1 5 10 15

<210> 51

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 51

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1 5 10 15

<210> 52

<211> 5

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<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 52

Gly Gly Ser Gly Gly
1 5

<210> 53

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 53

Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5

<210> 54
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<220>
 <223> Description of Artificial Sequence: Synthetic peptide

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

<210> 55
 <211> 15
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 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

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 1 5 10 15

<210> 56
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 Gly Lys Gly Gly Ser Gly Lys Gly Gly Ser Gly Lys Gly Gly Ser
 1 5 10 15

<210> 57
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<210> 58

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Gly Lys Gly Lys Ser Gly Lys Gly Lys Ser Gly Lys Gly Lys Ser Gly
1 5 10 15

Lys Gly Lys Ser
20

<210> 59

<211> 15

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 59

Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser
1 5 10 15

<210> 60

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 60

Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly
1 5 10 15

Lys Pro Gly Ser
20

<210> 61

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 61

Gly Pro Ala Lys Glu Leu Thr Pro Leu Lys Glu Ala Lys Val Ser
1 5 10 15

<210> 62

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 62

Gly Ser Ala Gly Ser Ala Ala Gly Ser Gly Glu Phe
1 5 10

<210> 63

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 63

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Ile Arg Pro Arg Ala Ile Gly Gly Ser Lys Pro Arg Val Ala
1 5 10

<210> 64

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 64

Lys Glu Ser Gly Ser Val Ser Ser Glu Gln Leu Ala Gln Phe Arg Ser
1 5 10 15

Leu Asp

<210> 65

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 65

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

<210> 66

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 66

Gln Pro Lys Ala Ala Pro
1 5

<210> 67
 <211> 13
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 67
 Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro
 1 5 10

<210> 68
 <211> 27
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 68
 Arg Ala Asp Ala Ala Ala Ala Gly Gly Gly Gly Ser Gly Gly Gly Gly
 1 5 10 15

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 20 25

<210> 69
 <211> 12
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 69
 Arg Ala Asp Ala Ala Ala Ala Gly Gly Pro Gly Ser
 1 5 10

<210> 70

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 70

Arg Ala Asp Ala Ala Pro

1 5

<210> 71

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 71

Arg Ala Asp Ala Ala Pro Thr Val Ser

1 5

<210> 72

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 72

Ser Ala Lys Thr Thr Pro

1 5

<210> 73

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 73

Ser Ala Lys Thr Thr Pro Lys Leu Glu Glu Gly Glu Phe Ser Glu Ala
1 5 10 15

Arg Val

<210> 74

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 74

Ser Ala Lys Thr Thr Pro Lys Leu Gly Gly
1 5 10

<210> 75

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 75

Ser Thr Ala Gly Asp Thr His Leu Gly Gly Glu Asp Phe Asp
1 5 10

<210> 76

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 76

Thr Val Ala Ala Pro

1 5

<210> 77

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 77

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro

1 5 10

<210> 78

<211> 24

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 78

Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Thr Val Ala Ala

1 5 10 15

Pro Ser Val Phe Ile Phe Pro Pro

20

<210> 79

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 79

NOV-001WO_SL.txt

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Lys Ala Thr Leu Thr Thr 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 Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Leu Thr Val Ser Ser
115

<210> 80

<211> 106

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 80

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 Ser Ser Ser Val Ser Tyr Met
20 25 30

NOV-001W0_SL.txt

Asn 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 His Phe Arg Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Gly Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Phe Thr
85 90 95

Phe Gly Ser Gly Thr Lys Leu Glu Ile Asn
100 105

<210> 81
<211> 125
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 81
Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Lys 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 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

NOV-001W0_SL.txt

Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp Ser Gln Ser Ile
65 70 75 80

Leu Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Met 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 Ala
115 120 125

<210> 82

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 82

Gln Ala Val Val Thr Gln Glu Ser Ala Leu Thr Thr Ser Pro Gly Glu
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 Glu Lys Pro Asp His Leu Phe Thr Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Ile Gly Asp Lys Ala Ala Leu Thr Ile Thr Gly Ala
65 70 75 80

Gln Thr Glu Asp Glu Ala Ile 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> 83

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 83

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg 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

Thr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Ile Asn Pro Ser Ser Gly Tyr Thr Lys 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 Trp Gln Asp Tyr Asp Val Tyr Phe Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Leu Thr Val Ser Ser
115

<210> 84

<211> 106

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 84

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 Ser Ser Ser Val Ser Tyr Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
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 Ser Ser Asn Pro Pro Thr
85 90 95

Phe Gly Gly Gly Thr Lys Leu Glu Thr Lys
100 105

<210> 85

<211> 106

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 85

NOV-001W0_SL.txt

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 Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Tyr 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 Ser Gly Thr Lys Leu Glu Ile Asn
100 105

<210> 86

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 86

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

NOV-001WO_SL.txt

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 Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Pro Val Thr Val Ser Ser
115

<210> 87

<211> 106

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 87

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
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

NOV-001WO_SL.txt

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> 88

<211> 118

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 88

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 Lys Phe Ser Gly 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 Trp Tyr Asp Gly Ser Lys Lys Tyr Tyr Val 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 Gln Met Gly Tyr Trp His Phe Asp Leu Trp Gly Arg Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 89
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 89
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

Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 90
<211> 124
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 90

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

Ala Met Asn Trp Val Arg Gln Ala Pro 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 Ile Ser Arg Asp Asp Ser Lys Asn Ser Leu
65 70 75 80

Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Phe Ala
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 91

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 91

NOV-001W0_SL.txt

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 Gly Lys Ala Ala Leu Ile Gly Ala Gln Ala
65 70 75 80

Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Leu Trp
85 90 95

Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 92

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 92

Asp Ile Lys Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Met Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Arg Tyr
20 25 30

Thr Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

NOV-001W0_SL.txt

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Lys Ala Thr Leu Thr Thr 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 Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
100 105 110

Thr Thr Leu Thr Val Ser Ser
115

<210> 93

<211> 105

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 93

Asp Ile Gln Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
1 5 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

Asn Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr
35 40 45

Asp Thr Ser Lys Val Ala Ser Gly Val Pro Tyr Arg Phe Ser Gly Ser
50 55 60

NOV-001WO_SL.txt

Gly Ser Gly Thr Ser Tyr Ser Leu Ile Ser Ser Met Glu Ala Glu Asp
65 70 75 80

Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe
85 90 95

Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 94

<211> 124

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 94

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 Asn Thr 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 Ile Ser Arg Asp Asp Ser Lys Asn Ser Leu
65 70 75 80

Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Phe Ala
100 105 110

Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 95

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 95

Glu Val Lys Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Lys 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 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 Gln Ser Ile
65 70 75 80

Leu Tyr Leu Gln Met Asn Asn Leu Lys Thr Glu Asp Thr Ala Met 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 Ala
115 120 125

<210> 96

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 96

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 Ser 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 Gly 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 Val Ser Trp Trp
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 97

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 97

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 Gln 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> 98

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 98

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

NOV-001W0_SL.txt

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> 99

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 99

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

NOV-001WO_SL.txt

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> 100

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 100

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 Arg Tyr
20 25 30

Thr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Arg Val Thr Met Thr Thr 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 Tyr Cys
85 90 95

Ala Arg Tyr Tyr Asp Asp His Tyr Cys Leu Asp Tyr Trp Gly Gln Gly
 100 105 110

Thr Leu Val Thr Val Ser Ser
 115

<210> 101

<211> 106

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 101

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 Ser Ala Ser Ser Ser Val Ser Tyr Met
 20 25 30

Asn Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr
 35 40 45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ala His Phe Arg Gly Ser
 50 55 60

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu
 65 70 75 80

Asp Phe Ala Val Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Phe Thr
 85 90 95

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 102

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 102

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

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser 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

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Ala Arg His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120 125

<210> 103

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 103

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 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 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> 104

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 104

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 Asn Thr Tyr
20 25 30

NOV-001W0_SL.txt

Ala Met Asn Trp Val Arg Gln Ala Pro 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 Asn Ser
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> 105

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 105

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 Glu Lys Pro Gly Gln Ala Pro Arg Gly
35 40 45

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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 Gly Lys Ala Ala Leu Thr Ile Thr Gly Ala
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr 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> 106

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 106

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 Asn Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro 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 Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

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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> 107

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 107

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 Gly 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 Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Glu Tyr Tyr 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> 108

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 108

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

Ala Met Asn Trp Val Arg Gln Ala Pro 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 Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp 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> 109

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 109

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 Gly Ser Ser Thr Gly Ala Val Thr Thr Ser
20 25 30

Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg Gly
35 40 45

Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe
50 55 60

Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly Ala
65 70 75 80

Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn
85 90 95

His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 110

<211> 101

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 110

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

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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
100

<210> 111

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 111

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

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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> 112

<211> 122

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 112

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15

Ser Met Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Gly Tyr
20 25 30

Thr Met Asn Trp Val Lys Gln Ser His Gly Lys Asn Leu Glu Trp Met
35 40 45

Gly Leu Ile Asn Pro Tyr Lys Gly Val Ser Thr Tyr Asn Gln Lys Phe
50 55 60

Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Leu Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Gly Tyr Tyr Gly Asp Ser Asp Trp Tyr Phe Asp Val Trp
 100 105 110

Gly Gln Gly Thr Thr Leu Thr Val Phe Ser
 115 120

<210> 113
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 113
 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 Arg Asn Tyr
 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile
 35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Lys 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 Trp
 85 90 95

Thr Phe Ala Gly Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> 114

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 114

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> 115

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 115

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> 116

<211> 254

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 116

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

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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 Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Asp Lys Ala Ala Leu Thr Leu Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Glu Tyr Phe Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 117

<211> 254

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 117

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

Ala Met Asn Trp Val Arg Gln Ala Pro 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 Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

NOV-001W0_SL.txt

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 118

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 118

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp 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> 119

<211> 254

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 119

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

NOV-001W0_SL.txt

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Gly Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

NOV-001W0_SL.txt

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 120

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 120

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

Ala Met Asn Trp Val Arg Gln Ala Pro 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 Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu 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> 121
 <211> 254
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic polypeptide

<400> 121
 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
 Ala Met Asn Trp Val Arg Gln Ala Pro 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 Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
 65 70 75 80
 Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
 85 90 95
 Tyr Cys Val Arg His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe
 100 105 110
 Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
 115 120 125
 Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
 130 135 140

NOV-001W0_SL.txt

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 122

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 122

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

Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

NOV-001W0_SL.txt

Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Pro 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> 123

<211> 254

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 123

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

Ala Met Asn Trp Val Arg Gln Ala Pro 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

NOV-001WO_SL.txt

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Pro Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 124

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 124

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

Ala Met Asn Trp Val Arg Gln Ala Pro 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 Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 125

<211> 254

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 125

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

Ala Met Asn Trp Val Arg Gln Ala Pro 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 Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

NOV-001W0_SL.txt

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 126

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 126

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

Ala Met Ser Trp Val Arg Gln Ala Pro 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 Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

NOV-001WO_SL.txt

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

Tyr Cys Val Arg His Gly Asn Phe Gly Asp 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> 127

<211> 254

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 127

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

Ala Met Ser Trp Val Arg Gln Ala Pro 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 Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr
85 90 95

NOV-001W0_SL.txt

Tyr Cys Val Arg His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe
100 105 110

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Lys Pro
115 120 125

Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly Ser Gly Lys Pro Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Lys Ser Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Gly Lys Ala Ala Leu Thr Ile Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn His Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
245 250

<210> 128

<211> 257

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

NOV-001WO_SL.txt

<400> 128

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 Asn Thr Tyr
20 25 30

Ala Met Asn Trp Val Arg Gln Ala Pro 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 Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Asn Thr
65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala 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 Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ala Val Val
130 135 140

Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu
145 150 155 160

Thr Cys Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn
165 170 175

Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly
180 185 190

NOV-001WO_SL.txt

Thr Asn Lys Arg Ala Pro Gly Val Pro Ala Arg Phe Ser Gly Ser Leu
 195 200 205

Leu Gly Gly Lys Ala Ala Leu Thr Leu Ser Gly Ala Gln Pro Glu Asp
 210 215 220

Glu Ala Glu Tyr Tyr Cys Ala Leu Trp Tyr Ser Asn Leu Trp Val Phe
 225 230 235 240

Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ser His His His His His
 245 250 255

His

<210> 129
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<220>
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<400> 129
 Arg Tyr Thr Met His
 1 5

<210> 130
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 <213> Artificial Sequence

<220>
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<400> 130
 Ser Ala Ser Ser Ser Val Ser Tyr Met Asn
 1 5 10

<210> 131
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Thr Tyr Ala Met Asn
1 5

<210> 132
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peptide

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Arg Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn
1 5 10

<210> 133
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Ser Tyr Thr Met His
1 5

<210> 134
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<400> 134

Arg Ala Ser Ser Ser Val Ser Tyr Met His
1 5 10

<210> 135

<211> 10

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 135

Arg Ala Ser Ser Ser Val Ser Tyr Met Asn
1 5 10

<210> 136

<211> 5

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<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 136

Gly Tyr Gly Met His
1 5

<210> 137

<211> 11

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 137

Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala
 1 5 10

<210> 138

<211> 5

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<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic
 peptide

<400> 138

Ser Tyr Ala Met Asn
 1 5

<210> 139

<211> 14

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<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic
 peptide

<400> 139

Gly Ser Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr Pro Asn
 1 5 10

<210> 140

<211> 5

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<223> Description of Artificial Sequence: Synthetic
 peptide

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Lys Tyr Ala Met Asn
 1 5

<210> 141

<211> 14

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Gly Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn
1 5 10

<210> 142

<211> 5

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<400> 142

Gly Tyr Thr Met Asn
1 5

<210> 143

<211> 11

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<400> 143

Arg Ala Ser Gln Asp Ile Arg Asn Tyr Leu Asn
1 5 10

<210> 144

<211> 5

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 144

Thr Tyr Ala Met Ser

1 5

<210> 145

<211> 5

<212> PRT

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 145

Thr Tyr Ala Met His

1 5

<210> 146

<211> 14

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 146

Gly Ser Ser Thr Gly Ala Val Thr Ser Ser Asn Tyr Ala Asn

1 5 10

<210> 147

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 147

Gly Ser Ser Thr Gly Ala Val Thr Ser Gly His Tyr Ala Asn

1 5 10

<210> 148

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 148

Lys Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn

1

5

10

<210> 149

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 149

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Phe Lys

1

5

10

15

Asp

<210> 150

<211> 7

<212> PRT

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 150

Asp Thr Ser Lys Leu Ala Ser

1

5

<210> 151

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 151

Arg	Ile	Arg	Ser	Lys	Tyr	Asn	Asn	Tyr	Ala	Thr	Tyr	Tyr	Ala	Asp	Ser
1				5				10						15	

Val Lys Asp

<210> 152

<211> 7

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 152

Gly	Thr	Asn	Lys	Arg	Ala	Pro
1			5			

<210> 153

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 153

Tyr	Ile	Asn	Pro	Ser	Ser	Gly	Tyr	Thr	Lys	Tyr	Asn	Gln	Lys	Phe	Lys
1				5				10						15	

Asp

<210> 154

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 154

Ala Thr Ser Asn Leu Ala Ser

1 5

<210> 155

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 155

Asp Thr Ser Lys Val Ala Ser

1 5

<210> 156

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 156

Tyr Ile Asn Pro Ser Arg Gly Tyr Thr Asn Tyr Asn Gln Lys Val Lys

1 5 10 15

Asp

<210> 157

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 157

Val	Ile	Trp	Tyr	Asp	Gly	Ser	Lys	Lys	Tyr	Tyr	Val	Asp	Ser	Val	Lys
1				5				10				15			

Gly

<210> 158

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 158

Asp	Ala	Ser	Asn	Arg	Ala	Thr
1			5			

<210> 159

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 159

Arg	Ile	Arg	Ser	Lys	Tyr	Asn	Asn	Tyr	Ala	Thr	Tyr	Tyr	Ala	Asp
1				5				10					15	

<210> 160

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 160

Arg	Ile	Arg	Ser	Lys	Tyr	Asn	Asn	Tyr	Ala	Thr	Tyr	Tyr	Ala	Asp	Ser
1				5				10						15	

Val Lys Gly

<210> 161

<211> 7

<212> PRT

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 161

Gly	Thr	Lys	Phe	Leu	Ala	Pro
1				5		

<210> 162

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 162

Leu	Ile	Asn	Pro	Tyr	Lys	Gly	Val	Ser	Thr	Tyr	Asn	Gln	Lys	Phe	Lys
1				5				10						15	

Asp

<210> 163

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 163

Tyr Thr Ser Arg Leu His
1 5

<210> 164

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 164

Arg Ile Arg Ser Lys Ala Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser
1 5 10 15

Val Lys Gly

<210> 165

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 165

Arg Ile Arg Ser Lys Ala Asn Asn Tyr Tyr Ala Thr Tyr Tyr Ala Asp
1 5 10 15

Ser Val Lys Gly
20

<210> 166

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 166

Arg	Ile	Arg	Ser	Lys	Ala	Asn	Ser	Tyr	Ala	Thr	Tyr	Tyr	Ala	Asp	Ser
1				5				10					15		

Val Lys Gly

<210> 167

<211> 19

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 167

Arg	Ile	Arg	Ser	Lys	Tyr	Asn	Asn	Tyr	Ala	Thr	Ala	Tyr	Ala	Asp	Ser
1				5				10					15		

Val Lys Gly

<210> 168

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 168

Asp	Thr	Asn	Lys	Arg	Ala	Pro
1			5			

<210> 169
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 169
Gly Thr Asn Asn Arg Ala Pro
1 5

<210> 170
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 170
Gly Thr Asn Lys Arg Ala Ser
1 5

<210> 171
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 171
Gly Thr Ser Asn Lys His Ser
1 5

<210> 172
<211> 18
<212> PRT
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<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 172

Arg	Ile	Arg	Ser	Asn	Gly	Gly	Tyr	Ser	Thr	Tyr	Tyr	Ala	Asp	Ser	Val
1				5					10					15	

Lys Gly

<210> 173

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 173

Tyr	Tyr	Asp	Asp	His	Tyr	Cys	Leu	Asp	Tyr
1				5					10

<210> 174

<211> 9

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Synthetic peptide

<400> 174

Gln	Gln	Trp	Ser	Ser	Asn	Pro	Phe	Thr
1				5				

<210> 175

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 175

His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Phe Ala Tyr
1 5 10

<210> 176

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 176

Ala Leu Trp Tyr Ser Asn Leu Trp Val
1 5

<210> 177

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 177

Trp Gln Asp Tyr Asp Val Tyr Phe Asp Tyr
1 5 10

<210> 178

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 178

Gln Gln Trp Ser Ser Asn Pro Pro Thr
1 5

<210> 179
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 179
Gln Gln Trp Ser Ser Asn Pro Leu Thr
1 5

<210> 180
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 180
Gln Met Gly Tyr Trp His Phe Asp Leu
1 5

<210> 181
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 181
Gln Gln Arg Ser Asn Trp Pro Pro Leu Thr
1 5 10

<210> 182
<211> 16
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 182

Val	Arg	His	Gly	Asn	Phe	Gly	Asn	Ser	Tyr	Val	Ser	Trp	Phe	Ala	Tyr
1				5				10					15		

<210> 183

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 183

His	Gly	Asn	Phe	Gly	Asn	Ser	Tyr	Val	Ser	Trp	Trp	Ala	Tyr
1				5				10					

<210> 184

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 184

Val	Leu	Trp	Tyr	Ser	Asn	Arg	Trp	Val
1				5				

<210> 185

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 185

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His Gly Asn Phe Gly Asn Ser Tyr Ile Ser Tyr Trp Ala Tyr
1 5 10

<210> 186

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 186

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Ala Tyr
1 5 10

<210> 187

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 187

Ala Leu Trp Tyr Ser Asn His Trp Val
1 5

<210> 188

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 188

Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr
1 5 10

<210> 189

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 189

Ser Gly Tyr Tyr Gly Asp Ser Asp Trp Tyr Phe Asp Val
1 5 10

<210> 190

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 190

Gln Gln Gly Asn Thr Leu Pro Trp Thr
1 5

<210> 191

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 191

His Gly Asn Phe Gly Asp Glu Tyr Val Ser Trp Phe Ala Tyr
1 5 10

<210> 192

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 192

His Gly Asn Phe Gly Asp Pro Tyr Val Ser Trp Phe Ala Tyr
1 5 10

<210> 193

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 193

His Gly Asn Phe Gly Asp Ser Tyr Val Ser Trp Phe Asp Tyr
1 5 10

<210> 194

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 194

His Gly Asn Phe Gly Gln Ser Tyr Val Ser Trp Phe Ala Tyr
1 5 10

<210> 195

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 195

His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Phe Asp Tyr
1 5 10

<210> 196

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 196

Leu Leu Trp Tyr Ser Asn Leu Trp Val

1 5

<210> 197

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 197

Gly Tyr Thr Phe Thr Arg Tyr

1 5

<210> 198

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 198

Ser Ser Ser Val Ser Tyr

1 5

<210> 199

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 199

Gly Phe Thr Phe Asn Thr Tyr
1 5

<210> 200

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 200

Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr
1 5 10

<210> 201

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 201

Gly Tyr Thr Phe Thr Ser Tyr
1 5

<210> 202

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 202

Gly Phe Lys Phe Ser Gly Tyr
1 5

<210> 203
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 203
Ser Gln Ser Val Ser Ser Tyr
1 5

<210> 204
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 204
Gly Phe Thr Phe Ser Thr Tyr
1 5

<210> 205
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 205
Gly Phe Thr Phe Asn Ser Tyr
1 5

<210> 206
<211> 10
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 206

Ser Thr Gly Ala Val Thr Ser Gly Asn Tyr
1 5 10

<210> 207

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 207

Gly Phe Thr Phe Asn Lys Tyr
1 5

<210> 208

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 208

Gly Tyr Ser Phe Thr Gly Tyr
1 5

<210> 209

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 209

Ser Gln Asp Ile Arg Asn Tyr
1 5

<210> 210
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 210
Asn Pro Ser Arg Gly Tyr
1 5

<210> 211
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<400> 211
Asp Thr Ser
1

<210> 212
<211> 8
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<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 212
Arg Ser Lys Tyr Asn Asn Tyr Ala
1 5

<210> 213
<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 213

Gly Thr Asn

1

<210> 214

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 214

Asn Pro Ser Ser Gly Tyr

1

5

<210> 215

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 215

Ala Thr Ser

1

<210> 216

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 216

Trp Tyr Asp Gly Ser Lys

1 5

<210> 217

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 217

Asp Ala Ser

1

<210> 218

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 218

Arg Ser Lys Tyr Asn Asn Tyr Ala Thr

1 5

<210> 219

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 219

Gly Thr Lys

1

<210> 220

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 220

Asn Pro Tyr Lys Gly Val

1 5

<210> 221

<211> 3

<212> PRT

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<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 221

Tyr Thr Ser

1

<210> 222

<211> 6

<212> PRT

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<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 222

Trp Ser Ser Asn Pro Phe

1 5

<210> 223

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 223

Trp Tyr Ser Asn Leu Trp
1 5

<210> 224

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 224

Trp Ser Ser Asn Pro Pro
1 5

<210> 225

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 225

Trp Ser Ser Asn Pro Leu
1 5

<210> 226

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 226

Arg Ser Asn Trp Pro Pro Leu
1 5

<210> 227
<211> 13
<212> PRT
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<223> Description of Artificial Sequence: Synthetic
peptide

<400> 227
His Gly Asn Phe Gly Asn Ser Tyr Val Ser Trp Phe Ala
1 5 10

<210> 228
<211> 6
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peptide

<400> 228
Trp Tyr Ser Asn Arg Trp
1 5

<210> 229
<211> 6
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peptide

<400> 229
Trp Tyr Ser Asn His Trp
1 5

<210> 230
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<223> Description of Artificial Sequence: Synthetic peptide

<400> 230

Gly Asn Thr Leu Pro Trp
1 5

<210> 231

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 231

Gly Tyr Thr Phe Thr Arg Tyr Thr Met His
1 5 10

<210> 232

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 232

Gly Phe Thr Phe Asn Thr Tyr Ala Met Asn
1 5 10

<210> 233

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 233

Gly Tyr Thr Phe Thr Ser Tyr Thr Met His
 1 5 10

<210> 234

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 peptide

<400> 234

Gly Phe Lys Phe Ser Gly Tyr Gly Met His
 1 5 10

<210> 235

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 peptide

<400> 235

Gly Phe Thr Phe Ser Thr Tyr Ala Met Asn
 1 5 10

<210> 236

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 peptide

<400> 236

Gly Phe Thr Phe Asn Ser Tyr Ala Met Asn
 1 5 10

<210> 237

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 237

Gly	Phe	Thr	Phe	Asn	Lys	Tyr	Ala	Met	Asn
1				5					10

<210> 238

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 238

Gly	Tyr	Ser	Phe	Thr	Gly	Tyr	Thr	Met	Asn
1				5					10

<210> 239

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 239

Arg	Ile	Arg	Ser	Lys	Tyr	Asn	Asn	Tyr	Ala	Thr	Tyr	Tyr	Ala	Asp	Ser
1				5					10					15	

Val Lys

<210> 240

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 240

Tyr Thr Ser Arg Leu His Ser
1 5

<210> 241

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 241

Lys Ala Ser Gly Tyr Lys Phe Thr Ser Tyr Val Met His
1 5 10

<210> 242

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 242

Tyr Ile Asn Pro Tyr Asn Asp Val Thr Lys Tyr Asn Glu Lys Phe Lys
1 5 10 15

<210> 243

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 243

Gly Ser Tyr Tyr Asp Tyr Asp Gly Phe Val Tyr
 1 5 10

<210> 244

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 peptide

<400> 244

Ser Ala Thr Ser Ser Val Ser Tyr Met His
 1 5 10

<210> 245

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 245

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

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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> 246

<211> 106

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 246

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> 247
 <211> 5
 <212> PRT
 <213> Rattus sp.

<400> 247
 Glu Tyr Tyr Met Tyr
 1 5

<210> 248
 <211> 17
 <212> PRT
 <213> Rattus sp.

<400> 248
 Arg Ile Asp Pro Glu Asp Gly Ser Ile Asp Tyr Val Glu Lys Phe Lys
 1 5 10 15

Lys

<210> 249
 <211> 9
 <212> PRT
 <213> Rattus sp.

<400> 249
 Gly Lys Phe Asn Tyr Arg Phe Ala Tyr
 1 5

<210> 250
 <211> 16
 <212> PRT
 <213> Rattus sp.

<400> 250
 Arg Ser Ser Gln Ser Leu Leu His Ser Ser Gly Asn Thr Tyr Leu Asn
 1 5 10 15

<210> 251
 <211> 7

<212> PRT

<213> Rattus sp.

<400> 251

Leu Val Ser Lys Leu Glu Ser
1 5

<210> 252

<211> 8

<212> PRT

<213> Rattus sp.

<400> 252

Gln Phe Thr His Tyr Pro Tyr Thr
1 5

<210> 253

<211> 118

<212> PRT

<213> Rattus sp.

<400> 253

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Gln Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Glu Tyr
20 25 30

Tyr Met Tyr Trp Val Lys Gln Arg Pro Lys 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 Ala Thr Leu Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

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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> 254
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 254
 Asp Val Val Leu Thr Gln Thr Pro Pro Thr Leu Leu Ala Thr Ile Gly
 1 5 10 15

Gln Ser Val 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 Thr 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

Asn 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 Leu Gly Val Tyr Tyr Cys Met Gln Phe
 85 90 95

Thr His Tyr Pro Tyr Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
 100 105 110

<210> 255
 <211> 118

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 255

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 Glu Tyr
20 25 30

Tyr Met Tyr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Leu Met
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> 256

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

NOV-001W0_SL.txt

<400> 256

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> 257

<211> 118

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 257

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Gln Arg Pro Gly Ala
1 5 10 15

Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Glu Tyr
20 25 30

NOV-001WO_SL.txt

Tyr Met Tyr Trp Val Lys Gln Arg Pro Lys 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 Ala Thr Leu Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Thr Tyr Phe 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> 258

<211> 250

<212> PRT

<213> Homo sapiens

<400> 258

Met Val Ala Gly Ser Asp Ala Gly Arg Ala Leu Gly Val Leu Ser Val
1 5 10 15

Val Cys Leu Leu His Cys Phe Gly Phe Ile Ser Cys Phe Ser Gln Gln
20 25 30

Ile Tyr Gly Val Val Tyr Gly Asn Val Thr Phe His Val Pro Ser Asn
35 40 45

Val Pro Leu Lys Glu Val Leu Trp Lys Lys Gln Lys Asp Lys Val Ala
50 55 60

Glu Leu Glu Asn Ser Glu Phe Arg Ala Phe Ser Ser Phe Lys Asn Arg
65 70 75 80

NOV-001WO_SL.txt

Val Tyr Leu Asp Thr Val Ser Gly Ser Leu Thr Ile Tyr Asn Leu Thr
85 90 95

Ser Ser Asp Glu Asp Glu Tyr Glu Met Glu Ser Pro Asn Ile Thr Asp
100 105 110

Thr Met Lys Phe Phe Leu Tyr Val Leu Glu Ser Leu Pro Ser Pro Thr
115 120 125

Leu Thr Cys Ala Leu Thr Asn Gly Ser Ile Glu Val Gln Cys Met Ile
130 135 140

Pro Glu His Tyr Asn Ser His Arg Gly Leu Ile Met Tyr Ser Trp Asp
145 150 155 160

Cys Pro Met Glu Gln Cys Lys Arg Asn Ser Thr Ser Ile Tyr Phe Lys
165 170 175

Met Glu Asn Asp Leu Pro Gln Lys Ile Gln Cys Thr Leu Ser Asn Pro
180 185 190

Leu Phe Asn Thr Thr Ser Ser Ile Ile Leu Thr Thr Cys Ile Pro Ser
195 200 205

Ser Gly His Ser Arg His Arg Tyr Ala Leu Ile Pro Ile Pro Leu Ala
210 215 220

Val Ile Thr Thr Cys Ile Val Leu Tyr Met Asn Gly Ile Leu Lys Cys
225 230 235 240

Asp Arg Lys Pro Asp Arg Thr Asn Ser Asn
245 250

<210> 259

<211> 187

NOV-001WO_SL.txt

<212> PRT

<213> Homo sapiens

<400> 259

Phe Ser Gln Gln Ile Tyr Gly Val Val Tyr Gly Asn Val Thr Phe His
1 5 10 15

Val Pro Ser Asn Val Pro Leu Lys Glu Val Leu Trp Lys Lys Gln Lys
20 25 30

Asp Lys Val Ala Glu Leu Glu Asn Ser Glu Phe Arg Ala Phe Ser Ser
35 40 45

Phe Lys Asn Arg Val Tyr Leu Asp Thr Val Ser Gly Ser Leu Thr Ile
50 55 60

Tyr Asn Leu Thr Ser Ser Asp Glu Asp Glu Tyr Glu Met Glu Ser Pro
65 70 75 80

Asn Ile Thr Asp Thr Met Lys Phe Phe Leu Tyr Val Leu Glu Ser Leu
85 90 95

Pro Ser Pro Thr Leu Thr Cys Ala Leu Thr Asn Gly Ser Ile Glu Val
100 105 110

Gln Cys Met Ile Pro Glu His Tyr Asn Ser His Arg Gly Leu Ile Met
115 120 125

Tyr Ser Trp Asp Cys Pro Met Glu Gln Cys Lys Arg Asn Ser Thr Ser
130 135 140

Ile Tyr Phe Lys Met Glu Asn Asp Leu Pro Gln Lys Ile Gln Cys Thr
145 150 155 160

Leu Ser Asn Pro Leu Phe Asn Thr Thr Ser Ser Ile Ile Leu Thr Thr
165 170 175

Cys Ile Pro Ser Ser Gly His Ser Arg His Arg
 180 185

<210> 260
 <211> 187
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic polypeptide

<220>
 <221> MOD_RES
 <222> (1)..(1)
 <223> Phe or Ser

<220>
 <221> MOD_RES
 <222> (9)..(9)
 <223> Val or Lys

<220>
 <221> MOD_RES
 <222> (21)..(21)
 <223> Val or Gln

<220>
 <221> MOD_RES
 <222> (58)..(58)
 <223> Val or Lys

<220>
 <221> MOD_RES
 <222> (85)..(85)
 <223> Thr or Ser

<220>
 <221> MOD_RES
 <222> (93)..(93)
 <223> Leu or Gly

<400> 260
 Xaa Ser Gln Gln Ile Tyr Gly Val Xaa Tyr Gly Asn Val Thr Phe His
 1 5 10 15

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Val Pro Ser Asn Xaa Pro Leu Lys Glu Val Leu Trp Lys Lys Gln Lys
20 25 30

Asp Lys Val Ala Glu Leu Glu Asn Ser Glu Phe Arg Ala Phe Ser Ser
35 40 45

Phe Lys Asn Arg Val Tyr Leu Asp Thr Xaa Ser Gly Ser Leu Thr Ile
50 55 60

Tyr Asn Leu Thr Ser Ser Asp Glu Asp Glu Tyr Glu Met Glu Ser Pro
65 70 75 80

Asn Ile Thr Asp Xaa Met Lys Phe Phe Leu Tyr Val Xaa Glu Ser Leu
85 90 95

Pro Ser Pro Thr Leu Thr Cys Ala Leu Thr Asn Gly Ser Ile Glu Val
100 105 110

Gln Cys Met Ile Pro Glu His Tyr Asn Ser His Arg Gly Leu Ile Met
115 120 125

Tyr Ser Trp Asp Cys Pro Met Glu Gln Cys Lys Arg Asn Ser Thr Ser
130 135 140

Ile Tyr Phe Lys Met Glu Asn Asp Leu Pro Gln Lys Ile Gln Cys Thr
145 150 155 160

Leu Ser Asn Pro Leu Phe Asn Thr Thr Ser Ser Ile Ile Leu Thr Thr
165 170 175

Cys Ile Pro Ser Ser Gly His Ser Arg His Arg
180 185

<210> 261

<211> 44

<212> PRT

<213> Homo sapiens

<400> 261

Ser	Gln	Gln	Ile	Tyr	Gly	Val	Val	Tyr	Gly	Asn	Val	Thr	Phe	His	Val
1				5					10					15	

Pro	Ser	Asn	Val	Pro	Leu	Lys	Glu	Val	Leu	Trp	Lys	Lys	Gln	Lys	Asp
			20					25					30		

Lys	Val	Ala	Glu	Leu	Glu	Asn	Ser	Glu	Phe	Arg	Ala
		35				40					

<210> 262

<211> 44

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<220>

<221> MOD_RES

<222> (8)..(8)

<223> Val or Lys

<220>

<221> MOD_RES

<222> (20)..(20)

<223> Val or Gln

<400> 262

Ser	Gln	Gln	Ile	Tyr	Gly	Val	Xaa	Tyr	Gly	Asn	Val	Thr	Phe	His	Val
1				5					10					15	

Pro	Ser	Asn	Xaa	Pro	Leu	Lys	Glu	Val	Leu	Trp	Lys	Lys	Gln	Lys	Asp
			20					25					30		

Lys	Val	Ala	Glu	Leu	Glu	Asn	Ser	Glu	Phe	Arg	Ala
		35				40					

<210> 263

<211> 115

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 263

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 Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 264

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 264

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln 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 Tyr
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 265

<211> 239

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 265

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 Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

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Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
115 120 125

Gly Gly Gly Ser Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser
130 135 140

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
145 150 155 160

Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
165 170 175

Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser
180 185 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
195 200 205

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr
210 215 220

Ser Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
225 230 235

<210> 266

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 266

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asn Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Gly Trp Val
35 40 45

Ser Gly Ile Ser Arg Ser Gly Glu Asn Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser Pro Ala His Tyr Tyr Gly Gly Met Asp Val Trp Gly Gln
100 105 110

Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 267

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 267

Asp Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Ser Ser Ser
20 25 30

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Arg Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Ser Ala Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro
85 90 95

Ser Trp Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 268

<211> 246

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 268

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

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Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
195 200 205

Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Ser Ala Val Tyr
210 215 220

Tyr Cys Gln Gln Tyr His Ser Ser Pro Ser Trp Thr Phe Gly Gln Gly
225 230 235 240

Thr Lys Leu Glu Ile Lys
245

<210> 269

<211> 115

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 269

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly 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 Leu Tyr Tyr Cys
85 90 95

Ser Val His Ser Phe Leu Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
 100 105 110

Val Ser Ser
 115

<210> 270
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 270
 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 His Ser
 20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala 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 Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
 85 90 95

Leu Gln Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> 271

<211> 244

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 271

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
 20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly 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 Leu Tyr Tyr Cys
 85 90 95

Ser Val His Ser Phe Leu Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr
 100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
 115 120 125

Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Pro
 130 135 140

Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
 145 150 155 160

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Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys
165 170 175

Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala
180 185 190

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
195 200 205

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr
210 215 220

Cys Met Gln Ala Leu Gln Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys
225 230 235 240

Val Glu Ile Lys

<210> 272

<211> 115

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 272

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

NOV-001W0_SL.txt

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 273

<211> 111

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 273

Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser Val Thr Pro Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser Leu Leu Arg Asn
20 25 30

Asp Gly Lys Thr Pro Leu Tyr Trp Tyr Leu Gln Lys Ala Gly Gln Pro
35 40 45

Pro Gln Leu Leu Ile Tyr Glu 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

NOV-001WO_SL.txt

Ser Arg Val Glu Ala Glu Asp Val Gly Ala Tyr Tyr Cys Met Gln Asn
85 90 95

Ile Gln Phe Pro Ser Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 274

<211> 243

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 274

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

NOV-001WO_SL.txt

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
115 120 125

Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr Pro Leu Ser Leu Ser
130 135 140

Val Thr Pro Gly Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser Gln Ser
145 150 155 160

Leu Leu Arg Asn Asp Gly Lys Thr Pro Leu Tyr Trp Tyr Leu Gln Lys
165 170 175

Ala Gly Gln Pro Pro Gln Leu Leu Ile Tyr Glu Val Ser Asn Arg Phe
180 185 190

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
195 200 205

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Ala Tyr Tyr
210 215 220

Cys Met Gln Asn Ile Gln Phe Pro Ser Phe Gly Gly Gly Thr Lys Leu
225 230 235 240

Glu Ile Lys

<210> 275

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 275

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Arg Lys Thr Gly Ala
1 5 10 15

NOV-001WO_SL.txt

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Asp Asn Phe
20 25 30

Gly Ile Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Lys Asn Asn Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala Tyr
65 70 75 80

Met Glu Val Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Pro Tyr Tyr Tyr Gln Ser Tyr Met Asp Val Trp Gly Gln
100 105 110

Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 276

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 276

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 His Ser
20 25 30

NOV-001WO_SL.txt

Asn Gly Tyr Asn Tyr Leu Asn Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Lys Arg Ala Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu His Ile
65 70 75 80

Thr Arg Val Gly Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Leu Gln Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 277

<211> 249

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 277

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Arg Lys Thr Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Asp Asn Phe
20 25 30

Gly Ile Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Lys Asn Asn Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Asn Thr Ala Tyr
65 70 75 80

NOV-001WO_SL.txt

Met Glu Val Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Pro Tyr Tyr Tyr Gln Ser Tyr Met Asp Val Trp Gly Gln
100 105 110

Gly Thr Met Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr
130 135 140

Pro Leu Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys
145 150 155 160

Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asn
165 170 175

Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu
180 185 190

Gly Ser Lys Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly
195 200 205

Ser Gly Thr Asp Phe Thr Leu His Ile Thr Arg Val Gly Ala Glu Asp
210 215 220

Val Gly Val Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Tyr Thr Phe
225 230 235 240

Gly Gln Gly Thr Lys Leu Glu Ile Lys
245

<210> 278

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 278

Gln Val Gln Leu Gln 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 Asp
20 25 30

Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Ser Gly Ser Gly Gly Thr Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Leu Asp Ser Ser Gly Tyr Tyr Tyr Ala Arg Gly Pro Arg Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 279

<211> 106

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

NOV-001WO_SL.txt

<400> 279

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln 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 Gly Ala Ser Thr Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr His Phe Thr Leu Thr Ile Asn Ser Leu Gln Ser
65 70 75 80

Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr Lys Arg Ala Ser
85 90 95

Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 280

<211> 246

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 280

Gln Val Gln Leu Gln 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 Asp
20 25 30

NOV-001WO_SL.txt

Ala Met Thr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Val Ile Ser Gly Ser Gly Gly Thr Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Leu Asp Ser Ser Gly Tyr Tyr Tyr Ala Arg Gly Pro Arg Tyr
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Arg Ala Ser Gly Gly Gly Gly Ser Asp Ile Gln Leu
130 135 140

Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr
145 150 155 160

Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Gly Ala Ser
180 185 190

Thr Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr His Phe Thr Leu Thr Ile Asn Ser Leu Gln Ser Glu Asp Ser Ala
210 215 220

NOV-001W0_SL.txt

Thr Tyr Tyr Cys Gln Gln Ser Tyr Lys Arg Ala Ser Phe Gly Gln Gly
225 230 235 240

Thr Lys Val Glu Ile Lys
245

<210> 281

<211> 118

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 281

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 Ser Asn Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile 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 Gly Pro Tyr Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr
100 105 110

Met Val Thr Val Ser Ser
115

<210> 282
 <211> 112
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic polypeptide

<400> 282
 Glu Ile Val Met Thr Gln Ser 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 Tyr Ser
 20 25 30

Asn Gly Tyr Asn Tyr Val Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
 35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
 50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Lys Leu Gln Ile
 65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Ile Tyr Tyr Cys Met Gln Gly
 85 90 95

Arg Gln Phe Pro Tyr Ser Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105 110

<210> 283
 <211> 247
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic polypeptide

NOV-001W0_SL.txt

<400> 283

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 Ser Asn Tyr
20 25 30

Gly Ile Thr Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg Asn Thr Ser Ile 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 Gly Pro Tyr Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr
100 105 110

Met Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg
115 120 125

Ala Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Leu
130 135 140

Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser
145 150 155 160

Ser Gln Ser Leu Leu Tyr Ser Asn Gly Tyr Asn Tyr Val Asp Trp Tyr
165 170 175

Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser
180 185 190

NOV-001WO_SL.txt

Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Phe Lys Leu Gln Ile Ser Arg Val Glu Ala Glu Asp Val Gly
210 215 220

Ile Tyr Tyr Cys Met Gln Gly Arg Gln Phe Pro Tyr Ser Phe Gly Gln
225 230 235 240

Gly Thr Lys Val Glu Ile Lys
245

<210> 284

<211> 115

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 284

Glu Val Gln Leu Leu Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

NOV-001W0_SL.txt

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 285

<211> 106

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 285

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15

Glu Ser Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
35 40 45

Tyr Gly Ala Ser Thr Arg Ala Ser Gly Ile Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala
65 70 75 80

Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Leu Thr
85 90 95

Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105

<210> 286
 <211> 238
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic polypeptide

<400> 286
 Glu Val Gln Leu Leu Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
 20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
 50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
 65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
 85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
 100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
 115 120 125

Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
 130 135 140

NOV-001W0_SL.txt

Val Ser Pro Gly Glu Ser Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145 150 155 160

Val Ser Ser Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
165 170 175

Arg Leu Leu Ile Tyr Gly Ala Ser Thr Arg Ala Ser Gly Ile Pro Asp
180 185 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
195 200 205

Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln Tyr Gly
210 215 220

Ser Ser Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
225 230 235

<210> 287

<211> 115

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 287

Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

NOV-001WO_SL.txt

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 288
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 288
Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Lys
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Met
35 40 45

Tyr Gly Ala Ser Ile Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
65 70 75 80

NOV-001W0_SL.txt

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Ser Trp
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 289

<211> 239

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 289

Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
115 120 125

NOV-001WO_SL.txt

Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser
130 135 140

Val Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145 150 155 160

Val Ser Ser Lys Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro
165 170 175

Arg Leu Leu Met Tyr Gly Ala Ser Ile Arg Ala Thr Gly Ile Pro Asp
180 185 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser
195 200 205

Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly
210 215 220

Ser Ser Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
225 230 235

<210> 290

<211> 115

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 290

Glu Val Gln Leu Val Glu Thr Gly Gly Gly Val Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

NOV-001W0_SL.txt

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
 50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
 65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
 85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
 100 105 110

Val Ser Ser
 115

<210> 291

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 291

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Gly Ser Thr
 20 25 30

Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
 35 40 45

Ile Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
 50 55 60

Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro
85 90 95

Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 292

<211> 241

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 292

Glu Val Gln Leu Val Glu Thr Gly Gly Gly Val Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

NOV-001W0_SL.txt

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
115 120 125

Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser
130 135 140

Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145 150 155 160

Val Gly Ser Thr Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
165 170 175

Pro Arg Leu Leu Ile Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro
180 185 190

Asp Arg Phe Ser Gly Gly Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
195 200 205

Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr
210 215 220

Gly Ser Ser Pro Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
225 230 235 240

Lys

<210> 293

<211> 117

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

NOV-001WO_SL.txt

<400> 293

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 Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr 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 Glu Ser Gly Asp Gly Met Asp Val Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser
115

<210> 294

<211> 105

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 294

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

NOV-001WO_SL.txt

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 Thr Leu Ala Phe
85 90 95

Gly Gln Gly Thr Lys Val Asp Ile Lys
100 105

<210> 295

<211> 239

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 295

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 Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

NOV-001W0_SL.txt

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 Glu Ser Gly Asp Gly Met Asp Val Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala
115 120 125

Ser Gly Gly Gly Gly Ser Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
130 135 140

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser
145 150 155 160

Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys
165 170 175

Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val
180 185 190

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
210 215 220

Ser Tyr Thr Leu Ala Phe Gly Gln Gly Thr Lys Val Asp Ile Lys
225 230 235

<210> 296

<211> 117

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 296

Gln Val Gln Leu Val Gln 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 Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Asn Thr 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 Ser Thr Met Val Arg Glu Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 297

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

NOV-001W0_SL.txt

<400> 297

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 Ser Ser Glu Ser Leu Val His Asn
20 25 30

Ser Gly Lys Thr Tyr Leu Asn Trp Phe His Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Arg Leu Ile Tyr Glu Val Ser Asn Arg Asp Ser Gly Val Pro
50 55 60

Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
85 90 95

Thr His Trp Pro Gly Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 298

<211> 246

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 298

Gln Val Gln Leu Val Gln 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

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Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Asn Thr 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 Ser Thr Met Val Arg Glu Asp Tyr Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala
115 120 125

Ser Gly Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Leu Ser
130 135 140

Leu Pro Val Thr Leu Gly Gln Pro Ala Ser Ile Ser Cys Lys Ser Ser
145 150 155 160

Glu Ser Leu Val His Asn Ser Gly Lys Thr Tyr Leu Asn Trp Phe His
165 170 175

Gln Arg Pro Gly Gln Ser Pro Arg Arg Leu Ile Tyr Glu Val Ser Asn
180 185 190

Arg Asp Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr
195 200 205

Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val
210 215 220

NOV-001W0_SL.txt

Tyr Tyr Cys Met Gln Gly Thr His Trp Pro Gly Thr Phe Gly Gln Gly
225 230 235 240

Thr Lys Leu Glu Ile Lys
245

<210> 299

<211> 115

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 299

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 Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser
115

<210> 300
 <211> 107
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic polypeptide

<400> 300
 Asp Ile Arg Leu Thr Gln Ser Pro Ser Pro Leu Ser Ala Ser Val Gly
 1 5 10 15

Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Glu Asp Ile Asn Lys Phe
 20 25 30

Leu Asn Trp Tyr His Gln Thr Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

Tyr Asp Ala Ser Thr Leu Gln Thr Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Gln Pro
 65 70 75 80

Glu Asp Ile Gly Thr Tyr Tyr Cys Gln Gln Tyr Glu Ser Leu Pro Leu
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 301
 <211> 239
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic polypeptide

NOV-001WO_SL.txt

<400> 301

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 Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
115 120 125

Gly Gly Gly Ser Asp Ile Arg Leu Thr Gln Ser Pro Ser Pro Leu Ser
130 135 140

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Gln Ala Ser Glu Asp
145 150 155 160

Ile Asn Lys Phe Leu Asn Trp Tyr His Gln Thr Pro Gly Lys Ala Pro
165 170 175

Lys Leu Leu Ile Tyr Asp Ala Ser Thr Leu Gln Thr Gly Val Pro Ser
180 185 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn
195 200 205

Ser Leu Gln Pro Glu Asp Ile Gly Thr Tyr Tyr Cys Gln Gln Tyr Glu
210 215 220

Ser Leu Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
225 230 235

<210> 302

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 302

Glu Thr Thr Leu Thr Gln Ser Pro Ala Thr Leu Ser Val Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Gly Ser Asn
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Gly Pro Arg Leu Leu Ile
35 40 45

Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asp Trp Leu Pro
85 90 95

Val Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 303

<211> 240

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 303

Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Val Ser Gly Phe Ala Leu Ser Asn His
 20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
 50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
 65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
 85 90 95

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
 100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
 115 120 125

Gly Gly Gly Ser Glu Thr Thr Leu Thr Gln Ser Pro Ala Thr Leu Ser
 130 135 140

NOV-001WO_SL.txt

Val Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145 150 155 160

Val Gly Ser Asn Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Gly Pro
165 170 175

Arg Leu Leu Ile Tyr Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Ala
180 185 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser
195 200 205

Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn
210 215 220

Asp Trp Leu Pro Val Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
225 230 235 240

<210> 304

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 304

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Ile Gly Ser Ser
20 25 30

Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

NOV-001WO_SL.txt

Met Tyr Gly Ala Ser Ser Arg Ala Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Ala Gly Ser Pro
85 90 95

Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 305

<211> 241

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 305

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 Val Ser Gly Phe Ala Leu Ser Asn His
20 25 30

Gly Met Ser Trp Val Arg Arg Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys
50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Arg Asn Thr Leu Tyr Leu
65 70 75 80

Gln Met Asn Ser Leu Arg Pro Glu Asp Thr Ala Ile Tyr Tyr Cys Ser
85 90 95

NOV-001WO_SL.txt

Ala His Gly Gly Glu Ser Asp Val Trp Gly Gln Gly Thr Thr Val Thr
100 105 110

Val Ser Ser Ala Ser Gly Gly Gly Gly Ser Gly Gly Arg Ala Ser Gly
115 120 125

Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser
130 135 140

Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145 150 155 160

Ile Gly Ser Ser Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
165 170 175

Pro Arg Leu Leu Met Tyr Gly Ala Ser Ser Arg Ala Ser Gly Ile Pro
180 185 190

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
195 200 205

Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr
210 215 220

Ala Gly Ser Pro Pro Phe Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
225 230 235 240

Lys

<210> 306

<211> 121

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 306

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 Gly Ser Ile Ser Ser Ser
20 25 30

Tyr Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Ala Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg His Trp Gln Glu Trp Pro Asp Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 307

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 307

Glu Thr Thr Leu Thr Gln Ser Pro Ala Phe Met Ser Ala Thr Pro Gly
1 5 10 15

NOV-001WO_SL.txt

Asp Lys Val Ile Ile Ser Cys Lys Ala Ser Gln Asp Ile Asp Asp Ala
20 25 30

Met Asn Trp Tyr Gln Gln Lys Pro Gly Glu Ala Pro Leu Phe Ile Ile
35 40 45

Gln Ser Ala Thr Ser Pro Val Pro Gly Ile Pro Pro Arg Phe Ser Gly
50 55 60

Ser Gly Phe Gly Thr Asp Phe Ser Leu Thr Ile Asn Asn Ile Glu Ser
65 70 75 80

Glu Asp Ala Ala Tyr Tyr Phe Cys Leu Gln His Asp Asn Phe Pro Leu
85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 308

<211> 243

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 308

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 Gly Ser Ile Ser Ser Ser
20 25 30

Tyr Tyr Tyr Trp Gly Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu
35 40 45

NOV-001WO_SL.txt

Trp Ile Gly Ser Ile Tyr Tyr Ser Gly Ser Ala Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg His Trp Gln Glu Trp Pro Asp Ala Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Glu Thr Thr Leu Thr Gln Ser Pro
130 135 140

Ala Phe Met Ser Ala Thr Pro Gly Asp Lys Val Ile Ile Ser Cys Lys
145 150 155 160

Ala Ser Gln Asp Ile Asp Asp Ala Met Asn Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Glu Ala Pro Leu Phe Ile Ile Gln Ser Ala Thr Ser Pro Val Pro
180 185 190

Gly Ile Pro Pro Arg Phe Ser Gly Ser Gly Phe Gly Thr Asp Phe Ser
195 200 205

Leu Thr Ile Asn Asn Ile Glu Ser Glu Asp Ala Ala Tyr Tyr Phe Cys
210 215 220

Leu Gln His Asp Asn Phe Pro Leu Thr Phe Gly Gln Gly Thr Lys Leu
225 230 235 240

Glu Ile Lys

<210> 309

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 309

Gln Val Asn Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Thr Gln
 1 5 10 15

Thr Leu Thr Leu Thr Cys Thr Phe Ser Gly Phe Ser Leu Arg Thr Ser
 20 25 30

Gly Met Cys Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Ala Leu Glu
 35 40 45

Trp Leu Ala Arg Ile Asp Trp Asp Glu Asp Lys Phe Tyr Ser Thr Ser
 50 55 60

Leu Lys Thr Arg Leu Thr Ile Ser Lys Asp Thr Ser Asp Asn Gln Val
 65 70 75 80

Val Leu Arg Met Thr Asn Met Asp Pro Ala Asp Thr Ala Thr Tyr Tyr
 85 90 95

Cys Ala Arg Ser Gly Ala Gly Gly Thr Ser Ala Thr Ala Phe Asp Ile
 100 105 110

Trp Gly Pro Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> 310

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 310

Asp	Ile	Gln	Met	Thr	Gln	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	Tyr	Asn	Asn
		20						25					30		

Leu	Ala	Trp	Phe	Gln	Leu	Lys	Pro	Gly	Ser	Ala	Pro	Arg	Ser	Leu	Met
		35					40					45			

Tyr	Ala	Ala	Asn	Lys	Ser	Gln	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly
	50					55					60				

Ser	Ala	Ser	Gly	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	His	Tyr	Tyr	Arg	Phe	Pro	Tyr
				85					90					95	

Ser	Phe	Gly	Gln	Gly	Thr	Lys	Leu	Glu	Ile	Lys
			100					105		

<210> 311

<211> 244

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 311

Val	Asn	Leu	Arg	Glu	Ser	Gly	Pro	Ala	Leu	Val	Lys	Pro	Thr	Gln	Thr
1				5					10					15	

NOV-001WO_SL.txt

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

Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr
 210 215 220

Cys Gln His Tyr Tyr Arg Phe Pro Tyr Ser Phe Gly Gln Gly Thr Lys
 225 230 235 240

Leu Glu Ile Lys

<210> 312

<211> 119

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 312

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 Tyr
 20 25 30

Ser 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

NOV-001WO_SL.txt

Ala Lys Thr Ile Ala Ala Val Tyr Ala Phe Asp Ile Trp Gly Gln Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> 313

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 313

Glu Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Pro Glu
1 5 10 15

Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser
20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala 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 Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Leu Gln Thr Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 314

<211> 246

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 314

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 Tyr
 20 25 30

Ser 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 Lys Thr Ile Ala Ala Val Tyr Ala Phe Asp Ile Trp Gly Gln Gly
 100 105 110

Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
 115 120 125

Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Leu Ser
 130 135 140

Leu Pro Val Thr Pro Glu Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser
 145 150 155 160

NOV-001W0_SL.txt

Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu
165 170 175

Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn
180 185 190

Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr
195 200 205

Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val
210 215 220

Tyr Tyr Cys Met Gln Ala Leu Gln Thr Pro Tyr Thr Phe Gly Gln Gly
225 230 235 240

Thr Lys Leu Glu Ile Lys
245

<210> 315

<211> 117

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 315

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 Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50 55 60

NOV-001W0_SL.txt

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 Asp Leu Arg Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met
100 105 110

Val Thr Val Ser Ser
115

<210> 316
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 316
Ser Tyr Val Leu Thr Gln Ser Pro Ser Val Ser Ala Ala Pro Gly Tyr
1 5 10 15

Thr Ala Thr Ile Ser Cys Gly Gly Asn Asn Ile Gly Thr Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu Leu Val Ile Arg
35 40 45

Asp Asp Ser Val Arg Pro Ser Lys Ile Pro Gly Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Met Ala Thr Leu Thr Ile Ser Gly Val Gln Ala Gly
65 70 75 80

NOV-001W0_SL.txt

Asp Glu Ala Asp Phe Tyr Cys Gln Val Trp Asp Ser Asp Ser Glu His
85 90 95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 317

<211> 240

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 317

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 Asp Tyr
20 25 30

Tyr Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Ser Thr 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 Asp Leu Arg Gly Ala Phe Asp Ile Trp Gly Gln Gly Thr Met
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

NOV-001WO_SL.txt

Gly Gly Gly Ser Ser Tyr Val Leu Thr Gln Ser Pro Ser Val Ser Ala
130 135 140

Ala Pro Gly Tyr Thr Ala Thr Ile Ser Cys Gly Gly Asn Asn Ile Gly
145 150 155 160

Thr Lys Ser Val His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Leu
165 170 175

Leu Val Ile Arg Asp Asp Ser Val Arg Pro Ser Lys Ile Pro Gly Arg
180 185 190

Phe Ser Gly Ser Asn Ser Gly Asn Met Ala Thr Leu Thr Ile Ser Gly
195 200 205

Val Gln Ala Gly Asp Glu Ala Asp Phe Tyr Cys Gln Val Trp Asp Ser
210 215 220

Asp Ser Glu His Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
225 230 235 240

<210> 318

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 318

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 Pro Ser Gly Tyr Thr Val Thr Ser His
20 25 30

NOV-001WO_SL.txt

Tyr Ile His Trp Val Arg Arg Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Met Ile Asn Pro Ser Gly Gly Val Thr Ala Tyr Ser Gln Thr Leu
 50 55 60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ser Ser Thr Val Tyr
 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
 85 90 95

Ala Arg Glu Gly Ser Gly Ser Gly Trp Tyr Phe Asp Phe Trp Gly Arg
 100 105 110

Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 319

<211> 106

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 319

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ser Pro Gly Gln
 1 5 10 15

Thr Ala Ser Ile Thr Cys Ser Gly Asp Gly Leu Ser Lys Lys Tyr Val
 20 25 30

Ser Trp Tyr Gln Gln Lys Ala Gly Gln Ser Pro Val Val Leu Ile Ser
 35 40 45

Arg Asp Lys Glu Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
 50 55 60

NOV-001W0_SL.txt

Asn Ser Ala Asp Thr Ala Thr Leu Thr Ile Ser Gly Thr Gln Ala Met
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Ala Trp Asp Asp Thr Thr Val Val
85 90 95

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> 320

<211> 241

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 320

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 Pro Ser Gly Tyr Thr Val Thr Ser His
20 25 30

Tyr Ile His Trp Val Arg Arg Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Met Ile Asn Pro Ser Gly Gly Val Thr Ala Tyr Ser Gln Thr Leu
50 55 60

Gln Gly Arg Val Thr Met Thr Ser Asp Thr Ser Ser Ser Thr Val Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

NOV-001WO_SL.txt

Ala Arg Glu Gly Ser Gly Ser Gly Trp Tyr Phe Asp Phe Trp Gly Arg
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 Ser Tyr Val Leu Thr Gln Pro Pro Ser
130 135 140

Val Ser Val Ser Pro Gly Gln Thr Ala Ser Ile Thr Cys Ser Gly Asp
145 150 155 160

Gly Leu Ser Lys Lys Tyr Val Ser Trp Tyr Gln Gln Lys Ala Gly Gln
165 170 175

Ser Pro Val Val Leu Ile Ser Arg Asp Lys Glu Arg Pro Ser Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Asn Ser Ala Asp Thr Ala Thr Leu Thr
195 200 205

Ile Ser Gly Thr Gln Ala Met Asp Glu Ala Asp Tyr Tyr Cys Gln Ala
210 215 220

Trp Asp Asp Thr Thr Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val
225 230 235 240

Leu

<210> 321

<211> 123

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

NOV-001WO_SL.txt

<400> 321

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 Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Ala Gly Ile Ala Ala Arg Leu Arg Gly Ala Phe Asp Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
115 120

<210> 322

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 322

Asp Ile Val Met Thr Gln Ser Pro Ser Ser Val Ser Ala Ser Val Gly
1 5 10 15

NOV-001WO_SL.txt

Asp Arg Val Ile Ile Thr Cys Arg Ala Ser Gln Gly Ile Arg Asn Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile
35 40 45

Tyr Ala Ala Ser Asn Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Ala Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Val Ala Thr Tyr Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Phe
85 90 95

Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100 105

<210> 323

<211> 245

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 323

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 Thr Val Ser Gly Gly Ser Ile Ser Ser Gly
20 25 30

Gly Tyr Tyr Trp Ser Trp Ile Arg Gln His Pro Gly Lys Gly Leu Glu
35 40 45

Trp Ile Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser
50 55 60

NOV-001W0_SL.txt

Leu Lys Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe
65 70 75 80

Ser Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr
85 90 95

Cys Ala Arg Ala Gly Ile Ala Ala Arg Leu Arg Gly Ala Phe Asp Ile
100 105 110

Trp Gly Gln Gly Thr Met Val Thr Val Ser 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

Ser Pro Ser Ser Val Ser Ala Ser Val Gly Asp Arg Val Ile Ile Thr
145 150 155 160

Cys Arg Ala Ser Gln Gly Ile Arg Asn Trp Leu Ala Trp Tyr Gln Gln
165 170 175

Lys Pro Gly Lys Ala Pro Asn Leu Leu Ile Tyr Ala Ala Ser Asn Leu
180 185 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Ala Asp
195 200 205

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Val Ala Thr Tyr
210 215 220

Tyr Cys Gln Lys Tyr Asn Ser Ala Pro Phe Thr Phe Gly Pro Gly Thr
225 230 235 240

Lys Val Asp Ile Lys
245

<210> 324
 <211> 129
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic polypeptide

<400> 324
 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 Gly Thr Phe Ser Ser Tyr
 20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
 50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu 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 Gly Gly Tyr Gln Leu Leu Arg Trp Asp Val Gly Leu Leu
 100 105 110

Arg Ser Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser
 115 120 125

Ser

<210> 325

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 325

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
 1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Leu Tyr
 35 40 45

Gly Lys Asn Asn Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
 50 55 60

Arg Ser Gly Thr Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
 65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Arg Asp Ser Ser Gly Asp His
 85 90 95

Leu Arg Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
 100 105

<210> 326

<211> 253

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 326

NOV-001W0_SL.txt

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 Gly Thr Phe Ser Ser Tyr
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu 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 Gly Gly Tyr Gln Leu Leu Arg Trp Asp Val Gly Leu Leu
100 105 110

Arg Ser Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val Thr Val Ser
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
130 135 140

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
145 150 155 160

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
165 170 175

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Leu Tyr
180 185 190

NOV-001WO_SL.txt

Gly Lys Asn Asn Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Arg Ser Gly Thr Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
210 215 220

Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Arg Asp Ser Ser Gly Asp His
225 230 235 240

Leu Arg Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
245 250

<210> 327

<211> 125

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 327

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 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 Tyr Tyr Arg Ser Lys Trp Tyr Ser Phe Tyr Ala
50 55 60

Ile Ser Leu Lys Ser Arg Ile Ile Ile Asn Pro Asp Thr Ser Lys Asn
65 70 75 80

Gln Phe Ser Leu Gln Leu Lys Ser Val Thr Pro Glu Asp Thr Ala Val
85 90 95

Tyr Tyr Cys Ala Arg Ser Ser Pro Glu Gly Leu Phe Leu Tyr Trp Phe
100 105 110

Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> 328

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 328

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1 5 10 15

Thr Ile Arg Ile Thr Cys Gln Gly Asp Ser Leu Gly Asn Tyr Tyr Ala
20 25 30

Thr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Gly Thr Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Ala Ser
50 55 60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly His His
85 90 95

Leu Leu Phe Gly Thr Gly Thr Lys Val Thr Val Leu
100 105

<210> 329

<211> 248

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 329

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 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 Tyr Tyr Arg Ser Lys Trp Tyr Ser Phe Tyr Ala
 50 55 60

Ile Ser Leu Lys Ser Arg Ile Ile Ile Asn Pro Asp Thr Ser Lys Asn
 65 70 75 80

Gln Phe Ser Leu Gln Leu Lys Ser Val Thr Pro Glu Asp Thr Ala Val
 85 90 95

Tyr Tyr Cys Ala Arg Ser Ser Pro Glu Gly Leu Phe Leu Tyr Trp Phe
 100 105 110

Asp Pro Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Asp
 115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Ser Glu Leu
 130 135 140

Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln Thr Ile Arg Ile
 145 150 155 160

NOV-001WO_SL.txt

Thr Cys Gln Gly Asp Ser Leu Gly Asn Tyr Tyr Ala Thr Trp Tyr Gln
165 170 175

Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr Gly Thr Asn Asn
180 185 190

Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Ala Ser Ser Ser Gly Asn
195 200 205

Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu Asp Glu Ala Asp
210 215 220

Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly His His Leu Leu Phe Gly
225 230 235 240

Thr Gly Thr Lys Val Thr Val Leu
245

<210> 330

<211> 118

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 330

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 Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

NOV-001WO_SL.txt

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Val Glu Gly Ser Gly Ser Leu Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 331

<211> 113

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 331

Glu Ile Val Met Thr Gln Ser Pro Gly 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 Ala
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro Arg Leu Leu
35 40 45

Ile Ser Gly Ala Ser Thr Arg Ala Thr Gly Ile Pro Asp Arg Phe Gly
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

NOV-001WO_SL.txt

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Ser Ser Phe
85 90 95

Asn Gly Ser Ser Leu Phe Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile
100 105 110

Lys

<210> 332

<211> 246

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 332

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 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

NOV-001W0_SL.txt

Ala Lys Val Glu Gly Ser Gly Ser Leu Asp Tyr Trp Gly Gln Gly Thr
 100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Gly Thr Leu
 130 135 140

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
 145 150 155 160

Ser Val Ser Ser Ala Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
 165 170 175

Pro Pro Arg Leu Leu Ile Ser Gly Ala Ser Thr Arg Ala Thr Gly Ile
 180 185 190

Pro Asp Arg Phe Gly Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
 195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His
 210 215 220

Tyr Gly Ser Ser Phe Asn Gly Ser Ser Leu Phe Thr Phe Gly Gln Gly
 225 230 235 240

Thr Arg Leu Glu Ile Lys
 245

<210> 333

<211> 118

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

NOV-001WO_SL.txt

<400> 333

Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ile Thr Phe Ser Arg Tyr
20 25 30

Pro Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Asp Ser Gly Val Ser Thr Tyr Tyr Ala Asp Ser Ala
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe
65 70 75 80

Leu Gln Met Ser Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Val Thr Arg Ala Gly Ser Glu Ala Ser Asp Ile Trp Gly Gln Gly Thr
100 105 110

Met Val Thr Val Ser Ser
115

<210> 334

<211> 108

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 334

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

NOV-001WO_SL.txt

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Asn Ser
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 Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro
65 70 75 80

Glu Asp Phe Ala Ile Tyr Tyr Cys Gln Gln Phe Gly Thr Ser Ser Gly
85 90 95

Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 335

<211> 241

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 335

Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Ile Thr Phe Ser Arg Tyr
20 25 30

Pro Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Asp Ser Gly Val Ser Thr Tyr Tyr Ala Asp Ser Ala
50 55 60

NOV-001W0_SL.txt

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe
65 70 75 80

Leu Gln Met Ser Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Val Thr Arg Ala Gly Ser Glu Ala Ser Asp Ile Trp Gly Gln Gly Thr
100 105 110

Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu
130 135 140

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
145 150 155 160

Ser Val Ser Asn Ser Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
165 170 175

Pro Arg Leu Leu Ile Tyr Asp Ala Ser Ser Arg Ala Thr Gly Ile Pro
180 185 190

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
195 200 205

Ser Arg Leu Glu Pro Glu Asp Phe Ala Ile Tyr Tyr Cys Gln Gln Phe
210 215 220

Gly Thr Ser Ser Gly Leu Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
225 230 235 240

Lys

<210> 336
 <211> 124
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic polypeptide

<400> 336
 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 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 Ala Lys Asn Ser Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ile Tyr Tyr Cys
 85 90 95

Ala Arg Ala Thr Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
 100 105 110

Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> 337
 <211> 109
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 337

Glu Ile Val Met Thr Gln Ser Pro Gly Thr Val Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Ser Ala Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro
85 90 95

Ser Trp Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 338

<211> 248

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 338

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

NOV-001WO_SL.txt

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 Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ile Tyr Tyr Cys
85 90 95

Ala Arg Ala Thr Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr
130 135 140

Gln Ser Pro Gly Thr Val Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu
145 150 155 160

Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser Phe Leu Ala Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser
180 185 190

Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

NOV-001WO_SL.txt

Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Ser Ala
210 215 220

Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro Ser Trp Thr Phe Gly
225 230 235 240

Gln Gly Thr Arg Leu Glu Ile Lys
245

<210> 339

<211> 124

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 339

Glu Val Gln Leu Val Glu Thr 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 Thr Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ala Thr Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120

<210> 340

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 340

Glu Ile Val Leu Thr Gln Ser Pro Ser Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Ser Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Thr Thr
20 25 30

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ser Ser Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Arg Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro
85 90 95

Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 341

<211> 248

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 341

Glu Val Gln Leu Val Glu Thr 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 Thr Leu Lys Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ala Thr Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
100 105 110

Val 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 Glu Ile Val Leu Thr
130 135 140

Gln Ser Pro Ser Thr Leu Ser Leu Ser Pro Gly Glu Ser Ala Thr Leu
145 150 155 160

Ser Cys Arg Ala Ser Gln Ser Val Ser Thr Thr Phe Leu Ala Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ser Ser
180 185 190

Asn Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Phe Thr Leu Thr Ile Arg Arg Leu Glu Pro Glu Asp Phe Ala
210 215 220

Val Tyr Tyr Cys Gln Gln Tyr His Ser Ser Pro Ser Trp Thr Phe Gly
225 230 235 240

Gln Gly Thr Lys Val Glu Ile Lys
245

<210> 342

<211> 117

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 342

Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly Tyr Ala Asp Ser Val
50 55 60

NOV-001W0_SL.txt

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 Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Gly Lys Ala Val Pro Asp Val Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser
115

<210> 343

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 343

Asp Ile Val Met Thr Gln Thr 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 Tyr
85 90 95

Ser Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 344

<211> 239

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 344

Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Trp Asn Ser Gly Ser Ile Gly 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 Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Gly Lys Ala Val Pro Asp Val Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

NOV-001W0_SL.txt

Gly Gly Gly Ser Asp Ile Val Met Thr Gln Thr Pro Ser Ser Leu Ser
130 135 140

Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser
145 150 155 160

Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro
165 170 175

Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val Pro Ser
180 185 190

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser
195 200 205

Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ser Tyr
210 215 220

Ser Thr Pro Tyr Ser Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
225 230 235

<210> 345

<211> 122

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 345

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Arg Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

NOV-001W0_SL.txt

Ala Ser Ile Asn Trp Lys Gly Asn Ser Leu Ala Tyr Gly Asp Ser Val
50 55 60

Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Phe
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Ser His Gln Gly Val Ala Tyr Tyr Asn Tyr Ala Met Asp Val Trp
100 105 110

Gly Arg Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 346

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 346

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Thr Gln Ser Ile Gly Ser Ser
20 25 30

Phe Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Gln Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

NOV-001WO_SL.txt

Gly Arg Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Val Glu
65 70 75 80

Pro Glu Asp Ser Ala Val Tyr Tyr Cys Gln His Tyr Glu Ser Ser Pro
85 90 95

Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 347

<211> 246

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 347

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Asp Asp Tyr
20 25 30

Ala Met His Trp Val Arg Gln Arg Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Ser Ile Asn Trp Lys Gly Asn Ser Leu Ala Tyr Gly Asp Ser Val
50 55 60

Lys Gly Arg Phe Ala Ile Ser Arg Asp Asn Ala Lys Asn Thr Val Phe
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Thr Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Ser His Gln Gly Val Ala Tyr Tyr Asn Tyr Ala Met Asp Val Trp
100 105 110

NOV-001W0_SL.txt

Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
 115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser
 130 135 140

Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
 145 150 155 160

Arg Ala Thr Gln Ser Ile Gly Ser Ser Phe Leu Ala Trp Tyr Gln Gln
 165 170 175

Arg Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Gln Arg
 180 185 190

Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Arg Gly Ser Gly Thr Asp
 195 200 205

Phe Thr Leu Thr Ile Ser Arg Val Glu Pro Glu Asp Ser Ala Val Tyr
 210 215 220

Tyr Cys Gln His Tyr Glu Ser Ser Pro Ser Trp Thr Phe Gly Gln Gly
 225 230 235 240

Thr Lys Val Glu Ile Lys
 245

<210> 348
 <211> 117
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 348

NOV-001WO_SL.txt

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 Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Val Val Arg Asp Gly Met Asp Val Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser
115

<210> 349

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 349

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 Ser
20 25 30

NOV-001W0_SL.txt

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Asn Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Pro Pro
85 90 95

Arg Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
100 105

<210> 350

<211> 241

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 350

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 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

NOV-001W0_SL.txt

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Val Val Arg Asp Gly Met Asp Val Trp Gly Gln Gly Thr Thr
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser
130 135 140

Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser
145 150 155 160

Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala
165 170 175

Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro
180 185 190

Asp Arg Phe Ser Gly Asn Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile
195 200 205

Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr
210 215 220

Gly Ser Pro Pro Arg Phe Thr Phe Gly Pro Gly Thr Lys Val Asp Ile
225 230 235 240

Lys

<210> 351

<211> 118

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 351

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ile Pro Gln Thr Gly Thr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> 352

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 352

Glu Ile Val Leu Thr Gln Ser Pro Gly 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 Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Ser Ser Pro
85 90 95

Ser Trp Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys
100 105

<210> 353

<211> 242

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 353

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

NOV-001W0_SL.txt

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ile Pro Gln Thr Gly Thr Phe Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
115 120 125

Gly Gly Gly Gly Ser Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu
130 135 140

Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln
145 150 155 160

Ser Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Arg Pro Gly Gln
165 170 175

Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile
180 185 190

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
195 200 205

Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His
210 215 220

Tyr Gly Ser Ser Pro Ser Trp Thr Phe Gly Gln Gly Thr Arg Leu Glu
225 230 235 240

Ile Lys

<210> 354

<211> 124

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 354

Glu Val Gln Leu Val Glu Thr 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 Met Ser Arg Glu Asn Asp Lys Asn Ser Val Phe
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Gly Val Tyr Tyr Cys
85 90 95

Ala Arg Ala Asn Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser
 115 120

<210> 355

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 355

Glu Ile Val Met Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
 1 5 10 15

Glu Ser Ala Thr Leu Ser Cys Arg Ala Ser Gln Arg Val Ala Ser Asn
 20 25 30

Tyr Leu Ala Trp Tyr Gln His Lys Pro Gly Gln Ala Pro Ser Leu Leu
 35 40 45

Ile Ser Gly Ala Ser Ser Arg Ala Thr Gly Val Pro Asp Arg Phe Ser
 50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Ala Ile Ser Arg Leu Glu
 65 70 75 80

Pro Glu Asp Ser Ala Val Tyr Tyr Cys Gln His Tyr Asp Ser Ser Pro
 85 90 95

Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 356

<211> 248

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 356

Glu Val Gln Leu Val Glu Thr 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 Met Ser Arg Glu Asn Asp Lys Asn Ser Val Phe
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Gly Val Tyr Tyr Cys
85 90 95

Ala Arg Ala Asn Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp
100 105 110

Val Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly
115 120 125

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr
130 135 140

Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Ser Ala Thr Leu
145 150 155 160

Ser Cys Arg Ala Ser Gln Arg Val Ala Ser Asn Tyr Leu Ala Trp Tyr
165 170 175

NOV-001W0_SL.txt

Gln His Lys Pro Gly Gln Ala Pro Ser Leu Leu Ile Ser Gly Ala Ser
180 185 190

Ser Arg Ala Thr Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Phe Thr Leu Ala Ile Ser Arg Leu Glu Pro Glu Asp Ser Ala
210 215 220

Val Tyr Tyr Cys Gln His Tyr Asp Ser Ser Pro Ser Trp Thr Phe Gly
225 230 235 240

Gln Gly Thr Lys Val Glu Ile Lys
245

<210> 357

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 357

Glu Val Gln Leu Leu Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser 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

NOV-001WO_SL.txt

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ala Leu Val Gly Ala Thr Gly Ala Phe Asp Ile Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 358

<211> 109

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 358

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Leu Ser Ser Asn
20 25 30

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Gly Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Asn Trp Ala Thr Gly Thr Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Thr Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Tyr Tyr Gly Thr Ser Pro
85 90 95

Met Tyr Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 359

<211> 244

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 359

Glu Val Gln Leu Leu Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ser Tyr
 20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Lys Ala Leu Val Gly Ala Thr Gly Ala Phe Asp Ile 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 Leu Thr Gln Ser Pro Gly
 130 135 140

NOV-001W0_SL.txt

Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala
145 150 155 160

Ser Gln Ser Leu Ser Ser Asn Phe Leu Ala Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Gln Ala Pro Gly Leu Leu Ile Tyr Gly Ala Ser Asn Trp Ala Thr
180 185 190

Gly Thr Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr
195 200 205

Leu Thr Ile Thr Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys
210 215 220

Gln Tyr Tyr Gly Thr Ser Pro Met Tyr Thr Phe Gly Gln Gly Thr Lys
225 230 235 240

Val Glu Ile Lys

<210> 360

<211> 117

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 360

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

NOV-001W0_SL.txt

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

Val Leu Trp Phe Gly Glu Gly Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser
115

<210> 361

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 361

Asp Ile Val Leu Thr Gln Ser 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 His Ser
20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro
50 55 60

NOV-001WO_SL.txt

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Ala
85 90 95

Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys
100 105 110

<210> 362

<211> 244

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 362

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe 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

NOV-001WO_SL.txt

Val Leu Trp Phe Gly Glu Gly Phe Asp Pro Trp Gly Gln Gly Thr Leu
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Leu Ser Leu Pro
130 135 140

Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser
145 150 155 160

Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys
165 170 175

Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala
180 185 190

Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe
195 200 205

Thr Leu Lys Ile Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr
210 215 220

Cys Met Gln Ala Leu Gln Thr Pro Leu Thr Phe Gly Gly Gly Thr Lys
225 230 235 240

Val Asp Ile Lys

<210> 363

<211> 126

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

NOV-001WO_SL.txt

<400> 363

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 Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Val Gly Tyr Asp Ser Ser Gly Tyr Tyr Arg Asp Tyr Tyr Gly
100 105 110

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser
115 120 125

<210> 364

<211> 110

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 364

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

NOV-001WO_SL.txt

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Thr Ser Ser Arg Ala Thr Gly Ile Ser Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Asn Ser Pro
85 90 95

Pro Lys Phe Thr Phe Gly Pro Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 365

<211> 251

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 365

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 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

NOV-001W0_SL.txt

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Val Gly Tyr Asp Ser Ser Gly Tyr Tyr Arg Asp Tyr Tyr Gly
100 105 110

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser Gly Gly
115 120 125

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Val
130 135 140

Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala
145 150 155 160

Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala
165 170 175

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly
180 185 190

Thr Ser Ser Arg Ala Thr Gly Ile Ser Asp Arg Phe Ser Gly Ser Gly
195 200 205

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp
210 215 220

Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Asn Ser Pro Pro Lys Phe
225 230 235 240

Thr Phe Gly Pro Gly Thr Lys Leu Glu Ile Lys
245 250

<210> 366
 <211> 122
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic polypeptide

<400> 366
 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 Ser Tyr
 20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Lys Met Gly Trp Ser Ser Gly Tyr Leu Gly Ala Phe Asp Ile Trp
 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser
 115 120

<210> 367
 <211> 109
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 367

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ala Ser Ser
20 25 30

Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu
35 40 45

Ile Tyr Gly Ala Ser Gly Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln His Tyr Gly Gly Ser Pro
85 90 95

Arg Leu Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys
100 105

<210> 368

<211> 246

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 368

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

NOV-001WO_SL.txt

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Met Gly Trp Ser Ser Gly Tyr Leu Gly Ala Phe Asp Ile 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 Glu Ile Val Leu Thr Gln Ser
130 135 140

Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys
145 150 155 160

Arg Ala Ser Gln Ser Val Ala Ser Ser Phe Leu Ala Trp Tyr Gln Gln
165 170 175

Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Gly Arg
180 185 190

Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp
195 200 205

NOV-001WO_SL.txt

Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr
 210 215 220

Tyr Cys Gln His Tyr Gly Gly Ser Pro Arg Leu Thr Phe Gly Gly Gly
 225 230 235 240

Thr Lys Val Asp Ile Lys
 245

<210> 369

<211> 122

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 369

Gln Ile Gln Leu Val Gln Ser Gly Pro Asp Leu Lys Lys Pro Gly Glu
 1 5 10 15

Thr Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Phe
 20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Phe Lys Trp Met
 35 40 45

Ala Trp Ile Asn Thr Tyr Thr Gly Glu Ser Tyr Phe Ala Asp Asp Phe
 50 55 60

Lys Gly Arg Phe Ala Phe Ser Val Glu Thr Ser Ala Thr Thr Ala Tyr
 65 70 75 80

Leu Gln Ile Asn Asn Leu Lys Thr Glu Asp Thr Ala Thr Tyr Phe Cys
 85 90 95

Ala Arg Gly Glu Ile Tyr Tyr Gly Tyr Asp Gly Gly Phe Ala Tyr Trp
 100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ala
 115 120

<210> 370

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 370

Asp Val Val Met Thr Gln Ser His Arg Phe Met Ser Thr Ser Val Gly
 1 5 10 15

Asp Arg Val Ser Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala
 20 25 30

Val Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile
 35 40 45

Phe Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly
 50 55 60

Ser Gly Ser Gly Ala Asp Phe Thr Leu Thr Ile Ser Ser Val Gln Ala
 65 70 75 80

Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Thr Pro Trp
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Asp Ile Lys
 100 105

<210> 371

<211> 244

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 371

Gln Ile Gln Leu Val Gln Ser Gly Pro Asp Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Phe
20 25 30

Gly Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Phe Lys Trp Met
35 40 45

Ala Trp Ile Asn Thr Tyr Thr Gly Glu Ser Tyr Phe Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Val Glu Thr Ser Ala Thr Thr Ala Tyr
65 70 75 80

Leu Gln Ile Asn Asn Leu Lys Thr Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Arg Gly Glu Ile Tyr Tyr Gly Tyr Asp Gly Gly Phe Ala Tyr Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ala Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Val Val Met Thr Gln Ser
130 135 140

His Arg Phe Met Ser Thr Ser Val Gly Asp Arg Val Ser Ile Thr Cys
145 150 155 160

Arg Ala Ser Gln Asp Val Asn Thr Ala Val Ser Trp Tyr Gln Gln Lys
165 170 175

Pro Gly Gln Ser Pro Lys Leu Leu Ile Phe Ser Ala Ser Tyr Arg Tyr
180 185 190

Thr Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Ala Asp Phe
195 200 205

Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr
210 215 220

Cys Gln Gln His Tyr Ser Thr Pro Trp Thr Phe Gly Gly Gly Thr Lys
225 230 235 240

Leu Asp Ile Lys

<210> 372

<211> 117

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 372

Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Ser Ile Asn Trp Val Lys Arg Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Glu Thr Arg Glu Pro Ala Tyr Ala Tyr Asp Phe
50 55 60

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Arg Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Asn Asn Leu Lys Tyr Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Leu Asp Tyr Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
100 105 110

Val Thr Val Ser Ser
115

<210> 373

<211> 111

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 373

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Met Ser Leu Gly
1 5 10 15

Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Ser Val Ile
20 25 30

Gly Ala His Leu Ile His Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

Lys Leu Leu Ile Tyr Leu Ala Ser Asn Leu Glu Thr Gly Val Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asp
65 70 75 80

Pro Val Glu Glu Asp Asp Val Ala Ile Tyr Ser Cys Leu Gln Ser Arg
85 90 95

Ile Phe Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 374

<211> 249

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 374

Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Ser Ile Asn Trp Val Lys Arg Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Trp Ile Asn Thr Glu Thr Arg Glu Pro Ala Tyr Ala Tyr Asp Phe
50 55 60

Arg Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Leu Gln Ile Asn Asn Leu Lys Tyr Glu Asp Thr Ala Thr Tyr Phe Cys
85 90 95

Ala Leu Asp Tyr Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Ser
100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

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Gly Gly Gly Ser Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys
130 135 140

Lys Pro Gly Glu Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr
145 150 155 160

Phe Thr Asp Tyr Ser Ile Asn Trp Val Lys Arg Ala Pro Gly Lys Gly
165 170 175

Leu Lys Trp Met Gly Trp Ile Asn Thr Glu Thr Arg Glu Pro Ala Tyr
180 185 190

Ala Tyr Asp Phe Arg Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala
195 200 205

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

Thr Tyr Phe Cys Ala Leu Asp Tyr Ser Tyr Ala Met Asp Tyr Trp Gly
225 230 235 240

Gln Gly Thr Ser Val Thr Val Ser Ser
245

<210> 375

<211> 117

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 375

Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Arg His Tyr
20 25 30

NOV-001WO_SL.txt

Ser Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Arg Ile Asn Thr Glu Ser Gly Val Pro Ile Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Val Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Leu Val Ile Asn Asn Leu Lys Asp Glu Asp Thr Ala Ser Tyr Phe Cys
85 90 95

Ser Asn Asp Tyr Leu Tyr Ser Leu Asp Phe Trp Gly Gln Gly Thr Ala
100 105 110

Leu Thr Val Ser Ser
115

<210> 376

<211> 111

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 376

Asp Ile Val Leu Thr Gln Ser Pro Pro Ser Leu Ala Met Ser Leu Gly
1 5 10 15

Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser Val Thr Ile Leu
20 25 30

Gly Ser His Leu Ile Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
35 40 45

NOV-001WO_SL.txt

Thr Leu Leu Ile Gln Leu Ala Ser Asn Val Gln Thr Gly Val Pro Ala
50 55 60

Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asp
65 70 75 80

Pro Val Glu Glu Asp Asp Val Ala Val Tyr Tyr Cys Leu Gln Ser Arg
85 90 95

Thr Ile Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

<210> 377

<211> 243

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 377

Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Arg His Tyr
20 25 30

Ser Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Arg Ile Asn Thr Glu Ser Gly Val Pro Ile Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Val Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Leu Val Ile Asn Asn Leu Lys Asp Glu Asp Thr Ala Ser Tyr Phe Cys
85 90 95

NOV-001W0_SL.txt

Ser Asn Asp Tyr Leu Tyr Ser Leu Asp Phe Trp Gly Gln Gly Thr Ala
100 105 110

Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Pro Ser Leu Ala
130 135 140

Met Ser Leu Gly Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser
145 150 155 160

Val Thr Ile Leu Gly Ser His Leu Ile Tyr Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Gln Pro Pro Thr Leu Leu Ile Gln Leu Ala Ser Asn Val Gln Thr
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr
195 200 205

Leu Thr Ile Asp Pro Val Glu Glu Asp Asp Val Ala Val Tyr Tyr Cys
210 215 220

Leu Gln Ser Arg Thr Ile Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu
225 230 235 240

Glu Ile Lys

<210> 378

<211> 117

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 378

Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr His Tyr
20 25 30

Ser Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Arg Ile Asn Thr Glu Thr Gly Glu Pro Leu Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Leu Val Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Phe Phe Cys
85 90 95

Ser Asn Asp Tyr Leu Tyr Ser Cys Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Leu Thr Val Ser Ser
115

<210> 379

<211> 243

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 379

Gln Ile Gln Leu Val Gln Ser Gly Pro Glu Leu Lys Lys Pro Gly Glu
1 5 10 15

NOV-001WO_SL.txt

Thr Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr His Tyr
20 25 30

Ser Met Asn Trp Val Lys Gln Ala Pro Gly Lys Gly Leu Lys Trp Met
35 40 45

Gly Arg Ile Asn Thr Glu Thr Gly Glu Pro Leu Tyr Ala Asp Asp Phe
50 55 60

Lys Gly Arg Phe Ala Phe Ser Leu Glu Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Leu Val Ile Asn Asn Leu Lys Asn Glu Asp Thr Ala Thr Phe Phe Cys
85 90 95

Ser Asn Asp Tyr Leu Tyr Ser Cys Asp Tyr Trp Gly Gln Gly Thr Thr
100 105 110

Leu Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
115 120 125

Gly Gly Gly Ser Asp Ile Val Leu Thr Gln Ser Pro Pro Ser Leu Ala
130 135 140

Met Ser Leu Gly Lys Arg Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser
145 150 155 160

Val Thr Ile Leu Gly Ser His Leu Ile Tyr Trp Tyr Gln Gln Lys Pro
165 170 175

Gly Gln Pro Pro Thr Leu Leu Ile Gln Leu Ala Ser Asn Val Gln Thr
180 185 190

Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr
195 200 205

Leu Thr Ile Asp Pro Val Glu Glu Asp Asp Val Ala Val Tyr Tyr Cys
 210 215 220

Leu Gln Ser Arg Thr Ile Pro Arg Thr Phe Gly Gly Gly Thr Lys Leu
 225 230 235 240

Glu Ile Lys

<210> 380

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 380

Arg Ala Ser Gln Ser Ile Ser Ser Tyr Leu Asn
 1 5 10

<210> 381

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 381

Arg Ala Ser Gln Ser Ile Ser Ser Ser Phe Leu Ala
 1 5 10

<210> 382

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 382

Arg	Ser	Ser	Gln	Ser	Leu	Leu	His	Ser	Asn	Gly	Tyr	Asn	Tyr	Leu	Asp
1				5					10					15	

<210> 383

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 383

Lys	Ser	Ser	Gln	Ser	Leu	Leu	Arg	Asn	Asp	Gly	Lys	Thr	Pro	Leu	Tyr
1				5					10					15	

<210> 384

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 384

Arg	Ser	Ser	Gln	Ser	Leu	Leu	His	Ser	Asn	Gly	Tyr	Asn	Tyr	Leu	Asn
1				5					10					15	

<210> 385

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 385

Arg	Ser	Ser	Gln	Ser	Leu	Leu	Tyr	Ser	Asn	Gly	Tyr	Asn	Tyr	Val	Asp
1				5					10					15	

<210> 386
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 386
 Arg Ala Ser Gln Ser Val Ser Ser Asn Leu Ala
 1 5 10

<210> 387
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 387
 Arg Ala Ser Gln Ser Val Ser Ser Lys Leu Ala
 1 5 10

<210> 388
 <211> 12
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 388
 Arg Ala Ser Gln Ser Val Gly Ser Thr Asn Leu Ala
 1 5 10

<210> 389
 <211> 16
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 389

Lys	Ser	Ser	Glu	Ser	Leu	Val	His	Asn	Ser	Gly	Lys	Thr	Tyr	Leu	Asn
1				5					10					15	

<210> 390

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 390

Gln	Ala	Ser	Glu	Asp	Ile	Asn	Lys	Phe	Leu	Asn
1			5				10			

<210> 391

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 391

Arg	Ala	Ser	Gln	Ser	Val	Gly	Ser	Asn	Leu	Ala
1			5				10			

<210> 392

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 392

Arg Ala Ser Gln Ser Ile Gly Ser Ser Ser Leu Ala
1 5 10

<210> 393

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 393

Lys Ala Ser Gln Asp Ile Asp Asp Ala Met Asn
1 5 10

<210> 394

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 394

Arg Ala Ser Gln Asp Ile Tyr Asn Asn Leu Ala
1 5 10

<210> 395

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 395

Gly Gly Asn Asn Ile Gly Thr Lys Ser Val His
1 5 10

<210> 396

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 396

Ser Gly Asp Gly Leu Ser Lys Lys Tyr Val Ser
1 5 10

<210> 397

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 397

Arg Ala Ser Gln Gly Ile Arg Asn Trp Leu Ala
1 5 10

<210> 398

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 398

Gly Gly Asn Asn Ile Gly Ser Lys Ser Val His
1 5 10

<210> 399

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 399

Gln Gly Asp Ser Leu Gly Asn Tyr Tyr Ala Thr
1 5 10

<210> 400

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 400

Arg Ala Ser Gln Ser Val Ser Ser Ala Tyr Leu Ala
1 5 10

<210> 401

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 401

Arg Ala Ser Gln Ser Val Ser Asn Ser Leu Ala
1 5 10

<210> 402

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 402

Arg Ala Ser Gln Ser Val Ser Ser Ser Phe Leu Ala
1 5 10

<210> 403

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 403

Arg Ala Ser Gln Ser Val Ser Thr Thr Phe Leu Ala

1

5

10

<210> 404

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 404

Arg Ala Thr Gln Ser Ile Gly Ser Ser Phe Leu Ala

1

5

10

<210> 405

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 405

Arg Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala

1

5

10

<210> 406

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 406

Arg Ala Ser Gln Arg Val Ala Ser Asn Tyr Leu Ala
1 5 10

<210> 407

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 407

Arg Ala Ser Gln Ser Leu Ser Ser Asn Phe Leu Ala
1 5 10

<210> 408

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 408

Arg Ala Ser Gln Ser Val Ala Ser Ser Phe Leu Ala
1 5 10

<210> 409

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 409

Arg Ala Ser Gln Asp Val Asn Thr Ala Val Ser
1 5 10

<210> 410
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 410
 Arg Ala Ser Glu Ser Val Ser Val Ile Gly Ala His Leu Ile His
 1 5 10 15

<210> 411
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 411
 Arg Ala Ser Glu Ser Val Thr Ile Leu Gly Ser His Leu Ile Tyr
 1 5 10 15

<210> 412
 <211> 7
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 412
 Ala Ala Ser Ser Leu Gln Ser
 1 5

<210> 413
 <211> 7
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 413

Gly Ala Ser Arg Arg Ala Thr
1 5

<210> 414

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 414

Leu Gly Ser Asn Arg Ala Ser
1 5

<210> 415

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 415

Glu Val Ser Asn Arg Phe Ser
1 5

<210> 416

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 416

Leu Gly Ser Lys Arg Ala Ser
1 5

<210> 417

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 417

Gly Ala Ser Thr Leu Ala Ser
1 5

<210> 418

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 418

Gly Ala Ser Thr Arg Ala Ser
1 5

<210> 419

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 419

Gly Ala Ser Ile Arg Ala Thr
1 5

<210> 420

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 420

Glu Val Ser Asn Arg Asp Ser
1 5

<210> 421

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 421

Asp Ala Ser Thr Leu Gln Thr
1 5

<210> 422

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 422

Gly Ala Ser Thr Arg Ala Thr
1 5

<210> 423

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 423

Gly Ala Ser Ser Arg Ala Ser
1 5

<210> 424

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 424

Ser Ala Thr Ser Pro Val Pro
1 5

<210> 425

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 425

Ala Ala Asn Lys Ser Gln Ser
1 5

<210> 426

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 426

Asp Asp Ser Val Arg Pro Ser
1 5

<210> 427

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 427

Arg Asp Lys Glu Arg Pro Ser

1 5

<210> 428

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 428

Ala Ala Ser Asn Leu Gln Ser

1 5

<210> 429

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 429

Gly Lys Asn Asn Arg Pro Ser

1 5

<210> 430

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 430

Gly Thr Asn Asn Arg Pro Ser
1 5

<210> 431

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 431

Asp Ala Ser Ser Arg Ala Thr
1 5

<210> 432

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 432

Gly Ala Ser Ser Arg Ala Thr
1 5

<210> 433

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 433

Gly Ser Ser Asn Arg Ala Thr
1 5

<210> 434
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 434
Gly Ala Ser Gln Arg Ala Thr
1 5

<210> 435
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 435
Gly Ala Ser Asn Trp Ala Thr
1 5

<210> 436
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 436
Gly Thr Ser Ser Arg Ala Thr
1 5

<210> 437
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 437

Gly Ala Ser Gly Arg Ala Thr
1 5

<210> 438

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 438

Ser Ala Ser Tyr Arg Tyr Thr
1 5

<210> 439

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 439

Leu Ala Ser Asn Leu Glu Thr
1 5

<210> 440

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 440

Leu Ala Ser Asn Val Gln Thr
1 5

<210> 441
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 441
Gln Gln Ser Tyr Ser Thr Pro Tyr Thr
1 5

<210> 442
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 442
Gln Gln Tyr His Ser Ser Pro Ser Trp Thr
1 5 10

<210> 443
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 443
Met Gln Ala Leu Gln Thr Pro Tyr Thr
1 5

<210> 444
<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 444

Met Gln Asn Ile Gln Phe Pro Ser
1 5

<210> 445

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 445

Gln Gln Ser Tyr Lys Arg Ala Ser
1 5

<210> 446

<211> 9

<212> PRT

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<210> 447

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Gln Gln Tyr Gly Ser Ser Leu Thr
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Gln Gln Tyr Gly Ser Ser Ser Trp Thr
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<210> 449

<211> 10

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Gln Gln Ser Tyr Thr Leu Ala
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Met Gln Gly Thr His Trp Pro Gly Thr

1 5

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Gln Gln Tyr Glu Ser Leu Pro Leu Thr

1 5

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Gln Gln Tyr Asn Asp Trp Leu Pro Val Thr

1 5 10

<210> 454

<211> 10

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Gln Gln Tyr Ala Gly Ser Pro Pro Phe Thr
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Leu Gln His Asp Asn Phe Pro Leu Thr
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Gln His Tyr Tyr Arg Phe Pro Tyr Ser
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Gln Val Trp Asp Ser Asp Ser Glu His Val Val
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Asn	Ser	Arg	Asp	Ser	Ser	Gly	His	His	Leu	Leu
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Gln	His	Tyr	Gly	Ser	Ser	Phe	Asn	Gly	Ser	Ser	Leu	Phe	Thr
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<210> 463

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Gln	Gln	Phe	Gly	Thr	Ser	Ser	Gly	Leu	Thr
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<210> 464

<211> 9

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Gln Gln Ser Tyr Ser Thr Pro Tyr Ser
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Gln His Tyr Glu Ser Ser Pro Ser Trp Thr
1 5 10

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Gln Gln Tyr Gly Ser Pro Pro Arg Phe Thr
1 5 10

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<211> 10

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Gln His Tyr Gly Ser Ser Pro Ser Trp Thr
1 5 10

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Gln His Tyr Asp Ser Ser Pro Ser Trp Thr
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Gln Tyr Tyr Gly Thr Ser Pro Met Tyr Thr
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<211> 9

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Met Gln Ala Leu Gln Thr Pro Leu Thr
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Gln His Tyr Gly Asn Ser Pro Pro Lys Phe Thr
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Ser Gln Ser Ile Ser Ser Tyr

1 5

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Ser Gln Ser Ile Ser Ser Ser Phe

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Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr
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Ser Gln Ser Leu Leu Arg Asn Asp Gly Lys Thr Pro
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Ser Gln Ser Leu Leu Tyr Ser Asn Gly Tyr Asn Tyr
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1 5

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Ser Gln Asp Ile Asp Asp Ala
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peptide

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Ser Gln Asp Ile Tyr Asn Asn
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Asn Asn Ile Gly Thr Lys Ser
1 5

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Asp Gly Leu Ser Lys Lys Tyr
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Ser Gln Gly Ile Arg Asn Trp
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<210> 493

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Asn Asn Ile Gly Ser Lys Ser
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<210> 494

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Asp Ser Leu Gly Asn Tyr Tyr
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Ser Gln Ser Val Ser Ser Ala Tyr

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1 5

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Ser Gln Ser Val Ser Ser Ser Phe

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Ser Gln Ser Val Ser Thr Thr Phe

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Thr Gln Ser Ile Gly Ser Ser Phe

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Ser Gln Ser Val Ser Ser Ser Tyr

1 5

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Ser Gln Arg Val Ala Ser Asn Tyr

1 5

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Ser Gln Ser Leu Ser Ser Asn Phe
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Ser Gln Ser Val Ala Ser Ser Phe
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Ser Gln Asp Val Asn Thr Ala
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Leu Gly Ser
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Glu Val Ser
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Ser Ala Thr
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Ala Ala Asn
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Gly Ser Ser

1

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Gly Thr Ser

1

<210> 518

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Ser Ala Ser

1

<210> 519

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Leu Ala Ser
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Ser Tyr Lys Arg Ala

1 5

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Gly Arg Gln Phe Pro Tyr

1 5

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Tyr Gly Ser Ser Leu
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Tyr Gly Ser Ser Ser Trp
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Ser Tyr Thr Leu
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Gly Thr His Trp Pro Gly
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<210> 531
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His Asp Asn Phe Pro Leu
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Tyr Tyr Arg Phe Pro Tyr
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<210> 540
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Tyr Gly Ser Ser Phe Asn Gly Ser Ser Leu Phe
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1 5

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Tyr Gly Thr Ser Pro Met Tyr

1 5

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Ala Leu Gln Thr Pro Leu

1 5

<210> 549

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Tyr Gly Asn Ser Pro Pro Lys Phe

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<210> 550

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peptide

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Asn Phe Gly Ile Asn
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Asn Tyr Gly Ile Thr
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peptide

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peptide

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peptide

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Ser His Tyr Ile His
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<223> Description of Artificial Sequence: Synthetic peptide

<400> 565

Ser Gly Gly Tyr Tyr Trp Ser
1 5

<210> 566

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 566

Ser Tyr Ala Ile Ser
1 5

<210> 567

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 567

Ser Asn Ser Ala Ala Trp Asn

1 5

<210> 568

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 568

Ser Tyr Ala Met Ser

1 5

<210> 569

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 569

Arg Tyr Pro Met Ser

1 5

<210> 570

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 570

Asn Phe Gly Met Asn

1 5

<210> 571

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 571

Asp Tyr Ser Ile Asn

1 5

<210> 572

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 572

His Tyr Ser Met Asn

1 5

<210> 573

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 573

Gly Ile Val Tyr Ser Gly Ser Thr Tyr Tyr Ala Ala Ser Val Lys Gly

1 5 10 15

<210> 574

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 574

Gly	Ile	Ser	Arg	Ser	Gly	Glu	Asn	Thr	Tyr	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10					15	

Gly

<210> 575

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 575

Gly	Ile	Ser	Trp	Asn	Ser	Gly	Ser	Ile	Gly	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10					15	

Gly

<210> 576

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 576

Trp	Ile	Asn	Pro	Lys	Asn	Asn	Asn	Thr	Asn	Tyr	Ala	Gln	Lys	Phe	Gln
1				5					10					15	

Gly

<210> 577

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 577

Val	Ile	Ser	Gly	Ser	Gly	Gly	Thr	Thr	Tyr	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10					15	

Gly

<210> 578

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 578

Trp	Ile	Ser	Ala	Tyr	Asn	Gly	Asn	Thr	Asn	Tyr	Ala	Gln	Lys	Phe	Gln
1				5					10					15	

Gly

<210> 579

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 579

Tyr	Ile	Ser	Ser	Ser	Gly	Ser	Thr	Ile	Tyr	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10					15	

Gly

<210> 580

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 580

Tyr Ile Ser Ser Ser Gly Asn Thr Ile Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 581

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 581

Ser Ile Tyr Tyr Ser Gly Ser Ala Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 582

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 582

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Arg	Ile	Asp	Trp	Asp	Glu	Asp	Lys	Phe	Tyr	Ser	Thr	Ser	Leu	Lys	Thr
1				5					10					15	

<210> 583

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 583

Ser	Ile	Ser	Ser	Ser	Ser	Ser	Tyr	Ile	Tyr	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10					15	

Gly

<210> 584

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 584

Met	Ile	Asn	Pro	Ser	Gly	Gly	Val	Thr	Ala	Tyr	Ser	Gln	Thr	Leu	Gln
1				5					10					15	

Gly

<210> 585

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 585

Tyr Ile Tyr Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 586

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 586

Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe Gln
1 5 10 15

Gly

<210> 587

<211> 18

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 587

Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Ser Phe Tyr Ala Ile Ser Leu
1 5 10 15

Lys Ser

<210> 588

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 588

Ala	Ile	Ser	Gly	Ser	Gly	Gly	Ser	Thr	Tyr	Tyr	Ala	Asp	Ser	Val	Lys
1				5					10					15	

Gly

<210> 589

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 589

Gly	Ile	Ser	Asp	Ser	Gly	Val	Ser	Thr	Tyr	Tyr	Ala	Asp	Ser	Ala	Lys
1				5					10					15	

Gly

<210> 590

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 590

Ser	Ile	Asn	Trp	Lys	Gly	Asn	Ser	Leu	Ala	Tyr	Gly	Asp	Ser	Val	Lys
1				5					10					15	

Gly

<210> 591

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 591

Trp	Ile	Asn	Thr	Tyr	Thr	Gly	Glu	Ser	Tyr	Phe	Ala	Asp	Asp	Phe	Lys
1				5					10					15	

Gly

<210> 592

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 592

Trp	Ile	Asn	Thr	Glu	Thr	Arg	Glu	Pro	Ala	Tyr	Ala	Tyr	Asp	Phe	Arg
1				5					10					15	

Gly

<210> 593

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 593

Arg	Ile	Asn	Thr	Glu	Ser	Gly	Val	Pro	Ile	Tyr	Ala	Asp	Asp	Phe	Lys
1				5					10					15	

Gly

<210> 594

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 594

Arg Ile Asn Thr Glu Thr Gly Glu Pro Leu Tyr Ala Asp Asp Phe Lys
1 5 10 15

Gly

<210> 595

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 595

His Gly Gly Glu Ser Asp Val
1 5

<210> 596

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 596

Ser Pro Ala His Tyr Tyr Gly Gly Met Asp Val
1 5 10

<210> 597

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 597

His Ser Phe Leu Ala Tyr
1 5

<210> 598

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 598

Gly Pro Tyr Tyr Tyr Gln Ser Tyr Met Asp Val
1 5 10

<210> 599

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 599

Leu Asp Ser Ser Gly Tyr Tyr Tyr Ala Arg Gly Pro Arg Tyr
1 5 10

<210> 600

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 600

Gly Pro Tyr Tyr Tyr Met Asp Val
1 5

<210> 601

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 601

Glu Ser Gly Asp Gly Met Asp Val
1 5

<210> 602

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 602

Ser Thr Met Val Arg Glu Asp Tyr
1 5

<210> 603

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 603

His Trp Gln Glu Trp Pro Asp Ala Phe Asp Ile
1 5 10

<210> 604

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 604

Ser Gly Ala Gly Gly Thr Ser Ala Thr Ala Phe Asp Ile
1 5 10

<210> 605

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 605

Thr Ile Ala Ala Val Tyr Ala Phe Asp Ile
1 5 10

<210> 606

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 606

Asp Leu Arg Gly Ala Phe Asp Ile
1 5

<210> 607

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 607

Glu Gly Ser Gly Ser Gly Trp Tyr Phe Asp Phe
1 5 10

<210> 608

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 608

Ala Gly Ile Ala Ala Arg Leu Arg Gly Ala Phe Asp Ile
1 5 10

<210> 609

<211> 20

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 609

Arg Gly Gly Tyr Gln Leu Leu Arg Trp Asp Val Gly Leu Leu Arg Ser
1 5 10 15

Ala Phe Asp Ile
20

<210> 610

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 610

Ser Ser Pro Glu Gly Leu Phe Leu Tyr Trp Phe Asp Pro
1 5 10

<210> 611

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 611

Val Glu Gly Ser Gly Ser Leu Asp Tyr
1 5

<210> 612

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 612

Arg Ala Gly Ser Glu Ala Ser Asp Ile
1 5

<210> 613

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 613

Ala Thr Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp Val
1 5 10 15

<210> 614

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 614

Val Gly Lys Ala Val Pro Asp Val
1 5

<210> 615

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 615

His Gln Gly Val Ala Tyr Tyr Asn Tyr Ala Met Asp Val
1 5 10

<210> 616

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 616

Val Val Arg Asp Gly Met Asp Val
1 5

<210> 617

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 617

Ile Pro Gln Thr Gly Thr Phe Asp Tyr

1 5

<210> 618

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 618

Ala Asn Tyr Lys Arg Glu Leu Arg Tyr Tyr Tyr Gly Met Asp Val

1 5 10 15

<210> 619

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 619

Ala Leu Val Gly Ala Thr Gly Ala Phe Asp Ile

1 5 10

<210> 620

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 620

Trp Phe Gly Glu Gly Phe Asp Pro
1 5

<210> 621

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 621

Val Gly Tyr Asp Ser Ser Gly Tyr Tyr Arg Asp Tyr Tyr Gly Met Asp
1 5 10 15

Val

<210> 622

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 622

Met Gly Trp Ser Ser Gly Tyr Leu Gly Ala Phe Asp Ile
1 5 10

<210> 623

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 623

Gly Glu Ile Tyr Tyr Gly Tyr Asp Gly Gly Phe Ala Tyr
1 5 10

<210> 624

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 624

Asp Tyr Ser Tyr Ala Met Asp Tyr
1 5

<210> 625

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 625

Asp Tyr Leu Tyr Ser Leu Asp Phe
1 5

<210> 626

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 626

Asp Tyr Leu Tyr Ser Cys Asp Tyr
1 5

<210> 627

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 627

Gly Phe Ala Leu Ser Asn His

1 5

<210> 628

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 628

Gly Phe Thr Phe Ser Asn Tyr

1 5

<210> 629

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 629

Gly Phe Thr Phe Asp Asp Tyr

1 5

<210> 630

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 630

Gly Tyr Ile Phe Asp Asn Phe
1 5

<210> 631

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 631

Gly Phe Thr Phe Ser Ser Asp
1 5

<210> 632

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 632

Gly Tyr Thr Phe Ser Asn Tyr
1 5

<210> 633

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 633

Gly Phe Thr Phe Ser Asp Tyr
1 5

<210> 634
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 634
Gly Gly Ser Ile Ser Ser Ser Tyr Tyr
1 5

<210> 635
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 635
Gly Phe Ser Leu Arg Thr Ser Gly Met
1 5

<210> 636
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 636
Gly Phe Thr Phe Ser Ser Tyr
1 5

<210> 637
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 637

Gly Tyr Thr Val Thr Ser His
1 5

<210> 638

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 638

Gly Gly Ser Ile Ser Ser Gly Gly Tyr
1 5

<210> 639

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 639

Gly Gly Thr Phe Ser Ser Tyr
1 5

<210> 640

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 640

Gly Asp Ser Val Ser Ser Asn Ser Ala
1 5

<210> 641
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 641
Gly Ile Thr Phe Ser Arg Tyr
1 5

<210> 642
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 642
Gly Phe Ser Phe Ser Ser Tyr
1 5

<210> 643
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 643
Gly Tyr Thr Phe Thr Asn Phe
1 5

<210> 644
<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 644

Gly Tyr Thr Phe Thr Asp Tyr
1 5

<210> 645

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 645

Gly Tyr Thr Phe Arg His Tyr
1 5

<210> 646

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 646

Gly Tyr Thr Phe Thr His Tyr
1 5

<210> 647

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 647

Val Tyr Ser Gly Ser
1 5

<210> 648

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 648

Ser Arg Ser Gly Glu Asn
1 5

<210> 649

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 649

Ser Trp Asn Ser Gly Ser
1 5

<210> 650

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 650

Asn Pro Lys Asn Asn Asn
1 5

<210> 651

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 651

Ser Gly Ser Gly Gly Thr

1 5

<210> 652

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 652

Ser Ala Tyr Asn Gly Asn

1 5

<210> 653

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 653

Ser Ser Ser Gly Ser Thr

1 5

<210> 654

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 654

Ser Ser Ser Gly Asn Thr
1 5

<210> 655

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 655

Tyr Tyr Ser Gly Ser
1 5

<210> 656

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 656

Asp Trp Asp Glu Asp
1 5

<210> 657

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 657

Ser Ser Ser Ser Ser Tyr
1 5

<210> 658
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 658
Asn Pro Ser Gly Gly Val
1 5

<210> 659
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 659
Ile Pro Ile Phe Gly Thr
1 5

<210> 660
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 660
Tyr Tyr Arg Ser Lys Trp Tyr
1 5

<210> 661
<211> 6
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 661

Ser Gly Ser Gly Gly Ser
1 5

<210> 662

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 662

Ser Asp Ser Gly Val Ser
1 5

<210> 663

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 663

Asn Trp Lys Gly Asn Ser
1 5

<210> 664

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 664

Asn Thr Tyr Thr Gly Glu
1 5

<210> 665

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 665

Asn Thr Glu Thr Arg Glu
1 5

<210> 666

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 666

Asn Thr Glu Ser Gly Val
1 5

<210> 667

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 667

Asn Thr Glu Thr Gly Glu
1 5

<210> 668

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 668

Gly Phe Ala Leu Ser Asn His Gly Met Ser
1 5 10

<210> 669

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 669

Gly Phe Thr Phe Ser Asn Tyr Ala Met Ser
1 5 10

<210> 670

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 670

Gly Phe Thr Phe Asp Asp Tyr Ala Met His
1 5 10

<210> 671

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 671

Gly Tyr Ile Phe Asp Asn Phe Gly Ile Asn
1 5 10

<210> 672

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 672

Gly Phe Thr Phe Ser Ser Asp Ala Met Thr
1 5 10

<210> 673

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 673

Gly Tyr Thr Phe Ser Asn Tyr Gly Ile Thr
1 5 10

<210> 674

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 674

Gly Phe Thr Phe Ser Asp Tyr Tyr Met Ser
1 5 10

<210> 675

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 675

Gly	Gly	Ser	Ile	Ser	Ser	Ser	Tyr	Tyr	Tyr	Trp	Gly
1				5						10	

<210> 676

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 676

Gly	Phe	Ser	Leu	Arg	Thr	Ser	Gly	Met	Cys	Val	Ser
1				5						10	

<210> 677

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 677

Gly	Phe	Thr	Phe	Ser	Ser	Tyr	Ser	Met	Asn
1				5					10

<210> 678

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 678

Gly Tyr Thr Val Thr Ser His Tyr Ile His
1 5 10

<210> 679

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 679

Gly Gly Ser Ile Ser Ser Gly Gly Tyr Tyr Trp Ser
1 5 10

<210> 680

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 680

Gly Gly Thr Phe Ser Ser Tyr Ala Ile Ser
1 5 10

<210> 681

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 681

Gly Asp Ser Val Ser Ser Asn Ser Ala Ala Trp Asn
1 5 10

<210> 682
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 682
 Gly Phe Thr Phe Ser Ser Tyr Ala Met Ser
 1 5 10

<210> 683
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 683
 Gly Ile Thr Phe Ser Arg Tyr Pro Met Ser
 1 5 10

<210> 684
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 684
 Gly Phe Ser Phe Ser Ser Tyr Ala Met Ser
 1 5 10

<210> 685
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 685

Gly Tyr Thr Phe Thr Asn Phe Gly Met Asn
1 5 10

<210> 686

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 686

Gly Tyr Thr Phe Thr Asp Tyr Ser Ile Asn
1 5 10

<210> 687

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 687

Gly Tyr Thr Phe Arg His Tyr Ser Met Asn
1 5 10

<210> 688

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 688

Gly Tyr Thr Phe Thr His Tyr Ser Met Asn
 1 5 10

<210> 689

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 peptide

<400> 689

Asp Tyr Gly Val Ser
 1 5

<210> 690

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 peptide

<400> 690

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys Ser
 1 5 10 15

<210> 691

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 peptide

<400> 691

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys Ser
 1 5 10 15

<210> 692

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 692

Val	Ile	Trp	Gly	Ser	Glu	Thr	Thr	Tyr	Tyr	Gln	Ser	Ser	Leu	Lys	Ser
1				5				10					15		

<210> 693

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 693

Val	Ile	Trp	Gly	Ser	Glu	Thr	Thr	Tyr	Tyr	Asn	Ser	Ser	Leu	Lys	Ser
1				5				10					15		

<210> 694

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 694

His	Tyr	Tyr	Tyr	Gly	Gly	Ser	Tyr	Ala	Met	Asp	Tyr
1				5				10			

<210> 695

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 695

Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn
1 5 10

<210> 696

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 696

His Thr Ser Arg Leu His Ser
1 5

<210> 697

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 697

Gln Gln Gly Asn Thr Leu Pro Tyr Thr
1 5

<210> 698

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 698

Glu Val Lys Leu Gln Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1 5 10 15

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Ser Leu Ser Val Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr
20 25 30

Gly Val Ser Trp Ile Arg Gln Pro Pro Arg Lys Gly Leu Glu Trp Leu
35 40 45

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ala Leu Lys
50 55 60

Ser Arg Leu Thr Ile Ile Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65 70 75 80

Lys Met Asn Ser Leu Gln Thr Asp Asp Thr Ala Ile 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 Ser Val Thr Val Ser Ser
115 120

<210> 699

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 699

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

NOV-001W0_SL.txt

Gly Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser 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> 700

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 700

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

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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> 701

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 701

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 Asn 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

NOV-001W0_SL.txt

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> 702

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 702

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
100 105

<210> 703

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 703

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> 704

<211> 242

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 704

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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	Ser	Ser	Ser	Leu	Lys	Ser	Arg	Val	Thr	Ile	Ser	180	185	190	

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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> 705

<211> 242

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 705

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

NOV-001WO_SL.txt

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> 706

<211> 242

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 706

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 Ser 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

NOV-001W0_SL.txt

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> 707

<211> 242

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 707

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

NOV-001W0_SL.txt

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> 708

<211> 247

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 708

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 Gly Gly Gly Gly Ser Gln
 115 120 125

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
 130 135 140

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
 145 150 155 160

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Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
165 170 175

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Ser Ser Ser Leu Lys Ser
180 185 190

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
195 200 205

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
210 215 220

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
225 230 235 240

Thr Leu Val Thr Val Ser Ser
245

<210> 709

<211> 247

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 709

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

NOV-001W0_SL.txt

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 Gly Gly Gly Gly Ser Gln
115 120 125

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
130 135 140

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
145 150 155 160

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
165 170 175

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser
180 185 190

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
195 200 205

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
210 215 220

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
225 230 235 240

Thr Leu Val Thr Val Ser Ser
245

<210> 710

<211> 247

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 710

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 Ser 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 Gly Gly Gly Gly Ser Glu Ile Val Met
130 135 140

NOV-001W0_SL.txt

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
145 150 155 160

Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
180 185 190

Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
225 230 235 240

Gly Thr Lys Leu Glu Ile Lys
245

<210> 711

<211> 247

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 711

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

NOV-001W0_SL.txt

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 Gly Gly Gly Gly Ser Glu Ile Val Met
130 135 140

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
145 150 155 160

Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
180 185 190

Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
225 230 235 240

Gly Thr Lys Leu Glu Ile Lys
245

<210> 712

<211> 247

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 712

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 Gly Gly Gly Gly Ser Gln
115 120 125

NOV-001WO_SL.txt

Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr
130 135 140

Leu Ser Leu Thr Cys Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly
145 150 155 160

Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly
165 170 175

Val Ile Trp Gly Ser Glu Thr Thr Tyr Tyr Asn Ser Ser Leu Lys Ser
180 185 190

Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys
195 200 205

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys
210 215 220

His Tyr Tyr Tyr Gly Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly
225 230 235 240

Thr Leu Val Thr Val Ser Ser
245

<210> 713

<211> 247

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 713

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

NOV-001W0_SL.txt

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 Asn 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 Gly Gly Gly Gly Ser Glu Ile Val Met
130 135 140

Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr
145 150 155 160

Leu Ser Cys Arg Ala Ser Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr
165 170 175

Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr His Thr Ser
180 185 190

Arg Leu His Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly
195 200 205

Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala
210 215 220

Val Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln
225 230 235 240

Gly Thr Lys Leu Glu Ile Lys
245

<210> 714

<211> 242

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 714

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

NOV-001WO_SL.txt

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 Asn 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> 715

<211> 242

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 715

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 5 10 15

NOV-001WO_SL.txt

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 Asn 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> 716
 <211> 4
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 716
 Gly Phe Leu Gly
 1

<210> 717
 <211> 4
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 717
 Ala Leu Ala Leu
 1

<210> 718
 <211> 4
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 718

Arg Gly Asp Ser

1

<210> 719

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 719

Gly Val Ser Leu Pro Asp Tyr

1

5

<210> 720

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 720

Trp Gly Ser Glu Thr

1

5

<210> 721

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 721

Ser Gln Asp Ile Ser Lys Tyr

1

5

<210> 722
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 722
His Thr Ser
1

<210> 723
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 723
Gly Asn Thr Leu Pro Tyr
1 5

<210> 724
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 724
Gln Asp Ile Ser Lys Tyr
1 5

<210> 725
<211> 8
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 725

Gly Phe Thr Phe Asn Thr Tyr Ala
1 5

<210> 726

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 726

Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr
1 5 10

<210> 727

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 727

Thr Gly Ala Val Thr Thr Ser Asn Tyr
1 5

<210> 728

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 728

Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro
 1 5 10

<210> 729

<211> 227

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 729

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 Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
 130 135 140

NOV-001W0_SL.txt

Leu Trp 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> 730

<211> 474

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 730

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

NOV-001W0_SL.txt

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

NOV-001W0_SL.txt

Ile Lys Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys
245 250 255

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
260 265 270

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
275 280 285

Val Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
290 295 300

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
305 310 315 320

Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
325 330 335

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
340 345 350

Lys Ala Leu Ala Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
355 360 365

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Asp Glu
370 375 380

Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr
385 390 395 400

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
405 410 415

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
420 425 430

NOV-001WO_SL.txt

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
435 440 445

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
450 455 460

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
465 470

<210> 731

<211> 227

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 731

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

NOV-001WO_SL.txt

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 Asp Glu Leu 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 His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

<210> 732

<211> 486

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 732

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

NOV-001W0_SL.txt

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 Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg
195 200 205

NOV-001W0_SL.txt

Phe Ser Gly Ser Leu Leu Gly Asp Lys Ala Ala Leu Thr Leu Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Glu Tyr Phe Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly
245 250 255

Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
260 265 270

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
275 280 285

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala
290 295 300

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
305 310 315 320

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
325 330 335

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
340 345 350

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala
355 360 365

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
370 375 380

Pro Gln Val Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
385 390 395 400

NOV-001W0_SL.txt

Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile
405 410 415

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
420 425 430

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys
435 440 445

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
450 455 460

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
465 470 475 480

Ser Leu Ser Pro Gly Lys
485

<210> 733

<211> 187

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 733

Phe Ser Gln Gln Ile Tyr Gly Val Val Tyr Gly Asn Val Thr Phe His
1 5 10 15

Val Pro Ser Asn Val Pro Leu Lys Glu Val Leu Trp Lys Lys Gln Lys
20 25 30

Asp Lys Val Ala Glu Leu Glu Asn Ser Glu Phe Arg Ala Phe Ser Ser
35 40 45

Phe Lys Asn Arg Val Tyr Leu Asp Thr Val Ser Gly Ser Leu Thr Ile
50 55 60

NOV-001WO_SL.txt

Tyr Asn Leu Thr Ser Ser Asp Glu Asp Glu Tyr Glu Met Glu Ser Pro
65 70 75 80

Asn Ile Thr Asp Thr Met Lys Phe Phe Leu Tyr Val Leu Glu Ser Leu
85 90 95

Pro Ser Pro Thr Leu Thr Cys Ala Leu Thr Asn Gly Ser Ile Glu Val
100 105 110

Gln Cys Met Ile Pro Glu His Tyr Asn Ser His Arg Gly Leu Ile Met
115 120 125

Tyr Ser Trp Asp Cys Pro Met Glu Gln Cys Lys Arg Asn Ser Thr Ser
130 135 140

Ile Tyr Phe Lys Met Glu Asn Asp Leu Pro Gln Lys Ile Gln Cys Thr
145 150 155 160

Leu Ser Asn Pro Leu Phe Asn Thr Thr Ser Ser Ile Ile Leu Thr Thr
165 170 175

Cys Ile Pro Ser Ser Gly His Ser Arg His Arg
180 185

<210> 734

<211> 419

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 734

Phe Ser Gln Gln Ile Tyr Gly Val Val Tyr Gly Asn Val Thr Phe His
1 5 10 15

NOV-001WO_SL.txt

Val Pro Ser Asn Val Pro Leu Lys Glu Val Leu Trp Lys Lys Gln Lys
20 25 30

Asp Lys Val Ala Glu Leu Glu Asn Ser Glu Phe Arg Ala Phe Ser Ser
35 40 45

Phe Lys Asn Arg Val Tyr Leu Asp Thr Val Ser Gly Ser Leu Thr Ile
50 55 60

Tyr Asn Leu Thr Ser Ser Asp Glu Asp Glu Tyr Glu Met Glu Ser Pro
65 70 75 80

Asn Ile Thr Asp Thr Met Lys Phe Phe Leu Tyr Val Leu Glu Ser Leu
85 90 95

Pro Ser Pro Thr Leu Thr Cys Ala Leu Thr Asn Gly Ser Ile Glu Val
100 105 110

Gln Cys Met Ile Pro Glu His Tyr Asn Ser His Arg Gly Leu Ile Met
115 120 125

Tyr Ser Trp Asp Cys Pro Met Glu Gln Cys Lys Arg Asn Ser Thr Ser
130 135 140

Ile Tyr Phe Lys Met Glu Asn Asp Leu Pro Gln Lys Ile Gln Cys Thr
145 150 155 160

Leu Ser Asn Pro Leu Phe Asn Thr Thr Ser Ser Ile Ile Leu Thr Thr
165 170 175

Cys Ile Pro Ser Ser Gly His Ser Arg His Arg Gly Gly Gly Gly Ser
180 185 190

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
195 200 205

NOV-001W0_SL.txt

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
210 215 220

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser His
225 230 235 240

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
245 250 255

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
260 265 270

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
275 280 285

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile
290 295 300

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
305 310 315 320

Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
325 330 335

Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
340 345 350

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
355 360 365

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val
370 375 380

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
385 390 395 400

NOV-001W0_SL.txt

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
 405 410 415

Pro Gly Lys

<210> 735

<211> 223

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 735

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 Ala Ser Thr Lys Gly Pro Ser Val
 115 120 125

NOV-001WO_SL.txt

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
210 215 220

<210> 736

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 736

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

NOV-001W0_SL.txt

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 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> 737

<211> 227

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 737

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	Gly	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			

Cys	Thr	Leu	Pro	Pro	Ser	Arg	Asp	Glu	Leu	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 His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
210 215 220

Pro Gly Lys
225

<210> 738
<211> 719
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 738
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

NOV-001W0_SL.txt

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 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 Glu Val Gln Leu Val Glu Ser
225 230 235 240

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala
245 250 255

Ala Ser Gly Phe Thr Phe Asn Thr Tyr Ala Met Asn Trp Val Arg Gln
260 265 270

NOV-001W0_SL.txt

Ala Ser Gly Lys Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr
 275 280 285

Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr
 290 295 300

Ile Ser Arg Asp Asp Ser Lys Ser Thr Leu Tyr Leu Gln Met Asn Ser
 305 310 315 320

Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn
 325 330 335

Phe Gly Asn Ser Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr
 340 345 350

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 355 360 365

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ala Val Val Thr Gln
 370 375 380

Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys
 385 390 395 400

Arg Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val
 405 410 415

Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Asn
 420 425 430

Lys Arg Ala Pro Trp Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly
 435 440 445

Asp Lys Ala Ala Leu Thr Leu Ser Gly Ala Gln Pro Glu Asp Glu Ala
 450 455 460

NOV-001W0_SL.txt

Glu Tyr Phe Cys Ala Leu Trp Tyr Ser Asn Leu Trp Val Phe Gly Gly
465 470 475 480

Gly Thr Lys Leu Thr Val Leu Gly Gly Gly Gly Ser Asp Lys Thr His
485 490 495

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
500 505 510

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
515 520 525

Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu Asp Pro Glu
530 535 540

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
545 550 555 560

Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser
565 570 575

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
580 585 590

Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu Lys Thr Ile
595 600 605

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro
610 615 620

Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Ser Cys Ala
625 630 635 640

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
645 650 655

NOV-001W0_SL.txt

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
660 665 670

Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg
675 680 685

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
690 695 700

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710 715

<210> 739

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 739

Gly Gly Gly Ser

1

<210> 740

<211> 227

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 740

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

NOV-001W0_SL.txt

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
 35 40 45

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
 50 55 60

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr
 65 70 75 80

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
 85 90 95

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
 100 105 110

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
 115 120 125

Tyr Thr Leu Pro Pro Cys Arg Glu Glu Met Thr Lys Asn Gln Val Ser
 130 135 140

Leu Trp 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 Arg Tyr Thr Gln Lys Ser Leu Ser Leu Ser
 210 215 220

Pro Gly Lys
225

<210> 741

<211> 418

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 741

Phe Ser Gln Gln Ile Tyr Gly Val Val Tyr Gly Asn Val Thr Phe His
1 5 10 15

Val Pro Ser Asn Val Pro Leu Lys Glu Val Leu Trp Lys Lys Gln Lys
20 25 30

Asp Lys Val Ala Glu Leu Glu Asn Ser Glu Phe Arg Ala Phe Ser Ser
35 40 45

Phe Lys Asn Arg Val Tyr Leu Asp Thr Val Ser Gly Ser Leu Thr Ile
50 55 60

Tyr Asn Leu Thr Ser Ser Asp Glu Asp Glu Tyr Glu Met Glu Ser Pro
65 70 75 80

Asn Ile Thr Asp Thr Met Lys Phe Phe Leu Tyr Val Leu Glu Ser Leu
85 90 95

Pro Ser Pro Thr Leu Thr Cys Ala Leu Thr Asn Gly Ser Ile Glu Val
100 105 110

Gln Cys Met Ile Pro Glu His Tyr Asn Ser His Arg Gly Leu Ile Met
115 120 125

Tyr Ser Trp Asp Cys Pro Met Glu Gln Cys Lys Arg Asn Ser Thr Ser
130 135 140

NOV-001W0_SL.txt

Ile Tyr Phe Lys Met Glu Asn Asp Leu Pro Gln Lys Ile Gln Cys Thr
145 150 155 160

Leu Ser Asn Pro Leu Phe Asn Thr Thr Ser Ser Ile Ile Leu Thr Thr
165 170 175

Cys Ile Pro Ser Ser Gly His Ser Arg His Arg Gly Gly Gly Ser Asp
180 185 190

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
195 200 205

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
210 215 220

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
225 230 235 240

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
245 250 255

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg
260 265 270

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
275 280 285

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
290 295 300

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
305 310 315 320

Thr Leu Pro Pro Cys Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu
325 330 335

NOV-001W0_SL.txt

Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 340 345 350

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
 355 360 365

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
 370 375 380

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
 385 390 395 400

Glu Ala Leu His Asn Arg Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
 405 410 415

Gly Lys

<210> 742

<211> 494

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 742

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 Pro Tyr
 20 25 30

Ser Val Phe Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

NOV-001W0_SL.txt

Ser Ser Ile Asn Thr Asp Ser Thr Tyr Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Glu Asn Ser Ile Phe
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 Asp Arg Ser Tyr Tyr Ala Phe Ser Ser Gly Ser Leu Ser Asp
100 105 110

Tyr Tyr Tyr Gly Leu Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val
115 120 125

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Gly Gly Ser Asp Ile Val Met Thr Gln Ser Pro Leu Ser
145 150 155 160

Leu Ser Val Thr Pro Gly Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser
165 170 175

Gln Ser Leu Leu His Thr Asn Leu Tyr Asn Tyr Leu Asp Trp Tyr Val
180 185 190

Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu Ile Tyr Leu Ala Ser Asn
195 200 205

Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr
210 215 220

Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Thr Glu Asp Val Gly Val
225 230 235 240

NOV-001W0_SL.txt

Tyr Tyr Cys Met Gln Ala Leu Gln Ile Pro Arg Thr Phe Gly Gln Gly
245 250 255

Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Asp Lys Thr His Thr
260 265 270

Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
275 280 285

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
290 295 300

Glu Val Thr Cys Val Val Val Ala Val Ser His Glu Asp Pro Glu Val
305 310 315 320

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
325 330 335

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
340 345 350

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
355 360 365

Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu Lys Thr Ile Ser
370 375 380

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
385 390 395 400

Cys Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val
405 410 415

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
420 425 430

NOV-001WO_SL.txt

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
435 440 445

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
450 455 460

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
465 470 475 480

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
485 490

<210> 743

<211> 719

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 743

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

NOV-001WO_SL.txt

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 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 Glu Val Gln Leu Val Glu Ser
225 230 235 240

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala
245 250 255

Ala Ser Gly Phe Thr Phe Asn Thr Tyr Ala Met Asn Trp Val Arg Gln
260 265 270

Ala Ser Gly Lys Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr
275 280 285

NOV-001W0_SL.txt

Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr
290 295 300

Ile Ser Arg Asp Asp Ser Lys Ser Thr Leu Tyr Leu Gln Met Asn Ser
305 310 315 320

Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn
325 330 335

Phe Gly Asn Ser Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr
340 345 350

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser
355 360 365

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ala Val Val Thr Gln
370 375 380

Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys
385 390 395 400

Arg Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val
405 410 415

Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Asn
420 425 430

Lys Arg Ala Pro Trp Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly
435 440 445

Asp Lys Ala Ala Leu Thr Leu Ser Gly Ala Gln Pro Glu Asp Glu Ala
450 455 460

Glu Tyr Phe Cys Ala Leu Trp Tyr Ser Asn Leu Trp Val Phe Gly Gly
465 470 475 480

NOV-001W0_SL.txt

Gly Thr Lys Leu Thr Val Leu Gly Gly Gly Gly Ser Asp Lys Thr His
485 490 495

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
500 505 510

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
515 520 525

Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu Asp Pro Glu
530 535 540

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
545 550 555 560

Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser
565 570 575

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
580 585 590

Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu Lys Thr Ile
595 600 605

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro
610 615 620

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Ser Cys Ala
625 630 635 640

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
645 650 655

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
660 665 670

Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg
675 680 685

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
690 695 700

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710 715

<210> 744

<211> 326

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 744

Ser Gln Gln Ile Tyr Gly Val Val Tyr Gly Asn Val Thr Phe His Val
1 5 10 15

Pro Ser Asn Val Pro Leu Lys Glu Val Leu Trp Lys Lys Gln Lys Asp
20 25 30

Lys Val Ala Glu Leu Glu Asn Ser Glu Phe Arg Ala Phe Ser Ser Phe
35 40 45

Lys Asn Arg Val Tyr Leu Asp Thr Val Ser Gly Ser Leu Thr Ile Tyr
50 55 60

Asn Leu Thr Ser Ser Asp Glu Asp Glu Tyr Glu Met Glu Ser Pro Asn
65 70 75 80

Ile Thr Asp Thr Met Lys Phe Phe Leu Tyr Val Leu Glu Ser Gly Gly
85 90 95

NOV-001W0_SL.txt

Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
100 105 110

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
115 120 125

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala
130 135 140

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
145 150 155 160

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala
165 170 175

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
180 185 190

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala
195 200 205

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
210 215 220

Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Glu Glu Met Thr Lys Asn
225 230 235 240

Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
245 250 255

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
260 265 270

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
275 280 285

NOV-001W0_SL.txt

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
290 295 300

Ser Val Met His Glu Ala Leu His Asn Arg Tyr Thr Gln Lys Ser Leu
305 310 315 320

Ser Leu Ser Pro Gly Lys
325

<210> 745

<211> 482

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 745

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

NOV-001W0_SL.txt

Leu 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 Val Val Met Thr Gln
130 135 140

Ser Pro Pro Ser Leu Leu Val Thr Leu Gly Gln Pro Ala Ser Ile Ser
145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Leu His Ser Ser Gly Asn Thr Tyr Leu
165 170 175

Asn Trp Leu Leu Gln Arg Pro Gly Gln Ser Pro Gln Pro Leu Ile Tyr
180 185 190

Leu Val Ser Lys Leu Glu Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Gly Val Glu Ala Glu
210 215 220

Asp Val Gly Val Tyr Tyr Cys Met Gln Phe Thr His Tyr Pro Tyr Thr
225 230 235 240

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Gly Gly Gly Gly Ser Asp
245 250 255

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
260 265 270

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
275 280 285

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu
290 295 300

NOV-001W0_SL.txt

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
305 310 315 320

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
325 330 335

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
340 345 350

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu
355 360 365

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys
370 375 380

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
385 390 395 400

Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
405 410 415

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
420 425 430

Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp
435 440 445

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
450 455 460

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
465 470 475 480

Gly Lys

<210> 746
 <211> 327
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic polypeptide

<400> 746
 Phe Ser Gln Gln Ile Tyr Gly Val Val Tyr Gly Asn Val Thr Phe His
 1 5 10 15

Val Pro Ser Asn Val Pro Leu Lys Glu Val Leu Trp Lys Lys Gln Lys
 20 25 30

Asp Lys Val Ala Glu Leu Glu Asn Ser Glu Phe Arg Ala Phe Ser Ser
 35 40 45

Phe Lys Asn Arg Val Tyr Leu Asp Thr Val Ser Gly Ser Leu Thr Ile
 50 55 60

Tyr Asn Leu Thr Ser Ser Asp Glu Asp Glu Tyr Glu Met Glu Ser Pro
 65 70 75 80

Asn Ile Thr Asp Thr Met Lys Phe Phe Leu Tyr Val Leu Glu Ser Gly
 85 90 95

Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
 100 105 110

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
 115 120 125

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
 130 135 140

NOV-001W0_SL.txt

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
145 150 155 160

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
165 170 175

Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
180 185 190

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
195 200 205

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
210 215 220

Glu Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Glu Glu Met Thr Lys
225 230 235 240

Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
245 250 255

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
260 265 270

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
275 280 285

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
290 295 300

Cys Ser Val Met His Glu Ala Leu His Asn Arg Tyr Thr Gln Lys Ser
305 310 315 320

Leu Ser Leu Ser Pro Gly Lys
325

<210> 747

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 747

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 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

NOV-001W0_SL.txt

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 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 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 His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 748

<211> 640

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 748

Ser Gln Gln Ile Tyr Gly Val Val Tyr Gly Asn Val Thr Phe His Val
1 5 10 15

Pro Ser Asn Val Pro Leu Lys Glu Val Leu Trp Lys Lys Gln Lys Asp
20 25 30

NOV-001W0_SL.txt

Lys Val Ala Glu Leu Glu Asn Ser Glu Phe Arg Ala Phe Ser Ser Phe
35 40 45

Lys Asn Arg Val Tyr Leu Asp Thr Val Ser Gly Ser Leu Thr Ile Tyr
50 55 60

Asn Leu Thr Ser Ser Asp Glu Asp Glu Tyr Glu Met Glu Ser Pro Asn
65 70 75 80

Ile Thr Asp Thr Met Lys Phe Phe Leu Tyr Val Leu Glu Ser Leu Pro
85 90 95

Ser Pro Thr Leu Thr Cys Ala Leu Thr Asn Gly Ser Ile Glu Val Gln
100 105 110

Cys Met Ile Pro Glu His Tyr Asn Ser His Arg Gly Leu Ile Met Tyr
115 120 125

Ser Trp Asp Cys Pro Met Glu Gln Cys Lys Arg Asn Ser Thr Ser Ile
130 135 140

Tyr Phe Lys Met Glu Asn Asp Leu Pro Gln Lys Ile Gln Cys Thr Leu
145 150 155 160

Ser Asn Pro Leu Phe Asn Thr Thr Ser Ser Ile Ile Leu Thr Thr Cys
165 170 175

Ile Pro Ser Ser Gly His Ser Arg His Arg Gly Gly Gly Gly Ser Gly
180 185 190

Gly Gly Gly Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val
195 200 205

Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala
210 215 220

NOV-001WO_SL.txt

Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Gln
225 230 235 240

Ala Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr
245 250 255

Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Asp Lys Ala Ala Leu Thr
260 265 270

Leu Ser Gly Ala Gln Pro Glu Asp Glu Ala Glu Tyr Phe Cys Ala Leu
275 280 285

Trp Tyr Ser Asn Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val
290 295 300

Leu Gly Gln Pro Lys Ala Ala Pro Ser Val Thr Leu Phe Pro Pro Ser
305 310 315 320

Ser Glu Glu Leu Gln Ala Asn Lys Ala Thr Leu Val Cys Leu Ile Ser
325 330 335

Asp Phe Tyr Pro Gly Ala Val Thr Val Ala Trp Lys Ala Asp Ser Ser
340 345 350

Pro Val Lys Ala Gly Val Glu Thr Thr Thr Pro Ser Lys Gln Ser Asn
355 360 365

Asn Lys Tyr Ala Ala Ser Ser Tyr Leu Ser Leu Thr Pro Glu Gln Trp
370 375 380

Lys Ser His Arg Ser Tyr Ser Cys Gln Val Thr His Glu Gly Ser Thr
385 390 395 400

Val Glu Lys Thr Val Ala Pro Thr Glu Cys Ser Gly Ser Asp Lys Thr
405 410 415

NOV-001W0_SL.txt

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
420 425 430

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
435 440 445

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
450 455 460

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
465 470 475 480

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val
485 490 495

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
500 505 510

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
515 520 525

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
530 535 540

Pro Pro Cys Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Trp Cys
545 550 555 560

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
565 570 575

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
580 585 590

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
595 600 605

NOV-001W0_SL.txt

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
610 615 620

Leu His Asn Arg Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
625 630 635 640

<210> 749

<211> 228

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 749

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 Ala Ser Thr
115 120 125

NOV-001W0_SL.txt

Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
130 135 140

Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu
145 150 155 160

Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His
165 170 175

Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser
180 185 190

Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys
195 200 205

Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu
210 215 220

Pro Lys Ser Cys
225

<210> 750

<211> 682

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 750

Ser Gln Gln Ile Tyr Gly Val Val Tyr Gly Asn Val Thr Phe His Val
1 5 10 15

Pro Ser Asn Val Pro Leu Lys Glu Val Leu Trp Lys Lys Gln Lys Asp
20 25 30

NOV-001W0_SL.txt

Lys Val Ala Glu Leu Glu Asn Ser Glu Phe Arg Ala Phe Ser Ser Phe
35 40 45

Lys Asn Arg Val Tyr Leu Asp Thr Val Ser Gly Ser Leu Thr Ile Tyr
50 55 60

Asn Leu Thr Ser Ser Asp Glu Asp Glu Tyr Glu Met Glu Ser Pro Asn
65 70 75 80

Ile Thr Asp Thr Met Lys Phe Phe Leu Tyr Val Leu Glu Ser Leu Pro
85 90 95

Ser Pro Thr Leu Thr Cys Ala Leu Thr Asn Gly Ser Ile Glu Val Gln
100 105 110

Cys Met Ile Pro Glu His Tyr Asn Ser His Arg Gly Leu Ile Met Tyr
115 120 125

Ser Trp Asp Cys Pro Met Glu Gln Cys Lys Arg Asn Ser Thr Ser Ile
130 135 140

Tyr Phe Lys Met Glu Asn Asp Leu Pro Gln Lys Ile Gln Cys Thr Leu
145 150 155 160

Ser Asn Pro Leu Phe Asn Thr Thr Ser Ser Ile Ile Leu Thr Thr Cys
165 170 175

Ile Pro Ser Ser Gly His Ser Arg His Arg Gly Gly Gly Gly Ser Gly
180 185 190

Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
195 200 205

Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr
210 215 220

NOV-001W0_SL.txt

Phe Asn Thr Tyr Ala Met Asn Trp Val Arg Gln Ala Ser Gly Lys Gly
225 230 235 240

Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr
245 250 255

Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp
260 265 270

Ser Lys Ser Thr Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp
275 280 285

Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr
290 295 300

Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
305 310 315 320

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
325 330 335

Gly Gly Gly Gly Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr
340 345 350

Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly
355 360 365

Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly
370 375 380

Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp
385 390 395 400

Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Asp Lys Ala Ala Leu
405 410 415

NOV-001W0_SL.txt

Thr Leu Ser Gly Ala Gln Pro Glu Asp Glu Ala Glu Tyr Phe Cys Ala
420 425 430

Leu Trp Tyr Ser Asn Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr
435 440 445

Val Leu Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys
450 455 460

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
465 470 475 480

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
485 490 495

Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
500 505 510

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
515 520 525

Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
530 535 540

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
545 550 555 560

Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
565 570 575

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Glu Glu
580 585 590

Met Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr
595 600 605

NOV-001W0_SL.txt

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
610 615 620

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
625 630 635 640

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
645 650 655

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn Arg Tyr Thr
660 665 670

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
675 680

<210> 751

<211> 679

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 751

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

NOV-001W0_SL.txt

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 Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Asp Lys Ala Ala Leu Thr Leu Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Glu Tyr Phe Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly
245 250 255

Gly Gly Ser Gly Gly Gly Gly Ser Ser Gln Gln Ile Tyr Gly Val Val
260 265 270

NOV-001W0_SL.txt

Tyr Gly Asn Val Thr Phe His Val Pro Ser Asn Val Pro Leu Lys Glu
275 280 285

Val Leu Trp Lys Lys Gln Lys Asp Lys Val Ala Glu Leu Glu Asn Ser
290 295 300

Glu Phe Arg Ala Phe Ser Ser Phe Lys Asn Arg Val Tyr Leu Asp Thr
305 310 315 320

Val Ser Gly Ser Leu Thr Ile Tyr Asn Leu Thr Ser Ser Asp Glu Asp
325 330 335

Glu Tyr Glu Met Glu Ser Pro Asn Ile Thr Asp Thr Met Lys Phe Phe
340 345 350

Leu Tyr Val Leu Glu Ser Leu Pro Ser Pro Thr Leu Thr Cys Ala Leu
355 360 365

Thr Asn Gly Ser Ile Glu Val Gln Cys Met Ile Pro Glu His Tyr Asn
370 375 380

Ser His Arg Gly Leu Ile Met Tyr Ser Trp Asp Cys Pro Met Glu Gln
385 390 395 400

Cys Lys Arg Asn Ser Thr Ser Ile Tyr Phe Lys Met Glu Asn Asp Leu
405 410 415

Pro Gln Lys Ile Gln Cys Thr Leu Ser Asn Pro Leu Phe Asn Thr Thr
420 425 430

Ser Ser Ile Ile Leu Thr Thr Cys Ile Pro Ser Ser Gly His Ser Arg
435 440 445

His Arg Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
450 455 460

NOV-001W0_SL.txt

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
465 470 475 480

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
485 490 495

Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
500 505 510

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
515 520 525

Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
530 535 540

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
545 550 555 560

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
565 570 575

Glu Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Glu Glu Met Thr Lys
580 585 590

Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
595 600 605

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
610 615 620

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
625 630 635 640

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
645 650 655

Cys Ser Val Met His Glu Ala Leu His Asn Arg Tyr Thr Gln Lys Ser
660 665 670

Leu Ser Leu Ser Pro Gly Lys
675

<210> 752
<211> 692
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 752
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

NOV-001WO_SL.txt

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Asp Lys Ala Ala Leu Thr Leu Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Glu Tyr Phe Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly
245 250 255

Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
260 265 270

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
275 280 285

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
290 295 300

NOV-001WO_SL.txt

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
305 310 315 320

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala
325 330 335

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
340 345 350

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
355 360 365

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
370 375 380

Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Glu Glu Met Thr Lys Asn
385 390 395 400

Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
405 410 415

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
420 425 430

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
435 440 445

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
450 455 460

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
465 470 475 480

Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
485 490 495

NOV-001W0_SL.txt

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Gln Gln Ile Tyr Gly
500 505 510

Val Val Tyr Gly Asn Val Thr Phe His Val Pro Ser Asn Val Pro Leu
515 520 525

Lys Glu Val Leu Trp Lys Lys Gln Lys Asp Lys Val Ala Glu Leu Glu
530 535 540

Asn Ser Glu Phe Arg Ala Phe Ser Ser Phe Lys Asn Arg Val Tyr Leu
545 550 555 560

Asp Thr Val Ser Gly Ser Leu Thr Ile Tyr Asn Leu Thr Ser Ser Asp
565 570 575

Glu Asp Glu Tyr Glu Met Glu Ser Pro Asn Ile Thr Asp Thr Met Lys
580 585 590

Phe Phe Leu Tyr Val Leu Glu Ser Leu Pro Ser Pro Thr Leu Thr Cys
595 600 605

Ala Leu Thr Asn Gly Ser Ile Glu Val Gln Cys Met Ile Pro Glu His
610 615 620

Tyr Asn Ser His Arg Gly Leu Ile Met Tyr Ser Trp Asp Cys Pro Met
625 630 635 640

Glu Gln Cys Lys Arg Asn Ser Thr Ser Ile Tyr Phe Lys Met Glu Asn
645 650 655

Asp Leu Pro Gln Lys Ile Gln Cys Thr Leu Ser Asn Pro Leu Phe Asn
660 665 670

Thr Thr Ser Ser Ile Ile Leu Thr Thr Cys Ile Pro Ser Ser Gly His
675 680 685

Ser Arg His Arg
690

<210> 753

<211> 753

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 753

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 Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130 135 140

NOV-001W0_SL.txt

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Asp Lys Ala Ala Leu Thr Leu Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Glu Tyr Phe Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly
245 250 255

Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
260 265 270

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
275 280 285

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala
290 295 300

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
305 310 315 320

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
325 330 335

NOV-001W0_SL.txt

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
340 345 350

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala
355 360 365

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
370 375 380

Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Glu Glu Met Thr Lys Asn
385 390 395 400

Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
405 410 415

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
420 425 430

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
435 440 445

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
450 455 460

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
465 470 475 480

Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
485 490 495

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu
500 505 510

Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys
515 520 525

NOV-001WO_SL.txt

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
530 535 540

Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser
545 550 555 560

Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser Arg Val Thr Ile Ser
565 570 575

Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr
580 585 590

Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
595 600 605

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
610 615 620

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
625 630 635 640

Ser Gly Gly Gly Gly Ser Glu Ile Val Met Thr Gln Ser Pro Ala Thr
645 650 655

Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser
660 665 670

Gln Asp Ile Ser Lys Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Gln
675 680 685

Ala Pro Arg Leu Leu Ile Tyr His Thr Ser Arg Leu His Ser Gly Ile
690 695 700

Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu Thr
705 710 715 720

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln
725 730 735

Gly Asn Thr Leu Pro Tyr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile
740 745 750

Lys

<210> 754

<211> 325

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 754

Ser Gln Gln Ile Tyr Gly Val Val Tyr Gly Asn Val Thr Phe His Val
1 5 10 15

Pro Ser Asn Val Pro Leu Lys Glu Val Leu Trp Lys Lys Gln Lys Asp
20 25 30

Lys Val Ala Glu Leu Glu Asn Ser Glu Phe Arg Ala Phe Ser Ser Phe
35 40 45

Lys Asn Arg Val Tyr Leu Asp Thr Val Ser Gly Ser Leu Thr Ile Tyr
50 55 60

Asn Leu Thr Ser Ser Asp Glu Asp Glu Tyr Glu Met Glu Ser Pro Asn
65 70 75 80

Ile Thr Asp Thr Met Lys Phe Phe Leu Tyr Val Leu Glu Ser Gly Gly
85 90 95

NOV-001W0_SL.txt

Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
100 105 110

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
115 120 125

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala Val
130 135 140

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
145 150 155 160

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly Ser
165 170 175

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
180 185 190

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala Ala
195 200 205

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
210 215 220

Gln Val Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
225 230 235 240

Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
245 250 255

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
260 265 270

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys Leu
275 280 285

NOV-001W0_SL.txt

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
290 295 300

Val Met His Glu Ala Leu His Asn Arg Tyr Thr Gln Lys Ser Leu Ser
305 310 315 320

Leu Ser Pro Gly Lys
325

<210> 755

<211> 729

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 755

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

NOV-001WO_SL.txt

Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
145 150 155 160

Gly Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Asp Lys Ala Ala Leu Thr Leu Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Glu Tyr Phe Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly
245 250 255

Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
260 265 270

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
275 280 285

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala
290 295 300

NOV-001W0_SL.txt

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
305 310 315 320

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
325 330 335

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
340 345 350

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala
355 360 365

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
370 375 380

Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Glu Glu Met Thr Lys Asn
385 390 395 400

Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
405 410 415

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
420 425 430

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
435 440 445

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
450 455 460

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
465 470 475 480

Ser Leu Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
485 490 495

NOV-001W0_SL.txt

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Val Gln Leu Gln Glu
500 505 510

Ser Gly Pro Gly Leu Val Lys Pro Ser Glu Thr Leu Ser Leu Thr Cys
515 520 525

Thr Val Ser Gly Val Ser Leu Pro Asp Tyr Gly Val Ser Trp Ile Arg
530 535 540

Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile Gly Val Ile Trp Gly Ser
545 550 555 560

Glu Thr Thr Tyr Tyr Gln Ser Ser Leu Lys Ser Arg Val Thr Ile Ser
565 570 575

Lys Asp Asn Ser Lys Asn Gln Val Ser Leu Lys Leu Ser Ser Val Thr
580 585 590

Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Lys His Tyr Tyr Tyr Gly
595 600 605

Gly Ser Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val
610 615 620

Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser
625 630 635 640

Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys
645 650 655

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu
660 665 670

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu
675 680 685

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr
690 695 700

Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val
705 710 715 720

Asp Lys Arg Val Glu Pro Lys Ser Cys
725

<210> 756

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 756

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

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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 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

NOV-001W0_SL.txt

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 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 His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 757

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 757

Gly	Tyr	Lys	Phe	Thr	Ser	Tyr	Val	Met	His
1				5				10	

<210> 758

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 758

Tyr	Ile	Asn	Pro	Tyr	Asn	Asp	Val	Thr	Lys	Tyr	Asn	Glu	Lys	Phe	Lys
1				5					10					15	

Gly

<210> 759

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 759

Ser	Tyr	Val	Met	His
1			5	

<210> 760

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 760

Gly Tyr Lys Phe Thr Ser Tyr
1 5

<210> 761

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 761

Asn Pro Tyr Asn Asp Val
1 5

<210> 762

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 762

Gly Tyr Lys Phe Thr Ser Tyr Val
1 5

<210> 763

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 763

Ile Asn Pro Tyr Asn Asp Val Thr
1 5

<210> 764
<211> 13
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 764
Ala Arg Gly Ser Tyr Tyr Asp Tyr Asp Gly Phe Val Tyr
1 5 10

<210> 765
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 765
Thr Ser Ser Val Ser Tyr
1 5

<210> 766
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic
peptide

<400> 766
Ser Ser Val Ser Tyr
1 5

<210> 767
<211> 477
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 767

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 Gly Gly Gly Gly Ser Gly Gly Gly
115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ile Val Leu
130 135 140

Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly Glu Lys Val Thr
145 150 155 160

Met Thr Cys Ser Ala Thr Ser Ser Val Ser Tyr Met His Trp Tyr Gln
165 170 175

NOV-001W0_SL.txt

Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr Asp Thr Ser Lys
180 185 190

Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr
195 200 205

Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu Asp Ala Ala Thr
210 215 220

Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr Phe Gly Ala Gly
225 230 235 240

Thr Lys Leu Glu Leu Lys 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 Ala 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

NOV-001WO_SL.txt

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> 768

<211> 711

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 768

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

NOV-001W0_SL.txt

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 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

NOV-001W0_SL.txt

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Gln Gln Ser
225 230 235 240

Gly Pro Glu Leu Val Lys Pro Gly Ala Ser Val Lys Met Ser Cys Lys
245 250 255

Ala Ser Gly Tyr Lys Phe Thr Ser Tyr Val Met His Trp Val Lys Gln
260 265 270

Lys Pro Gly Gln Gly Leu Glu Trp Ile Gly Tyr Ile Asn Pro Tyr Asn
275 280 285

Asp Val Thr Lys Tyr Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr
290 295 300

Ser Asp Lys Ser Ser Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Thr
305 310 315 320

Ser Glu Asp Ser Ala Val His Tyr Cys Ala Arg Gly Ser Tyr Tyr Asp
325 330 335

Tyr Asp Gly Phe Val Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
340 345 350

Ala Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
355 360 365

Gly Gly Gly Gly Ser Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met
370 375 380

Ser Ala Ser Pro Gly Glu Lys Val Thr Met Thr Cys Ser Ala Thr Ser
385 390 395 400

Ser Val Ser Tyr Met His Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro
405 410 415

NOV-001W0_SL.txt

Lys Arg Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ala
420 425 430

Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser
435 440 445

Ser Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser
450 455 460

Ser Asn Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Gly
465 470 475 480

Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro
485 490 495

Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
500 505 510

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
515 520 525

Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp
530 535 540

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr
545 550 555 560

Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
565 570 575

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu
580 585 590

Ala Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
595 600 605

NOV-001W0_SL.txt

Glu Pro Gln Val Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys
610 615 620

Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp
625 630 635 640

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
645 650 655

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser
660 665 670

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser
675 680 685

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
690 695 700

Leu Ser Leu Ser Pro Gly Lys
705 710

<210> 769

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 769

Gly Tyr Thr Phe Thr Arg Tyr Thr
1 5

<210> 770

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 770

Ile Asn Pro Ser Arg Gly Tyr Thr
1 5

<210> 771

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 771

Ala Arg Tyr Tyr Asp Asp His Tyr Ser Leu Asp Tyr
1 5 10

<210> 772

<211> 477

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 772

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

NOV-001W0_SL.txt

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 Lys
115 120 125

Ser Lys Lys 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

NOV-001W0_SL.txt

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 Ala 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 Ala 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 Ala 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

NOV-001W0_SL.txt

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> 773

<211> 710

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 773

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 Ala Ser Thr Lys Gly Pro Ser Val
 115 120 125

NOV-001W0_SL.txt

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

NOV-001W0_SL.txt

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 Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
485 490 495

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
500 505 510

NOV-001W0_SL.txt

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala
515 520 525

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
530 535 540

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Gly
545 550 555 560

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
565 570 575

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala
580 585 590

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
595 600 605

Pro Gln Val Cys Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
610 615 620

Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr Pro Ser Asp Ile
625 630 635 640

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
645 650 655

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Val Ser Lys
660 665 670

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
675 680 685

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
690 695 700

Ser Leu Ser Pro Gly Lys
705 710

<210> 774
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 774
Gly Phe Asn Ile Lys Asp Thr Tyr Ile His
1 5 10

<210> 775
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 775
Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

<210> 776
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Synthetic peptide

<400> 776

Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr
1 5 10

<210> 777

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 777

Asp Thr Tyr Ile His
1 5

<210> 778

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 778

Gly Phe Asn Ile Lys Asp Thr
1 5

<210> 779

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 779

Tyr Pro Thr Asn Gly Tyr
1 5

<210> 780

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 780

Gly Phe Asn Ile Lys Asp Thr Tyr
1 5

<210> 781

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 781

Ile Tyr Pro Thr Asn Gly Tyr Thr
1 5

<210> 782

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 782

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr
1 5 10

<210> 783

<211> 120

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

NOV-001WO_SL.txt

<400> 783

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 Asn Ile Lys Asp Thr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> 784

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 784

Arg Ala Ser Gln Asp Val Asn Thr Ala Val Ala
1 5 10

<210> 785

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 785

Ser Ala Ser Phe Leu Tyr Ser

1 5

<210> 786

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 786

Gln Gln His Tyr Thr Thr Pro Pro Thr

1 5

<210> 787

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 787

His Tyr Thr Thr Pro Pro

1 5

<210> 788

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 788

Gln Asp Val Asn Thr Ala
1 5

<210> 789

<211> 107

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 789

Asp Ile Gln Met Thr Gln 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 Val Asn Thr Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Arg Ser Gly 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 His Tyr Thr Thr Pro Pro
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105

<210> 790

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 790

Asp	Ile	Gln	Met	Thr	Gln	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	Val	Asn	Thr	Ala
		20						25					30		

Val	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Lys	Ala	Pro	Lys	Leu	Leu	Ile
	35						40					45			

Tyr	Ser	Ala	Ser	Phe	Leu	Tyr	Ser	Gly	Val	Pro	Ser	Arg	Phe	Ser	Gly
	50					55					60				

Ser	Arg	Ser	Gly	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	His	Tyr	Thr	Thr	Pro	Pro
				85					90					95	

Thr	Phe	Gly	Gln	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

NOV-001W0_SL.txt

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> 791

<211> 450

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 791

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 Asn Ile Lys Asp Thr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

NOV-001W0_SL.txt

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr 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

NOV-001W0_SL.txt

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 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 His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
435 440 445

Gly Lys
450

<210> 792

<211> 486

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 792

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 Gly Gly Gly
 115 120 125

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
 130 135 140

Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr Val Ser Pro Gly
 145 150 155 160

NOV-001WO_SL.txt

Gly Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly Ala Val Thr Thr
165 170 175

Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly Gln Ala Pro Arg
180 185 190

Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp Thr Pro Ala Arg
195 200 205

Phe Ser Gly Ser Leu Leu Gly Asp Lys Ala Ala Leu Thr Leu Ser Gly
210 215 220

Ala Gln Pro Glu Asp Glu Ala Glu Tyr Phe Cys Ala Leu Trp Tyr Ser
225 230 235 240

Asn Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Gly
245 250 255

Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
260 265 270

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
275 280 285

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Ala
290 295 300

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
305 310 315 320

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Ala
325 330 335

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
340 345 350

NOV-001W0_SL.txt

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Ala
 355 360 365

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
 370 375 380

Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Glu Glu Met Thr Lys Asn
 385 390 395 400

Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
 405 410 415

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
 420 425 430

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
 435 440 445

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
 450 455 460

Ser Val Met His Glu Ala Leu His Asn Arg Tyr Thr Gln Lys Ser Leu
 465 470 475 480

Ser Leu Ser Pro Gly Lys
 485

<210> 793

<211> 719

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 793

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

NOV-001WO_SL.txt

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Asp Thr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr 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

NOV-001W0_SL.txt

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 Glu Val Gln Leu Val Glu Ser
225 230 235 240

Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala
245 250 255

Ala Ser Gly Phe Thr Phe Asn Thr Tyr Ala Met Asn Trp Val Arg Gln
260 265 270

Ala Ser Gly Lys Gly Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr
275 280 285

Asn Asn Tyr Ala Thr Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr
290 295 300

Ile Ser Arg Asp Asp Ser Lys Ser Thr Leu Tyr Leu Gln Met Asn Ser
305 310 315 320

Leu Lys Thr Glu Asp Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn
325 330 335

Phe Gly Asn Ser Tyr Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr
340 345 350

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
355 360 365

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ala Val Val Thr Gln
370 375 380

Glu Pro Ser Leu Thr Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys
385 390 395 400

NOV-001W0_SL.txt

Arg Ser Ser Thr Gly Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val
405 410 415

Gln Gln Lys Pro Gly Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Asn
420 425 430

Lys Arg Ala Pro Trp Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly
435 440 445

Asp Lys Ala Ala Leu Thr Leu Ser Gly Ala Gln Pro Glu Asp Glu Ala
450 455 460

Glu Tyr Phe Cys Ala Leu Trp Tyr Ser Asn Leu Trp Val Phe Gly Gly
465 470 475 480

Gly Thr Lys Leu Thr Val Leu Gly Gly Gly Gly Ser Asp Lys Thr His
485 490 495

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
500 505 510

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
515 520 525

Pro Glu Val Thr Cys Val Val Val Ala Val Ser His Glu Asp Pro Glu
530 535 540

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
545 550 555 560

Thr Lys Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser
565 570 575

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
580 585 590

NOV-001WO_SL.txt

Cys Lys Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu Lys Thr Ile
595 600 605

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro
610 615 620

Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Ser Cys Ala
625 630 635 640

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
645 650 655

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
660 665 670

Asp Gly Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg
675 680 685

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
690 695 700

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710 715

<210> 794

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
peptide

<400> 794

Gly Tyr Thr Phe Thr Asp Tyr Tyr Met His
1 5 10

<210> 795

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 795

Trp	Ile	Asn	Pro	Asn	Ser	Gly	Gly	Thr	Asn	Tyr	Ala	Gln	Lys	Phe	Gln
1				5				10						15	

Gly

<210> 796

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 796

Gly	Trp	Asp	Phe	Asp	Tyr
1				5	

<210> 797

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 797

Asp	Tyr	Tyr	Met	His
1			5	

<210> 798

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 798

Asn Pro Asn Ser Gly Gly
1 5

<210> 799

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 799

Gly Tyr Thr Phe Thr Asp Tyr Tyr
1 5

<210> 800

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 800

Ile Asn Pro Asn Ser Gly Gly Thr
1 5

<210> 801

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 801

Ala Ser Gly Trp Asp Phe Asp Tyr
1 5

<210> 802

<211> 115

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 802

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Glu Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Met Thr Arg 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 Tyr Cys
85 90 95

Ala Ser Gly Trp Asp Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> 803

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 803

Arg Ala Ser Gln Ser Ile Arg Tyr Tyr Leu Ser

1

5

10

<210> 804

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 804

Thr Ala Ser Ile Leu Gln Asn

1

5

<210> 805

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 805

Leu Gln Thr Tyr Thr Thr Pro Asp

1

5

<210> 806

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 806

Ser Gln Ser Ile Arg Tyr Tyr
1 5

<210> 807

<211> 3

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 807

Thr Ala Ser
1

<210> 808

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 808

Thr Tyr Thr Thr Pro
1 5

<210> 809

<211> 6

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic peptide

<400> 809

Gln Ser Ile Arg Tyr Tyr
1 5

<210> 810
 <211> 10
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic peptide

<400> 810
 Thr Ala Ser Ile Leu Gln Asn Gly Val Pro
 1 5 10

<210> 811
 <211> 106
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic polypeptide

<400> 811
 Asp Ile Val Met Thr Gln 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 Arg Tyr Tyr
 20 25 30

Leu Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

Tyr Thr Ala Ser Ile Leu Gln Asn Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Thr Tyr Thr Thr Pro Asp
 85 90 95

Phe Gly Pro Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 812

<211> 213

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic polypeptide

<400> 812

Asp Ile Val Met Thr Gln 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 Arg Tyr Tyr
 20 25 30

Leu Ser Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

Tyr Thr Ala Ser Ile Leu Gln Asn Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Thr Tyr Thr Thr Pro Asp
 85 90 95

Phe Gly Pro Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala Pro
 100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr
 115 120 125

NOV-001WO_SL.txt

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys
130 135 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu
145 150 155 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser
165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe
195 200 205

Asn Arg Gly Glu Cys
210

<210> 813

<211> 445

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Synthetic
polypeptide

<400> 813

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Glu Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

NOV-001W0_SL.txt

Gln Gly Arg Val Thr Met Thr Arg 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 Tyr Cys
85 90 95

Ala Ser Gly Trp Asp Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
100 105 110

Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
115 120 125

Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
130 135 140

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
145 150 155 160

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
165 170 175

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
180 185 190

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
195 200 205

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys
210 215 220

Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu
225 230 235 240

Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu
245 250 255

NOV-001W0_SL.txt

Val Thr Cys Val Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys
260 265 270

Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys
275 280 285

Pro Arg Glu Glu Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu
290 295 300

Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys
305 310 315 320

Val Ser Asn Lys Ala Leu Ala Ala Pro Ile Glu Lys Thr Ile Ser Lys
325 330 335

Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro Pro Ser
340 345 350

Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Ser Cys Ala Val Lys
355 360 365

Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln
370 375 380

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly
385 390 395 400

Ser Phe Phe Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln
405 410 415

Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn
420 425 430

His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
435 440 445

<210> 814
 <211> 714
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic polypeptide

<400> 814
 Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Glu Lys Pro Gly Ala
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asp Tyr
 20 25 30
 Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
 35 40 45
 Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
 50 55 60
 Gln Gly Arg Val Thr Met Thr Arg 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 Tyr Cys
 85 90 95
 Ala Ser Gly Trp Asp Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr
 100 105 110
 Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro
 115 120 125
 Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
 130 135 140

NOV-001W0_SL.txt

Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala
145 150 155 160

Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly
165 170 175

Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly
180 185 190

Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys
195 200 205

Val Asp Lys Arg Val Glu Pro Lys Ser Cys Gly Gly Gly Gly Ser Gly
210 215 220

Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
225 230 235 240

Gln Pro Gly Gly Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr
245 250 255

Phe Asn Thr Tyr Ala Met Asn Trp Val Arg Gln Ala Ser Gly Lys Gly
260 265 270

Leu Glu Trp Val Gly Arg Ile Arg Ser Lys Tyr Asn Asn Tyr Ala Thr
275 280 285

Tyr Tyr Ala Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asp
290 295 300

Ser Lys Ser Thr Leu Tyr Leu Gln Met Asn Ser Leu Lys Thr Glu Asp
305 310 315 320

Thr Ala Val Tyr Tyr Cys Val Arg His Gly Asn Phe Gly Asn Ser Tyr
325 330 335

NOV-001W0_SL.txt

Val Ser Trp Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser
340 345 350

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
355 360 365

Gly Gly Gly Gly Ser Gln Ala Val Val Thr Gln Glu Pro Ser Leu Thr
370 375 380

Val Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Arg Ser Ser Thr Gly
385 390 395 400

Ala Val Thr Thr Ser Asn Tyr Ala Asn Trp Val Gln Gln Lys Pro Gly
405 410 415

Gln Ala Pro Arg Gly Leu Ile Gly Gly Thr Asn Lys Arg Ala Pro Trp
420 425 430

Thr Pro Ala Arg Phe Ser Gly Ser Leu Leu Gly Asp Lys Ala Ala Leu
435 440 445

Thr Leu Ser Gly Ala Gln Pro Glu Asp Glu Ala Glu Tyr Phe Cys Ala
450 455 460

Leu Trp Tyr Ser Asn Leu Trp Val Phe Gly Gly Gly Thr Lys Leu Thr
465 470 475 480

Val Leu Gly Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys
485 490 495

Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro
500 505 510

Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys
515 520 525

NOV-001W0_SL.txt

Val Val Val Ala Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp
530 535 540

Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu
545 550 555 560

Glu Gln Tyr Gly Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu
565 570 575

His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn
580 585 590

Lys Ala Leu Ala Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly
595 600 605

Gln Pro Arg Glu Pro Gln Val Cys Thr Leu Pro Pro Ser Arg Asp Glu
610 615 620

Leu Thr Lys Asn Gln Val Ser Leu Ser Cys Ala Val Lys Gly Phe Tyr
625 630 635 640

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn
645 650 655

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe
660 665 670

Leu Val Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn
675 680 685

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr
690 695 700

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
705 710

NOV-001WO_SL.txt

<210> 815

<211> 194

<212> PRT

<213> Homo sapiens

<400> 815

Gln Gly His Leu Val His Met Thr Val Val Ser Gly Ser Asn Val Thr
1 5 10 15

Leu Asn Ile Ser Glu Ser Leu Pro Glu Asn Tyr Lys Gln Leu Thr Trp
20 25 30

Phe Tyr Thr Phe Asp Gln Lys Ile Val Glu Trp Asp Ser Arg Lys Ser
35 40 45

Lys Tyr Phe Glu Ser Lys Phe Lys Gly Arg Val Arg Leu Asp Pro Gln
50 55 60

Ser Gly Ala Leu Tyr Ile Ser Lys Val Gln Lys Glu Asp Asn Ser Thr
65 70 75 80

Tyr Ile Met Arg Val Leu Lys Lys Thr Gly Asn Glu Gln Glu Trp Lys
85 90 95

Ile Lys Leu Gln Val Leu Asp Pro Val Pro Lys Pro Val Ile Lys Ile
100 105 110

Glu Lys Ile Glu Asp Met Asp Asp Asn Cys Tyr Leu Lys Leu Ser Cys
115 120 125

Val Ile Pro Gly Glu Ser Val Asn Tyr Thr Trp Tyr Gly Asp Lys Arg
130 135 140

Pro Phe Pro Lys Glu Leu Gln Asn Ser Val Leu Glu Thr Thr Leu Met
145 150 155 160

Pro His Asn Tyr Ser Arg Cys Tyr Thr Cys Gln Val Ser Asn Ser Val
165 170 175

Ser Ser Lys Asn Gly Thr Val Cys Leu Ser Pro Pro Cys Thr Leu Ala
 180 185 190

Arg Ser

<210> 816
 <211> 425
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Synthetic
 polypeptide

<400> 816
 Gln Gly His Leu Val His Met Thr Val Val Ser Gly Ser Asn Val Thr
 1 5 10 15

Leu Asn Ile Ser Glu Ser Leu Pro Glu Asn Tyr Lys Gln Leu Thr Trp
 20 25 30

Phe Tyr Thr Phe Asp Gln Lys Ile Val Glu Trp Asp Ser Arg Lys Ser
 35 40 45

Lys Tyr Phe Glu Ser Lys Phe Lys Gly Arg Val Arg Leu Asp Pro Gln
 50 55 60

Ser Gly Ala Leu Tyr Ile Ser Lys Val Gln Lys Glu Asp Asn Ser Thr
 65 70 75 80

Tyr Ile Met Arg Val Leu Lys Lys Thr Gly Asn Glu Gln Glu Trp Lys
 85 90 95

Ile Lys Leu Gln Val Leu Asp Pro Val Pro Lys Pro Val Ile Lys Ile
 100 105 110

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Glu Lys Ile Glu Asp Met Asp Asp Asn Cys Tyr Leu Lys Leu Ser Cys
 115 120 125

Val Ile Pro Gly Glu Ser Val Asn Tyr Thr Trp Tyr Gly Asp Lys Arg
 130 135 140

Pro Phe Pro Lys Glu Leu Gln Asn Ser Val Leu Glu Thr Thr Leu Met
 145 150 155 160

Pro His Asn Tyr Ser Arg Cys Tyr Thr Cys Gln Val Ser Asn Ser Val
 165 170 175

Ser Ser Lys Asn Gly Thr Val Cys Leu Ser Pro Pro Cys Thr Leu Ala
 180 185 190

Arg Ser Gly Gly Gly Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro
 195 200 205

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
 210 215 220

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
 225 230 235 240

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
 245 250 255

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
 260 265 270

Gln Tyr Ala Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
 275 280 285

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
 290 295 300

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Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
305 310 315 320

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Cys Arg Glu Glu Met
325 330 335

Thr Lys Asn Gln Val Ser Leu Trp Cys Leu Val Lys Gly Phe Tyr Pro
340 345 350

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
355 360 365

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
370 375 380

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
385 390 395 400

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn Arg Tyr Thr Gln
405 410 415

Lys Ser Leu Ser Leu Ser Pro Gly Lys
420 425