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(72) Inventeurs/Inventors:
WILTZIUS, JED, US;
SIEVERS, STUART, US;
PEREZ GARCIA, ARIANNE, US

(73) Propriétaire/Owner:
KITE PHARMA, INC., US

(74) Agent: ROBIC

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(57) Abrégé/Abstract:
Isolated antigen binding molecules that specifically binds to a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) are provided. The antigen binding molecules can be used in the methods provided herein.

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(71) Applicant: **KITE PHARMA, INC.** [US/US]; 2225 Colorado Avenue, Santa Monica, California 90404 (US).

(72) Inventors: **WILTZIUS, Jed**; 2225 Colorado Avenue, Santa Monica, California 90404 (US). **SIEVERS, Stuart**; 2225 Colorado Avenue, Santa Monica, California 90404 (US). **PEREZ GARCIA, Arianne**; 2225 Colorado Avenue, Santa Monica, California 90404 (US).

(74) Agent: **LAMERDIN, John A.** et al.; 2225 Colorado Avenue, Santa Monica, California 90404 (US).

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(54) Title: ANTIGEN BINDING MOLECULES AND METHODS OF USE THEREOF

(57) Abstract: Isolated antigen binding molecules that specifically binds to a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) are provided. The antigen binding molecules can be used in the methods provided herein.

WO 2018/013563 A1

ANTIGEN BINDING MOLECULES AND METHODS OF USE THEREOF

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to United States Provisional Patent Application serial numbers 62/361,420 filed on July 12, 2016 and 62/415,786 and November 1, 2016.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing, which has been submitted electronically in ASCII format. Said ASCII copy, created on July 10, 2017 is named K1033_03_SL.txt and is 571,539 bytes in size.

FIELD OF THE INVENTION

[0003] This disclosure relates to antigen binding molecules, such as antibodies, which specifically bind to the sequence GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising these sequences and cells presenting such molecules, polynucleotides encoding such antigen binding molecules, as well as humanized forms of the antigen binding molecules; methods of using the antigen binding molecules are also disclosed.

BACKGROUND OF THE INVENTION

[0004] Antigen binding molecules, including antibodies, are used in immunotherapy and solid phase-based applications such as biosensors, affinity chromatography, and immunoassays. These antibodies and antigen binding molecules gain their utility by virtue of their ability to specifically bind their targets.

[0005] Linker sequences, which are often peptide-based when employed in biotechnological and biotherapeutic applications, can serve a range of scientifically-relevant applications. For example, a linker can be used as simply a spacer moiety in order to impart a desired structural and/or functional property to a larger molecule. In another example, a

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linker can impart little or no structural or functional properties to a larger molecule, but can be used simply as a distinguishing feature (*e.g.*, a "marker" or "biomarker" or "tag"), uniquely identifying a larger molecule. In still another example, a linker can be used to impart a recognizable feature that can serve as a binding site for an antibody directed against a larger molecule comprising the linker sequence.

[0006] When a linker sequence is used as a distinguishing, detectable or identifiable feature of a larger molecule, an antibody that specifically binds the linker sequence, to the exclusion of other sequences present in the larger molecule, the antibody can serve as a detection agent. Such antibodies can be labeled with a moiety that is detectable under certain conditions. Additional applications for such an antibody include purification and isolation of a molecule comprising the linker, characterization of a molecule in a particular setting, enrichment of the concentration of a population of molecules comprising and/or presenting the linker, and therapeutic applications as well.

[0007] In 1993, Whitlow *et al.* disclosed a synthetic linker peptide comprising the amino acid sequence GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) (Whitlow *et al.*, (1993) *Prot. Eng.* 6(8):989-95). The disclosed peptide was studied as a component of an scFv, and was designed to remove a proteolytic site identified in a previous linker peptide. Whitlow *et al.* concluded that this newly-designed synthetic linker peptide was more stable to proteolysis *in vitro* when compared to the prior linker peptide upon which its sequence was based, and also showed less aggregation compared to the same prior linker. Whitlow *et al.* did not disclose any antigen binding molecules directed to their second generation linker peptide.

[0008] Disclosed herein are antigen binding molecules, including antibodies, that specifically bind the sequence GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising these sequences and cells presenting such molecules. Humanized forms of the antigen binding molecules are also provided. Applications and uses thereof are also disclosed.

SUMMARY OF THE INVENTION

[0009] An isolated antigen binding molecule that specifically binds to a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2),

GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and KPGSG (SEQ ID NO: 500) is provided. In various embodiments, the antigen binding molecule is selected from the group consisting of an antibody, an scFv, a Fab, a Fab', a Fv, a $F(ab')_2$, a dAb, a non-human antibody (e.g., rabbit) a human antibody, a humanized antibody, a chimeric antibody, a monoclonal antibody, a polyclonal antibody, a recombinant antibody, an IgE antibody, an IgD antibody, an IgM antibody, an IgG1 antibody, an IgG1 antibody having at least one mutation in the hinge region, an IgG2 antibody, an IgG2 antibody having at least one mutation in the hinge region, an IgG3 antibody, an IgG1 antibody having at least one mutation in the hinge region, an IgG4 antibody, an IgG4 antibody having at least one mutation in the hinge region, an antibody comprising at least one non-naturally occurring amino acid, and any combination thereof. In a specific embodiment, the antigen binding molecule comprises an antibody.

[0010] In various embodiments, the antigen binding molecule comprises a heavy chain (HC) and in some embodiments, the HC comprises a heavy chain variable region (VH) sequence selected from the group consisting of SEQ ID NOs: 5 and 17. In other embodiments, the variable region (VH) comprises one or more of (a) a CDR1, (b) a CDR2, and (c) a CDR3. In some embodiments, the antigen binding molecule comprises a heavy chain CDR1 selected from the group consisting of SEQ ID NOs: 7 and 19; in other embodiments, the antigen binding molecule comprises a heavy chain CDR2 selected from the group consisting of SEQ ID NOs: 8 and 20, and still other embodiments, the antigen binding molecule comprises a heavy chain CDR3 selected from the group consisting of SEQ ID NOs: 9 and 21. In a various embodiments, an antigen binding molecule comprises a heavy chain CDR1, a heavy chain CDR2, and a heavy chain CDR3, each CDR comprising an amino acid sequence shown in FIGURES 6 and 8, and in further embodiments, an antigen binding molecule comprises a VH amino acid sequence that is at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or about 100% identical to a VH of an antigen binding molecule provided herein, *e.g.*, in the attached Sequence Listing and in FIGURES 6 and 8.

[0011] In various embodiments, the antigen binding molecule comprises a light chain (LC) and in some embodiments, the LC comprises a light chain variable region (VL) sequence selected from the group consisting of SEQ ID NOs: 11 and 23. In other embodiments, the variable region (VL) comprises one or more of (a) a CDR1, (b) a CDR2, and (c) a CDR3. In

some embodiments, the antigen binding molecule comprises a light chain CDR1 selected from the group consisting of SEQ ID NOs: 13 and 25; in other embodiments, the antigen binding molecule comprises a light chain CDR2 selected from the group consisting of SEQ ID NOs: 14 and 26, and still other embodiments, the antigen binding molecule comprises a light chain CDR3 selected from the group consisting of SEQ ID NOs: 15 and 27. In a various embodiments, an antigen binding molecule comprises a light chain CDR1, a light chain CDR2, and a light chain CDR3, each CDR comprising an amino acid sequence shown in FIGURES 6 and 8, and in further embodiments, an antigen binding molecule comprises a VL amino acid sequence that is at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or about 100% identical to a VL of an antigen binding molecule provided herein, *e.g.*, in the attached Sequence Listing and in FIGURES 6 and 8.

[0012] In a specific embodiment, the antigen binding molecule comprises: (a) a VH comprising the amino acid sequence of SEQ ID NO: 5; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 11. In a further specific embodiment, the antigen binding molecule comprises: (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 7; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 8; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 9; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 13; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 14; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 15.

[0013] In a specific embodiment, the antigen binding molecule comprises: (a) a VH comprising the amino acid sequence of SEQ ID NO: 17; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 23. In a further specific embodiment, the antigen binding molecule comprises: (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 19; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 20; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 21; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 25; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 26; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 27.

[0014] In some embodiments, an antigen binding molecule provided herein further comprises a detectable label, which can be selected from the group consisting of a fluorescent label, a photochromic compound, a proteinaceous fluorescent label, a magnetic label, a radiolabel, and a hapten. In a specific embodiment, the detectable label comprises a fluorescent label and is selected from the group consisting of an Atto™ dye, an Alexa Fluor™ dye, quantum dots, Hydroxycoumarin, Aminocouramin, Methoxycourmarin, Cascade Blue™, Pacific Blue™, Pacific Orange™, Lucifer Yellow™, NBD, R-Phycoerythrin (PE), PE-Cy™5 conjugates, PE-Cy7 conjugates, Red 613, PerCP, TruRed™, FluorX™, Fluorescein, BODIPY™-FL, Cy2, Cy3, Cy3B, Cy3.5, Cy5, Cy5.5, Cy7, TRITC, X-Rhodamine, Lissamine™, Rhodamine B, Texas Red™, Allophycocyanin (APC), APC-Cy7 conjugates, Indo-1, Fluo-3, Fluo-4, DCFH, DHR, SNARF™, GFP (Y66H mutation), GFP (Y66F mutation), EBFP, EBFP2, Azurite, GFPuv, T-Sapphire, Cerulean, mCFP, mTurquoise2, ECFP, CyPet, GFP (Y66W mutation), mKeima-Red, TagCFP, AmCyan1, mTFP1, GFP (S65A mutation), Midorishi Cyan, Wild Type GFP, GFP (S65C mutation), TurboGFP, TagGFP, GFP (S65L mutation), Emerald, GFP (S65T mutation), EGFP, Azami Green, ZsGreen1, TagYFP, EYFP, Topaz, Venus, mCitrine, YPet, TurboYFP, ZsYellow1, Kusabira Orange, mOrange, Allophycocyanin (APC), mKO, TurboRFP, tdTomato, TagRFP, DsRed monomer, DsRed2 ("RFP"), mStrawberry, TurboFP602, AsRed2, mRFP1, J-Red, R-phycoerythrin (RPE), B-phycoerythrin (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

[0015] Also provided are compositions comprising the antigen binding molecules, polynucleotides encoding the heavy chain of the antigen binding molecules and polynucleotides encoding the light chain of an antigen binding molecules. Vectors comprising the polynucleotides and cells comprising such vectors form additional aspects of the disclosure. In various embodiments, a cell can be selected from the group consisting of a CHO cell, a Sp2/0 cell, a rabbit cell other mammalian cells, yeast cells, or bacterial cells, such as an *E. coli* cell. Methods of making an antigen binding molecule disclosed herein, which can comprise incubating the cell under suitable conditions, are also provided.

[0016] In another aspect, a method of administering a dose of a medicament to a subject, the dose comprising a preselected number of cells presenting a therapeutic molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO:

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500) is provided. In an embodiment, the method comprises (a) providing a sample of known volume comprising a population comprising a known number of cells, the population known or suspected to be expressing a therapeutic molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500); (b) providing an aliquot of the sample comprising a population of cells presenting a molecule comprising the selected amino acid sequence; (c) providing an antigen binding molecule that specifically binds the selected amino acid sequence and comprises a detectable label; (d) contacting the aliquot of (b) with the antigen binding molecule of (c) under conditions that permit the formation of a binding complex comprising a cell present in the sample and the antigen binding molecule; (e) determining the fraction of cells present in a binding complex of (d) in the aliquot; (f) determining the concentration of cells presenting a molecule comprising the selected amino acid sequence in the sample, based on the fraction of cells determined in (e); (g) determining the volume of the sample that comprises the selected number of cells; and (h) administering the volume of the sample determined in (g) to the subject.

[0017] In some embodiments, (a) the therapeutic molecule is a CAR; and (b) the cell is an immune cell selected from the group consisting of CD8+ T cells, CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells. In specific embodiments, the CAR comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314

(NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof. In some embodiments, the immune cell is a T cell, which can be disposed *in vitro* or *in vivo*, and can be in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media. A T cell can be an autologous T cell or an allogenic T cell. In some embodiments, the dose comprises 0.5 x10^6 cells per kilogram of the subject, 1.0x10^6 cells per kilogram of the subject, 2.0x10^6 cells per kilogram of the subject, 3.0x10^6 cells per kilogram of the subject, 4.0x10^6 cells per kilogram of the subject, or 5.0x10^6 cells per kilogram of the subject. In a specific embodiment, the dose comprises 1.0x10^6 cells per kg. In other embodiments, the detectable label is selected from the group consisting of a fluorescent label, a photochromic compound, a proteinaceous fluorescent label, a magnetic label, a radiolabel, and a hapten. When the detectable label is a fluorescent label, the fluorescent label can be selected from the group consisting of an Atto dye, an Alexafluor dye, quantum dots, Hydroxycoumarin, Aminocouramin, Methoxycourmarin, Cascade Blue, Pacific Blue, Pacific Orange, Lucifer Yellow, NBD, R-Phycoerythrin (PE), PE-Cy5 conjugates, PE-Cy7 conjugates, Red 613, PerCP, TruRed, FluorX, Fluorescein, BODIPY-FL, Cy2, Cy3, Cy3B, Cy3.5, Cy5, Cy5.5, Cy7, TRITC, X-Rhodamine, Lissamine Rhocamine B, Texas Red, Allophycocyanin (APC), APC-Cy7 conjugates, Indo-1, Fluo-3, Fluo-4, DCFH, DHR, SNARF, GFP (Y66H mutation), GFP (Y66F mutation), EBFP, EBFP2, Azurite, GFPuv, T-Sapphire, Cerulean, mCFP, mTurquoise2, ECFP, CyPet, GFP (Y66W mutation), mKeima-Red, TagCFP, AmCyan1, mTFP1, GFP (S65A mutation), Midorishi Cyan, Wild Type GFP, GFP (S65C mutation), TurboGFP, TagGFP, GFP (S65L mutation), Emerald, GFP (S65T mutation), EGFP, Azami Green, ZsGreen1, TagYFP, EYFP, Topaz, Venus, mCitrine, YPet, TurboYFP, ZsYellow1, Kusabira Orange, mOrange, Allophycocyanin (APC), mKO, TurboRFP, tdTomato, TagRFP, DsRed monomer, DsRed2 ("RFP"), mStrawberry, TurboFP602, AsRed2, mRFP1, J-Red, R-phycoerythrin (RPE), B-phycoerythrin (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry. In yet further embodiments, the antigen binding molecule is a humanized antigen binding molecule.

[0018] In another aspect, a method of activating an immune cell expressing a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) is provided. In an embodiment, the method comprises (a) providing a sample comprising an immune cell known or suspected to be expressing a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500); and (b) contacting an antigen binding molecule with the sample, under conditions that permit the formation of a binding complex comprising the antigen binding molecule and two molecules comprising the selected amino acid sequence, wherein the molecules comprising the selected amino acid sequences are disposed on two different immune cells.

[0019] In some embodiments, the immune cell selected from the group consisting of CD8+ T cells, CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells. In specific embodiments, the molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) is a CAR. In further embodiments, the CAR comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1),

CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof. In some embodiments, the immune cell is a T cell, which can be disposed *in vitro* or *in vivo*, and can be in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media. A T cell can be an autologous T cell or an allogenic T cell. In yet further embodiments, the antigen binding molecule is a humanized antigen binding molecule.

[0020] In another aspect, a method of determining a number of cells presenting a molecule in a sample wherein the molecule comprises an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) is provided. In an embodiment, the method comprises (a) providing a sample comprising cells known or suspected to be presenting a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500); (b) contacting the sample of (a) with an antigen binding molecule that specifically binds the selected amino acid sequence and comprises a detectable label, under conditions that permit the formation of a binding complex comprising a cell present in the sample and the antigen binding molecule; and (c) determining the number of cells present in a binding complex of (b) in the sample.

[0021] In some embodiments, the molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2) and GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) is a CAR. In specific embodiments, the CAR comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1),

CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof. In other embodiments, the cells are immune cells selected from the group consisting of CD8+ T cells, CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells. In some embodiments, the cells are T cells, which can be disposed *in vitro* or *in vivo*, and can be in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media. T cells can be autologous T cells or allogenic T cells. In yet further embodiments, the antigen binding molecule is a humanized antigen binding molecule.

[0022] In another aspect, a method of isolating a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) is provided. The molecule can comprise the selected amino acid at the N-terminus, C-terminus, between domains, in loops, or anywhere in the molecule that may or may not disrupt the structure. In an embodiment, the method comprises (a) providing a sample known or suspected to comprise a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500); (b) providing an antigen binding molecule that specifically binds the selected amino acid sequence, optionally

comprising a detectable label; (c) contacting the sample with the antigen binding molecule, under conditions that permit the formation of a binding complex comprising a molecule comprising the selected amino acid sequence and the antigen binding molecule; and (d) separating any molecules not part of a binding complex from formed binding complexes; and (e) separating a formed binding complex into: (1) a molecule comprising the selected amino acid sequence, and (2) an antigen binding molecule.

[0023] In some embodiments, the molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) is a CAR. In specific embodiments, the CAR comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof. In other embodiments, the antigen binding molecule is disposed on a surface selected from the group consisting of an agarose bead, a magnetic bead, a plastic welled plate, a glass welled plate, a ceramic welled plate and

a cell culture bag. In other embodiments, the detectable label is selected from the group consisting of a fluorescent label, a photochromic compound, a proteinaceous fluorescent label, a magnetic label, a radiolabel, and a hapten. When the detectable label is a fluorescent label, the fluorescent label can be selected from the group consisting of an Atto dye, an Alexafluor dye, quantum dots, Hydroxycoumarin, Aminocouramin, Methoxycourmarin, Cascade Blue, Pacific Blue, Pacific Orange, Lucifer Yellow, NBD, R-Phycoerythrin (PE), PE-Cy5 conjugates, PE-Cy7 conjugates, Red 613, PerCP, TruRed, FluorX, Fluorescein, BODIPY-FL, Cy2, Cy3, Cy3B, Cy3.5, Cy5, Cy5.5, Cy7, TRITC, X-Rhodamine, Lissamine Rhocamine B, Texas Red, Allophycocyanin (APC), APC-Cy7 conjugates, Indo-1, Fluo-3, Fluo-4, DCFH, DHR, SNARF, GFP (Y66H mutation), GFP (Y66F mutation), EBFP, EBFP2, Azurite, GFPuv, T-Sapphire, Cerulean, mCFP, mTurquoise2, ECFP, CyPet, GFP (Y66W mutation), mKeima-Red, TagCFP, AmCyan1, mTFP1, GFP (S65A mutation), Midorishi Cyan, Wild Type GFP, GFP (S65C mutation), TurboGFP, TagGFP, GFP (S65L mutation), Emerald, GFP (S65T mutation), EGFP, Azami Green, ZsGreen1, TagYFP, EYFP,Topaz, Venus, mCitrine, YPet, TurboYFP, ZsYellow1, Kusabira Orange, mOrange, Allophycocyanin (APC), mKO, TurboRFP, tdTomato, TagRFP, DsRed monomer, DsRed2 ("RFP"), mStrawberry, TurboFP602, AsRed2, mRFP1, J-Red, R-phycoerythrin (RPE), B-phycoerythrin (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry. In yet further embodiments, the antigen binding molecule is a humanized antigen binding molecule.

[0024] In a further aspect, a method of determining the presence or absence of a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) is provided. In embodiments, the method comprises (a) providing a sample known or suspected to comprise a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500); (b) providing an antigen binding molecule that specifically binds the selected amino acid sequence, the antigen binding protein further comprising a detectable label; (c) contacting the sample with the antigen binding molecule under conditions that permit the formation of a binding complex; (d) separating any molecules not part of a binding complex

from formed binding complexes; and (e) detecting the presence or absence of a binding complex.

[0025] In embodiments, the molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) is a CAR. In further embodiments, the CAR comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof. In other embodiments, the antigen binding molecule is disposed on a surface selected from the group consisting of an agarose bead, a magnetic bead, a plastic welled plate, a glass welled plate, a ceramic welled plate and a cell culture bag. In other embodiments, the detectable label is selected from the group consisting of a fluorescent label, a photochromic compound, a proteinaceous fluorescent label, a magnetic label, a radiolabel, and a hapten. When the detectable label is a fluorescent label, the fluorescent label can be selected from the group consisting of an Atto dye, an

Alexafluor dye, quantum dots, Hydroxycoumarin, Aminocouramin, Methoxycourmarin, Cascade Blue, Pacific Blue, Pacific Orange, Lucifer Yellow, NBD, R-Phycoerythrin (PE), PE-Cy5 conjugates, PE-Cy7 conjugates, Red 613, PerCP, TruRed, FluorX, Fluorescein, BODIPY-FL, Cy2, Cy3, Cy3B, Cy3.5, Cy5, Cy5.5, Cy7, TRITC, X-Rhodamine, Lissamine Rhocamine B, Texas Red, Allophycocyanin (APC), APC-Cy7 conjugates, Indo-1, Fluo-3, Fluo-4, DCFH, DHR, SNARF, GFP (Y66H mutation), GFP (Y66F mutation), EBFP, EBFP2, Azurite, GFPuv, T-Sapphire, Cerulean, mCFP, mTurquoise2, ECFP, CyPet, GFP (Y66W mutation), mKeima-Red, TagCFP, AmCyan1, mTFP1, GFP (S65A mutation), Midorishi Cyan, Wild Type GFP, GFP (S65C mutation), TurboGFP, TagGFP, GFP (S65L mutation), Emerald, GFP (S65T mutation), EGFP, Azami Green, ZsGreen1, TagYFP, EYFP,Topaz, Venus, mCitrine, YPet, TurboYFP, ZsYellow1, Kusabira Orange, mOrange, Allophycocyanin (APC), mKO, TurboRFP, tdTomato, TagRFP, DsRed monomer, DsRed2 ("RFP"), mStrawberry, TurboFP602, AsRed2, mRFP1, J-Red, R-phycoerythrin (RPE), B-phycoerythrin (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry. In yet further embodiments, the antigen binding molecule is a humanized antigen binding molecule.

[0026] Also provided is a method of increasing the concentration of cells presenting a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500). In some embodiments, the method comprises (a) providing a sample comprising cells known or suspected to comprise a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500); (b) providing an antigen binding molecule that specifically binds the selected amino acid sequence and optionally comprises a detectable label; (c) contacting the sample with the antigen binding molecule under conditions that permit the formation of a binding complex comprising molecule comprising the selected amino acid sequence and the antigen binding molecule; (d) removing any components not part of a binding complex; and (e) repeating steps (a)-(d) a desired number of times.

[0027] In embodiments, (a) the molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and

KPGSG (SEQ ID NO: 500) is a CAR; and (b) the cells are immune cells selected from the group consisting of CD8+ T cells, CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells. In further embodiments, the CAR comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof. In some embodiments, the cells are T cells, which can be disposed *in vitro* or *in vivo*, and can be in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media. T cells can be autologous T cells or allogenic T cells. In yet further embodiments, the antigen binding molecule is a humanized antigen binding molecule.

[0028] In still a further aspect, a method of depleting a population of cells (e.g., immune cells) presenting a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) is provided. In embodiments, the method comprises (a) providing a population

of immune cells to be depleted, wherein the immune cells are known or suspected to be expressing a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500); and (b) contacting the immune cells with an antigen binding molecule that specifically binds to (a) the molecule comprising the selected amino acid sequence, and (b) an activating molecule presented on the surface of that immune cell that does not comprise the selected amino acid sequence, under conditions that permit the formation of a ternary binding complex comprising the molecule comprising the molecule comprising the selected amino acid sequence, the activating molecule and the antigen binding molecule.

[0029] In specific embodiments, the molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) is a CAR. In further embodiments, the CAR comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor

protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof. In some embodiments, the immune cell is a T cell, which can be disposed *in vitro* or *in vivo*, and can be in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media. A T cell can be an autologous T cell or an allogenic T cell. In yet further embodiments, the antigen binding molecule is a humanized antigen binding molecule.

[0030] In one aspect, the present invention provides a method of monitoring distribution *in vivo* of a population of cells presenting a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500). In some embodiments, the population of cells are CAR cells. In some embodiments, the present invention provides a method of monitoring distribution *in vivo* of a population of cells presenting a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) comprising providing an antigen binding molecule; and performing a positron emission tomography (PET) scan. In some embodiments, providing the antigen binding molecule stimulates or depletes the CAR T-cells in vivo.

BRIEF DESCRIPTION OF THE FIGURES

[0031] Figure 1A is a ribbon diagram and Figure 1B is a space-filling diagram of an scFv sequence comprising the linker sequence of SEQ ID NO: 1; the linker is shown in gray.

[0032] Figure 2 is series of plots showing the results of flow cytometry experiments performed using cells presenting a chimeric antigen receptor (CAR) comprising the linker sequence of SEQ ID NO: 1; results were generated using 1, 10 or 100 ng of an antibody generated from two different clones (clone 8, left; and clone 16, right), and demonstrate specific binding of the antibodies to the expressed CAR at all three amounts.

[0033] Figure 3 is series of plots showing the results of flow cytometry experiments performed using cells presenting 5 different CARs comprising the linker sequence of SEQ ID NO: 1; and demonstrate specific binding of the antibodies to the expressed CARs.

[0034] Figure 4 is a series of photographs depicting the results of immunohistochemistry (IHC) studies performed using cells presenting a CAR; the upper figures demonstrate the specific binding of antibody Clone 8 and directed against a CAR

comprising the linker sequence of SEQ ID NO: 1 to cells presenting the CAR, while the lower figures demonstrate the specific binding of antibody Clone 16 and directed against a CAR comprising the linker sequence of SEQ ID NO: 1 to cells presenting the CAR.

[0035] Figure 5 is a histogram depicting the results of epitope mapping ELISA experiments performed on the antibodies Clone 8 and Clone 16; the results demonstrate that although all antibodies bind to the full length 18mer (SEQ ID NO: 1), Clone 8 specifically binds to the 10mer subsequence GSGKPGSGEG (SEQ ID NO: 2) and Clone 16 specifically binds to the 8mer subsequence GKPGSGEG (SEQ ID NO: 3). Figure discloses SEQ ID NOS 1, 485-488, 1, and 489-491, respectively, in order of appearance.

[0036] Figure 6 is a series of tables showing the CDR1, 2 and 3 regions of the heavy chain (HC) and light chain (LC) of antibodies secreted by Clones 8 and 16; heavy and light chain CDRs are shown for each antibody using the Kabat (SEQ ID NOS 492, 8, 9, 493, 20, 21, 13-15, and 25-27, respectively, in order of appearance), Chothia (SEQ ID NOS 7-9, 19-21, 13-15, and 25-27, respectively, in order of appearance) and IMGT (SEQ ID NOS 494, 8, 9, 495, 20, 21, 13-15, and 25-27, respectively, in order of appearance) numbering systems.

[0037] Figure 7 is a table showing the 18mer sequence GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) as well as the epitopes on this sequence where the antibodies of clone 8 bind (GSGKPGSGEG; SEQ ID NO: 2 and SGKPGSGE; SEQ ID NO: 499) and where the antibodies of clone 16 bind (GKPGSGEG; SEQ ID NO: 3 and KPGSG; SEQ ID NO: 500).

[0038] Figure 8 is a series of tables showing humanized forms of the antigen binding molecules provided herein.

[0039] Figure 9 is a bar chart indicating regions of SEQ ID NO: 1 where the antigen binding molecules disclosed herein were found to bind via epitope mapping by ELISA. This assay further narrows the linker antibody epitopes from the ELISA shown in Figure 5 using a more narrow range of peptide sequences focusing on the region identified in the previous experiment.

[0040] Figure 10 is the result of Fluorescense activated cell sorting (FACS) plots showing CAR-T cells that were negatively- and positively-gated using the antigen binding molecules disclosed herein.

[0041] Figure 11 is a series of bar charts showing the results of *in vitro* stimulation of CAR-T cells using OKT3 antibodies and the anti-linker antibody disclosed herein. Whereas OKT3 activates all T cells in a given population, the anti-linker MAb preferentially activates

and thereby enriches the population of CAR-T cells over time as shown by using a gradient of CAR+ to CAR- population ratios.

[0042] Figures 12A and 12B are a series of bar charts and plots showing the effects of *in vitro* stimulation of CAR-T positive cells; the figures show that that OKT3 antibodies stimulated all T-cells, while the antigen binding molecules disclosed herein selectively stimulated only CAR-T positive cells.

[0043] Figure 13 shows FDG-PET imaging of female NSG mice previously injected with CAR T cells before and after stimulation with anti-linker Clone 8 Mab.

[0044] Figure 14A and 14B demonstrates the diabody incubated with CAR constructs comprising the peptide GSTSGSGKPGSGEGSTKG leads to increased cell death. As shown in Fig. 14A, as the diabody concentration is increased, a larger median fluorescent intensity is seen in the average of three replicates of CAR constructs containing the specific peptide. When a control CAR or Mock-transduced cells are incubated with the diabody, there is not a significant increase in the amount of cytotoxic dye fluorescence. In Fig. 14B, the percentage of CAR+ T-cells is measured as a function of increasing diabody concentration.

DETAILED DESCRIPTION OF THE INVENTION

[0045] The present disclosure relates to antigen binding molecules, including antibodies, which specifically bind a moiety comprising the sequence GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), as well as humanized forms of the antigen binding molecules, molecules comprising SEQ ID NOs: 1, 2, 3, 499 and/or 500, cells presenting such molecules, polynucleotides encoding the molecules, and vectors comprising the polynucleotides; *in vitro* cells comprising the polynucleotides and vectors are also disclosed.

[0046] Methods of using the disclosed antigen binding molecules are provided. The antigen binding molecules, polynucleotides, vectors, *in vitro* cells and methods described herein can be used in a range of applications, *e.g.*, as reagents to detect the presence of molecules comprising GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3),

SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), and cells presenting such molecules, quantifying the amount of a molecule comprising SEQ ID NOs: 1, 2, 3, 499 and/or 500, molecules and cells presenting such molecules, screening for molecules comprising SEQ ID NOs: 1, 2, 3, 499 and/or 500, and cells presenting such molecules, purifying molecules comprising SEQ ID NOs: 1, 2, 3, 499 and/or 500, and cells presenting such molecules, and biomarker studies focused on molecules comprising SEQ ID NOs: 1, 2, 3, 499 and/or 500, and cells presenting such molecules. Therapeutic uses are also provided, for example applications in which the biological activity of a molecule comprising SEQ ID NOs: 1, 2, 3, 499 and/or 500, and cells presenting such molecules, is modulated (enhanced or repressed), as well as dose ranging studies related to therapeutics comprising SEQ ID NOs: 1, 2, 3, 499 and/or 500, and cells presenting such molecules.

[0047] The antigen binding molecules (antibodies) disclosed herein were generated from hybridomas generated using B-cells of rabbit origin, but can be readily humanized using standard methods known to those of skill in the art, as well as those described herein. Representative humanized forms of the disclosed antigen binding molecules are provided herein.

I. Definitions

[0048] In order that the present disclosure may be more readily understood, certain terms are first defined. As used in this application, except as otherwise expressly provided herein, each of the following terms shall have the meaning set forth below. Additional definitions are set forth throughout the application. The headings provided herein are not limitations of the various aspects of the disclosure, which aspects can be understood by reference to the specification as a whole.

[0049] It is understood that wherever aspects are described herein with the language "comprising," otherwise analogous aspects described in terms of "consisting of" and/or "consisting essentially of" are also provided.

[0050] Units, prefixes, and symbols used herein are provided using their Système International de Unites (SI) accepted form. Numeric ranges are inclusive of the numbers defining the range.

[0051] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure is related. For example, Juo, The Concise Dictionary of Biomedicine and

Molecular Biology, 2nd ed., (2001), CRC Press; The Dictionary of Cell & Molecular Biology, 5th ed., (2013), Academic Press; and The Oxford Dictionary Of Biochemistry And Molecular Biology, Cammack et al. eds., 2nd ed, (2006), Oxford University Press, provide those of skill in the art with a general dictionary for many of the terms used in this disclosure.

[0052] As used herein, the twenty conventional (*e.g.*, naturally occurring) amino acids and their abbreviations follow conventional usage. *See, e.g.*, Immunology - A Synthesis (2nd Edition), Golub and Green, eds., Sinauer Assoc., Sunderland, Mass. (1991). Stereoisomers (*e.g.*, D-amino acids) of the twenty conventional amino acids, unnatural amino acids such as alpha-, alpha-disubstituted amino acids, N-alkyl amino acids, lactic acid, and other unconventional amino acids can also be suitable components for polypeptides of the present invention. Examples of unconventional amino acids include: 4-hydroxyproline, gamma-carboxyglutamate, epsilon-N,N,N-trimethyllysine, e-N-acetyllysine, O-phosphoserine, N-acetylserine, N-formylmethionine, 3-methylhistidine, 5-hydroxylysine, sigma-N-methylarginine, and other similar amino acids and imino acids (*e.g.*, 4-hydroxyproline). In the polypeptide notation used herein, the left-hand direction is the amino terminal direction and the right-hand direction is the carboxy-terminal direction, in accordance with standard usage and convention.

[0053] As used herein, the term the terms "a" and "an" are used per standard convention and mean one or more, unless context dictates otherwise.

[0054] As used herein, the term "about" refers to a value or composition that is within an acceptable error range for the particular value or composition as determined by one of ordinary skill in the art, which will depend in part on how the value or composition is measured or determined, *i.e.*, the limitations of the measurement system. For example, "about" or "comprising essentially of" can mean within one or more than one standard deviation per the practice in the art. Alternatively, "about" or "comprising essentially of" can mean a range of up to 10% (*i.e.*, ±10%). For example, about 5mg can include any number between 4.5 mg and 5.5 mg. Furthermore, particularly with respect to biological systems or processes, the terms can mean up to an order of magnitude or up to 5-fold of a value. When particular values or compositions are provided in the instant disclosure, unless otherwise stated, the meaning of "about" or "comprising essentially of" should be assumed to be within an acceptable error range for that particular value or composition.

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[0055] As described herein, any concentration range, percentage range, ratio range or integer range is to be understood to be inclusive of the value of any integer within the recited range and, when appropriate, fractions thereof (such as one-tenth and one-hundredth of an integer), unless otherwise indicated.

[0056] As used herein, the term "and/or" is to be taken as specific disclosure of each of the two specified features or components with or without the other. Thus, the term "and/or" as used in a phrase such as "A and/or B" herein is intended to include "A and B," "A or B," "A" (alone), and "B" (alone). Likewise, the term "and/or" as used in a phrase such as 'A, B, and/or C" is intended to encompass each of the following aspects: A, B, and C; A, B, or C; A or C; A or B; B or C; A and C; A and B; B and C; A (alone); B (alone); and C (alone).

[0057] As used herein, the term the use of the alternative (*e.g.*, "or") should be understood to mean either one, both, or any combination thereof of the alternatives.

[0058] As used herein, the term "allogeneic" refers to any material derived from one individual which is then introduced to another individual of the same species, *e.g.*, allogeneic T cell transplantation.

[0059] As used herein, the term "antibody" (Ab) includes, without limitation, a glycoprotein immunoglobulin which binds specifically to an antigen. In general, an antibody can comprise at least two heavy (HC) chains and two light (LC) chains interconnected by disulfide bonds, or an antigen binding molecule thereof. Each HC chain comprises a heavy chain variable region (abbreviated herein as VH) and a heavy chain constant region. The heavy chain constant region comprises three constant domains, CH1, CH2 and CH3. Each LC chain comprises a light chain variable region (abbreviated herein as VL) and a light chain constant region. The light chain constant region is comprises one constant domain, CL. The VH and VL regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDRs), interspersed with regions that are more conserved, termed framework regions (FR). Each VH and VL comprises 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 Abs 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 of the classical complement system (C1q).

[0060] The term "antibody" also encompasses an intact immunoglobulin or an antigen binding portion thereof that competes with the intact antibody for specific binding, unless otherwise specified. Antigen binding portions can be produced by recombinant DNA techniques or by enzymatic or chemical cleavage of intact antibodies. Antigen binding portions include, inter alia, Fab, Fab', $F(ab')_2$, Fv, domain antibodies (dAbs), fragments including complementarity determining regions (CDRs), single-chain antibodies (scFv), chimeric antibodies, diabodies, triabodies, tetrabodies, and polypeptides that contain at least a portion of an immunoglobulin that is sufficient to confer specific antigen binding to the polypeptide.

[0061] The term "antibody" includes, both naturally occurring and non-naturally occurring (recombinantly-produced) antibodies, human and non-human antibodies, monospecific antibodies, multispecific antibodies (including bispecific antibodies), immunoglobulins, synthetic antibodies, tetrameric antibodies comprising two heavy chain and two light chain molecules, an antibody light chain monomer, an antibody heavy chain monomer, an antibody light chain dimer, an antibody heavy chain dimer, an antibody light chain-antibody heavy chain pair, intrabodies (*see, e.g.*, Stocks, (2004) *Drug Discovery Today* 9(22):960-66), antibody fusions (which term encompasses antibody-drug conjugates) and which are sometimes referred to herein as "antibody conjugates"), heteroconjugate antibodies, single domain antibodies, monovalent antibodies, single chain antibodies or single-chain Fvs (scFv), camelized antibodies, affybodies, Fab fragments, $F(ab')_2$ fragments, disulfide-linked Fvs (sdFv), anti-idiotypic (anti-Id) antibodies (including, *e.g.*, anti-anti-Id antibodies), minibodies, domain antibodies, synthetic antibodies (sometimes referred to herein as "antibody mimetics"), and antigen-binding fragments thereof. In certain embodiments, antibodies described herein refer to polyclonal antibody populations.

[0062] A non-human antibody can be humanized using recombinant methods to reduce its immunogenicity in humans, as disclosed herein with respect to antibodies that specifically bind GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules. Examples of humanized antibodies are provided herein. Where not expressly stated, and unless the context indicates otherwise, the term "antibody" also includes an antigen-binding fragment of an antigen binding molecule of any of the

aforementioned immunoglobulins, and includes a monovalent and a divalent fragment or portion, and a single chain antibody (*i.e.*, a scFv).

[0063] In various embodiments, an antibody specifically binds GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising these sequences and cells presenting such molecules. In some embodiments, the antibody specifically binds to a CAR (or component thereof) comprising SEQ ID NOs: 1, 2, 3, 499 and/or 500, molecules comprising this sequence, and cells presenting such molecules; cells presenting SEQ ID NOs: 1, 2, 3, 499 and/or 500 can, but need not be, an immune cell, such as a T cell.

[0064] As used herein, the term "antigen" means any molecule that provokes an immune response or is capable of being bound by an antibody or other antigen binding molecule. The immune response can involve either antibody production, or the activation of specific immunologically-competent cells, or both. Those of skill in the art will readily understand that any macromolecule, including virtually all proteins or peptides (including SEQ ID NOs: 1, 2, 3, 499 and/or 500), molecules comprising this sequence and cells presenting such molecules), can serve as an antigen. Generally, an antigen can be endogenously expressed, *i.e.* expressed by genomic DNA, or it can be recombinantly expressed, or it can be chemically synthesized. In one particular embodiment, an antigen comprises all or a portion of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising these sequences, which is optionally conjugated to an adjuvant such as keyhole limpet hemocyanin (KLH).

[0065] As used herein, the term "antigen binding molecule" means a protein comprising a portion that binds to an antigen or target protein and, optionally, a scaffold or framework portion that allows the antigen binding portion to adopt a conformation that promotes binding of the antigen binding molecule to the antigen. Examples of the representative types of antigen binding molecules include a scFv, a human, mouse or rabbit antibody; a humanized antibody; a chimeric antibody; a recombinant antibody; a single chain antibody; a diabody; a triabody; a tetrabody; a Fab fragment; a F(ab')2 fragment; an IgD antibody; an IgE antibody; an IgM antibody; an IgGl antibody; an IgG2 anti-body; an IgG3 antibody; or an IgG4 antibody, and fragments thereof.

[0066] An antigen binding molecule can comprise, for example, an alternative protein scaffold or artificial scaffold with grafted complementarity determining regions (CDRs) or CDR derivatives. Such scaffolds include, but are not limited to, antibody-derived scaffolds comprising mutations introduced to, for example, stabilize the three-dimensional structure of the antigen binding molecule as well as wholly synthetic scaffolds comprising, for example, a biocompatible polymer. *See, e.g.*, Korndorfer et al., 2003, *Proteins: Structure, Function, and Bioinformatics*, 53(1):121-129 (2003); Roque et al., *Biotechnol. Prog.* 20:639-654 (2004). In addition, peptide antibody mimetics ("PAMs") can be used, as well as scaffolds based on antibody mimetics utilizing various components (*e.g.*, fibronectin) as a scaffold. An antigen binding molecule can have, for example, the structure of a naturally occurring immunoglobulin.

[0067] An antigen binding molecule can have one or more binding sites. If there is more than one binding site, the binding sites can be identical to one another or they can be different. For example, a naturally occurring human immunoglobulin typically has two identical binding sites, while a "bispecific" or "bifunctional" antibody has two different binding sites, and is capable of specifically binding two different antigens (*e.g.*, SEQ ID NOs: 1, 2, 3, 499 and/or 500 and a cell surface activator molecule).

[0068] In various embodiments, an antigen binding molecule is an antibody or fragment thereof, including one or more of the complementarity determining regions (CDRs) disclosed herein and shown in FIGURES 6 and 8, which specifically bind GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising SEQ ID NOs: 1, 2, 3, 499 and/or 500, and cells presenting such molecules. In further embodiments, the antigen binding molecule binds to a CAR comprising the SEQ ID NOs: 1, 2, 3, 499 and/or 500, and can be expressed on an immune cell, such as a T cell.

[0069] The term "autologous" refers to any material derived from the same individual to which it is later to be re-introduced. For example, the engineered autologous cell therapy (eACT™) methods described herein involve collection of lymphocytes from a patient, which are then engineered to express a construct, *e.g.*, a CAR construct, and then administered back to the same patient.

[0070] As used herein, the term "binding affinity" means the strength of the sum total of non-covalent interactions between a single binding site of a molecule (*e.g.*, an antigen

binding molecule such as an antibody) and its binding partner (*e.g.*, an antigen). Unless indicated otherwise, as used herein, "binding affinity" refers to intrinsic binding affinity which reflects a 1:1 interaction between members of a binding pair (*e.g.*, antibody and antigen). The affinity of a molecule X for its partner Y can generally be represented by the dissociation constant (K_D). Affinity can be measured and/or expressed in a number of ways known in the art, including, but not limited to, equilibrium dissociation constant (K_D), and equilibrium association constant (K_A). The K_D is calculated from the quotient of k_{off}/k_{on}, whereas K_A is calculated from the quotient of k_{on}/k_{off}. k_{on} refers to the association rate constant of, *e.g.*, an antibody to an antigen, and k_{off} refers to the dissociation of, *e.g.*, an antibody to an antigen. The k_{on} and k_{off} can be determined by standard techniques known to one of ordinary skill in the art, such as BIAcore® or KinExA or surface plasmon resonance.

[0071] As used herein, the term "complementarity determining region" or "CDR" means an amino acid sequence that contributes to antigen binding specificity and affinity. Framework regions can aid in maintaining the proper confirmation of the CDRs to promote binding between the antigen binding molecule and an antigen. There are three CDRs in each of the variable regions of the heavy chain and the light chain, which are designated CDR1, CDR2 and CDR3, for each of the variable regions. The exact boundaries of CDRs have been defined differently according to different systems.

[0072] A number of definitions of the CDRs are commonly in use: Kabat numbering, Chothia numbering, AbM numbering, or contact numbering. The AbM definition is a compromise between the Kabat and Chothia systems, and is used by Oxford Molecular's AbM antibody modelling software.

[0073] The system described by Kabat (Kabat *et al.*, Sequences of Proteins of Immunological Interest (National Institutes of Health, Bethesda, Md. (1987) and (1991)) provides a residue numbering system applicable to any variable region of an antibody, and also provides precise residue boundaries defining the three CDRs.

[0074] Chothia and coworkers (Chothia and Lesk, (1987) *J. Mol. Biol.*, 196:901-917; and Chothia *et al.*, (1989) *Nature*, 342: 877-883) found that certain sub-portions within Kabat CDRs adopt nearly identical peptide backbone conformations, despite having great diversity at the level of amino acid sequence. Chothia CDRs have boundaries that overlap with Kabat CDRs. Other boundaries defining CDRs overlapping with the Kabat CDRs have been described by Padlan et al. ((1995) *FASEB J.*, 9:133-139) and MacCallum *et al.* ((1996) *J. Mol. Biol.*, 262(5):732-745). Still other CDR boundary definitions may not strictly follow

one of the described systems, but will nonetheless overlap with the Kabat CDRs, although they may be shortened or lengthened in light of prediction or experimental findings that particular residues or groups of residues or even entire CDRs do not significantly impact antigen binding. The methods used herein may utilize CDRs defined according to any of these systems, although exemplary embodiments use ***Chothia*** defined CDRs.

[0075] Table A defines CDRs using each numbering system. The contact definition is based on an analysis of the available complex crystal structures.

Table A

Loop	Kabat	AbM	Chothia	Contact
L1	L24--L34	L24--L34	L24--L34	L30--L36
L2	L50--L56	L50--L56	L50--L56	L46--L55
L3	L89--L97	L89--L97	L89--L97	L89--L96
H1	H31--H35B	H26--H35B	H26--H32..34	H30--H35B
H1	H31--H35	H26--H35	H26--H32	H30--H35
H2	H50--H65	H50--H58	H52--H56	H47--H58
H3	H95--H102	H95--H102	H95--H102	H93--H101

The term "Kabat numbering" and like terms are recognized in the art and refer to a system of numbering amino acid residues in the heavy and light chain variable regions of an antibody, or an antigen binding molecule thereof. In certain aspects, the CDRs of an antibody can be determined according to the Kabat numbering system (*see, e.g.*, Kabat *et al.* in Sequences of Proteins of Immunological Interest, 5th Ed., NIH Publication 91-3242, Bethesda MD 1991). Using the Kabat numbering system, CDRs within an antibody heavy chain molecule are typically present at amino acid positions 31 to 35, which optionally can include one or two additional amino acids, following 35 (referred to in the Kabat numbering scheme as 35A and 35B) (CDR1), amino acid positions 50 to 65 (CDR2), and amino acid positions 95 to 102 (CDR3). Using the Kabat numbering system, CDRs within an antibody light chain molecule are typically present at amino acid positions 24 to 34 (CDR1), amino acid positions 50 to 56 (CDR2), and amino acid positions 89 to 97 (CDR3). In a specific embodiment, the CDRs of the antibodies described herein can be described according to the Kabat numbering scheme although they can readily be construed in other numbering systems using Table A.

[0076] In certain aspects, the CDRs of an antibody can be determined according to the Chothia numbering scheme, which refers to the location of immunoglobulin structural loops (*see, e.g.*, Chothia C & Lesk AM, (1987), *J Mol Biol* 196: 901-917; Al-Lazikani B *et al.*, (1997) *J Mol Biol* 273: 927-948; Chothia C *et al.*, (1992) *J Mol Biol* 227: 799-817; Tramontano A *et al.*, (1990) *J Mol Biol* 215(1): 175-82; and U.S. Patent No. 7,709,226). Typically, when using the Kabat numbering convention, the Chothia CDR-H1 loop is present at heavy chain amino acids 26 to 32, 33, or 34, the Chothia CDR-H2 loop is present at heavy chain amino acids 52 to 56, and the Chothia CDR-H3 loop is present at heavy chain amino acids 95 to 102, while the Chothia CDR-L1 loop is present at light chain amino acids 24 to 34, the Chothia CDR-L2 loop is present at light chain amino acids 50 to 56, and the Chothia CDR-L3 loop is present at light chain amino acids 89 to 97. The end of the Chothia CDR-HI loop when numbered using the Kabat numbering convention varies between H32 and H34 depending on the length of the loop (this is because the Kabat numbering scheme places the insertions at H35A and H35B; if neither 35A nor 35B is present, the loop ends at 32; if only 35A is present, the loop ends at 33; if both 35A and 35B are present, the loop ends at 34). See Table A. In a specific embodiment, the CDRs of the antibodies described herein have been determined according to the Chothia numbering scheme, as shown in FIGURES 6 and 8.

[0077] As used herein, a "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having 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). In certain embodiments, one or more amino acid residues within a CDR(s) or within a framework region(s) of an antibody or antigen binding molecule provided herein (or fragment thereof) can be replaced with an amino acid residue with a similar side chain.

[0078] Conservative amino acid substitutions, which are encompassed by the present disclosure, can encompass non-naturally occurring amino acid residues, which are typically incorporated by chemical peptide synthesis rather than by synthesis in biological systems.

These include peptidomimetics and other reversed or inverted forms of amino acid moieties. Naturally occurring residues can be divided into classes based on common side chain properties:

hydrophobic: norleucine, Met, Ala, Val, Leu, Ile;

neutral hydrophilic: Cys, Ser, Thr, Asn, Gln;

acidic: Asp, Glu;

basic: His, Lys, Arg;

residues that influence chain orientation: Gly, Pro; and

aromatic: Trp, Tyr, Phe.

[0079] Non-conservative substitutions can involve the exchange of a member of one of these classes for a member from another class. Such substituted residues can be introduced, for example, into regions of a human antibody that are homologous with non-human antibodies, or into the non-homologous regions of the molecule. Exemplary conservative amino acid substitutions are set forth in Table B below.

Table B

Original Residues	Exemplary Substitutions	Preferred Substitutions
Ala	Val, Leu, Ile	Val
Arg	Lys, Gln, Asn	Lys
Asn	Gln	Gln
Asp	Glu	Glu
Cys	Ser, Ala	Ser
Gln	Asn	Asn
Glu	Asp	Asp
Gly	Pro, Ala	Ala
His	Asn, Gln, Lys, Arg	Arg
Ile	Leu, Val, Met, Ala, Phe, Norleucine	Leu

Leu	Norleucine, Ile, Val, Met, Ala, Phe	Ile
Lys	Arg, 1,4 Diamino-butyric acid, Gln, Asn	Arg
Met	Leu, Phe, Ile	Leu
Phe	Leu, Val, Ile, Ala,Tyr	Leu
Pro	Ala	Gly
Ser	Thr, Ala, Cys	Thr
Thr	Ser	Ser
Trp	Tyr, Phe	Tyr
Tyr	Trp, Phe, Thr, Ser	Phe
Val	Ile, Met, Leu, Phe, Ala, Norleucine	Leu

[0080] As used herein, the terms "constant region" and "constant domain" are interchangeable and have a meaning common in the art. The constant region is an antibody portion, *e.g.*, a carboxyl terminal portion of a light and/or heavy chain which is not directly involved in binding of an antibody to antigen but which can exhibit various effector functions, such as interaction with the Fc receptor. The constant region of an immunoglobulin molecule generally has a more conserved amino acid sequence relative to an immunoglobulin variable domain.

[0081] As used herein, the term "cross competes" means the situation in which the interaction between an antigen and a first antigen binding molecule or binding fragment thereof blocks, limits, inhibits, or otherwise reduces the ability of a reference antigen binding molecule or binding fragment thereof to interact with the antigen. Cross competition can be complete, *e.g.*, binding of the binding molecule to the antigen completely blocks the ability of the reference binding molecule to bind the antigen, or it can be partial, *e.g.*, binding of the binding molecule to the antigen reduces the ability of the reference binding molecule to bind the antigen. In certain embodiments, an antigen binding molecule that cross competes with a reference antigen binding molecule binds the same or an overlapping epitope as the reference antigen binding molecule. In other embodiments, the antigen binding molecule that

cross competes with a reference antigen binding molecule binds a different epitope than the reference antigen binding molecule. Numerous types of competitive binding assays can be used to determine if one antigen binding molecule competes with another, for example: solid phase direct or indirect radioimmunoassay (RIA); solid phase direct or indirect enzyme immunoassay (EIA); sandwich competition assay (Stahli *et al.*, (1983) *Method Enzymol* 9:242-53); solid phase direct biotin-avidin EIA (Kirkland *et al.*, (1986) *J Immunol* 137:3614-19); solid phase direct labeled assay, solid phase direct labeled sandwich assay (Harlow and Lane, 1988, Antibodies, A Laboratory Manual, Cold Spring Harbor Press); solid phase direct label RIA using I^{125} label (Morel *et al.*, (1988) *Molec Immunol* 25:7-15); solid phase direct biotin-avidin EIA (Cheung *et al.*, (1990) *Virology* 176:546-52); and direct labeled RIA (Moldenhauer *et al.*, (1990) *Scand J Immunol* 32:77-82).

[0082] The term "derivative" refers to a molecule that includes a chemical modification other than an insertion, deletion, or substitution of amino acids (or nucleic acids). In certain embodiments, derivatives comprise covalent modifications, including, but not limited to, chemical bonding with polymers, lipids, or other organic or inorganic moieties. In certain embodiments, a chemically modified antigen binding molecule (a derivative) can have a greater circulating half-life than an antigen binding molecule that is not chemically modified. In some embodiments, a derivative antigen binding molecule is covalently modified to include one or more water soluble polymer attachments, including, but not limited to, polyethylene glycol, polyoxyethylene glycol, or polypropylene glycol.

[0083] As used herein, the term "diabody" or dAB means bivalent antibodies comprising two polypeptide chains, wherein each polypeptide chain comprises VH and VL domains joined by a linker that is too short to allow for pairing between two domains on the same chain, thus allowing each domain to pair with a complementary domain on another polypeptide chain (*see, e.g.*, Holliger *et al.*, (1993) *Proc Natl Acad Sci U.S.A.* 90:6444-48, Poljak *et al.*, (1994) *Structure* 2: 1121-23, and Perisic *et al.*, (1994) *Strucure* 2(12): 1217-26). If the two polypeptide chains of a diabody are identical, then a diabody resulting from their pairing will have two identical antigen binding sites. Polypeptide chains having different sequences can be used to make a diabody with two different antigen binding sites. Similarly, tribodies and tetrabodies are antibodies comprising three and four polypeptide chains, respectively, and forming three and four antigen binding sites, respectively, which can be the same or different.

[0084] As used herein, an "epitope" is a term in the art and refers to a localized region of an antigen to which an antibody can specifically bind. An epitope can be, for example, contiguous amino acids of a polypeptide (linear or contiguous epitope) or an epitope can, for example, come together from two or more non-contiguous regions of a polypeptide or polypeptides (conformational, non-linear, discontinuous, or non-contiguous epitope). In certain embodiments, the epitope to which an antibody binds can be determined by, *e.g.*, NMR spectroscopy, X-ray diffraction crystallography studies, ELISA assays, hydrogen/deuterium exchange coupled with mass spectrometry (*e.g.*, liquid chromatography electrospray mass spectrometry), array-based oligo-peptide scanning assays, and/or mutagenesis mapping (*e.g.*, site-directed mutagenesis mapping). For X-ray crystallography, crystallization may be accomplished using any of the known methods in the art (*e.g.*, Giege *et al.*, (1994) *Acta Crystallogr D Biol Crystallogr* 50(Pt 4): 339-350; McPherson, (1990) *Eur J Biochem* 189: 1-23; Chayen, (1997) *Structure* 5: 1269-1274; McPherson, (1976) *J Biol Chem* 251: 6300-6303). Antibody:antigen crystals can be studied using well known X-ray diffraction techniques and may be refined using computer software such as X-PLOR (Yale University, 1992, distributed by Molecular Simulations, Inc.; *see*, *e.g.*, *Meth Enzymol* (1985) Vols 114 & 115, eds Wyckoff *et al.*,), and BUSTER (Bricogne, (1993) *Acta Crystallogr D Biol Crystallogr* 49(Pt 1): 37-60; Bricogne, (1997) *Meth Enzymol* 276A: 361-423, ed. Carter; Roversi *et al.*, (2000) *Acta Crystallogr D Biol Crystallogr* 56(Pt 10): 1316-1323). Mutagenesis mapping studies can be accomplished using any method known to one of skill in the art. *See*, *e.g.*, Champe *et al.*, (1995) *J Biol Chem* 270: 1388-94 and Cunningham & Wells, (1989) *Science* 244: 1081-85 for a description of mutagenesis techniques, including alanine and arginine scanning mutagenesis techniques.

[0085] As used herein, the term "Fab fragment" means is a monovalent fragment having the VL, VH, CL and CH domains; a "F(ab')$_2$ fragment" is a bivalent fragment having two Fab fragments linked by a disulfide bridge at the hinge region; a "Fv fragment" has the VH and VL domains of a single arm of an antibody; and a "dAb fragment" has a VH domain, a VL domain, or an antigen-binding fragment of a VH or VL domain.

[0086] As used herein, the terms "immunospecifically binds," "immunospecifically recognizes," "specifically binds," and "specifically recognizes" are analogous terms and are used interchangeably in the context of antigen binding molecules, and means that a given molecule preferentially binds to an antigen (*e.g.*, epitope or immune complex) as such binding is understood by one skilled in the art. For example, an antigen binding molecule that

specifically binds to an antigen may bind to other peptides or polypeptides, but with a comparatively lower affinity as determined by, *e.g.*, immunoassays, BIAcore®, KinExA 3000 instrument (Sapidyne Instruments, Boise, ID), or other assays known in the art. In a specific embodiment, molecules that specifically bind to an antigen bind to the antigen with a K_A that is at least 2 logs, 2.5 logs, 3 logs, 4 logs or greater than the K_A when the molecules bind to another antigen.

[0087] In another embodiment, molecules that specifically bind to an antigen (*e.g.*, GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500)), molecules comprising this sequence and cells presenting such molecules) bind with a dissociation constant (K_d) of about 1×10^{-7} M. In some embodiments, the antigen binding molecule specifically binds an antigen (*e.g.*, SEQ ID NOs: 1, 2, 3, 499 and/or 500, molecules comprising this sequence and cells presenting such molecules) with "high affinity" when the K_d is about 1×10^{-9} M to about 5×10^{-9} M. In some embodiments, the antigen binding molecule specifically binds an antigen (*e.g.*, SEQ ID NOs: 1, 2, 3, 499 and/or 500, molecules comprising this sequence and cells presenting such molecules) with "very high affinity" when the K_d is 1×10^{-10} M to about 5×10^{-10} M.

[0088] In still another embodiment, molecules that specifically bind to an antigen (*e.g.*, SEQ ID NOs: 1, 2, 3, 499 and/or 500, molecules comprising these sequences and cells presenting such molecules) do not cross react with other proteins under similar binding conditions. In another specific embodiment, molecules that specifically bind to an antigen (*e.g.*, SEQ ID NOs: 1, 2, 3, 499 and/or 500, molecules comprising these sequences and cells presenting such molecules) do not cross react with other proteins that do not comprise SEQ ID NOs: 1, 2, 3, 499 and/or 500, molecules comprising these sequences and cells presenting such molecules. In a specific embodiment, provided herein is an antibody or fragment thereof that binds to SEQ ID NOs: 1, 2, 3, 499 and/or 500, molecules comprising these sequences and cells presenting such molecules, with higher affinity than to another unrelated antigen. In certain embodiments, provided herein is an antigen binding molecule (*e.g.*, an antibody) or fragment thereof that binds to SEQ ID NOs: 1, 2, 3, 499 and/or 500, molecules comprising these sequences and cells presenting such molecules as molecules comprising this sequence and cells presenting such molecules, with a 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or higher affinity than to another, unrelated antigen as measured by, *e.g.*, a radioimmunoassay, surface plasmon resonance, or kinetic

exclusion assay. In a specific embodiment, the extent of binding of an antigen binding molecule, antibody or antigen binding fragment thereof that specifically binds SEQ ID NOs: 1, 2, 3, 499 and/or 500, molecules comprising these sequences and cells presenting such molecules, described herein compared to an unrelated protein which does not comprise SEQ ID NOs: 1, 2, 3, 499 and/or 500, is less than 10%, 15%, or 20% of the binding of the antibody to linker fragment protein as measured by, *e.g.*, a radioimmunoassay.

[0089] As used herein, the term "heavy chain" when used in reference to an antibody can refer to any distinct type, *e.g.*, alpha (α), delta (δ), epsilon (ε), gamma (γ) and mu (μ), based on the amino acid sequence of the constant domain, which give rise to IgA, IgD, IgE, IgG and IgM classes of antibodies, respectively, including subclasses of IgG, *e.g.*, IgG_1, IgG_2, IgG_3 and IgG_4.

[0090] As used herein, the term "immunoglobulin" means an immune molecule from any of the commonly known isotypes, including but not limited to IgA, secretory IgA, IgG and IgM. IgG subclasses are also well known to those in the art and include but are not limited to human IgG1, IgG2, IgG3 and IgG4. Many of the molecules described herein are immunoglobulins. As used herein, "isotype" means the antibody class or subclass (*e.g.*, IgM or IgG1) that is encoded by the heavy chain constant region genes.

[0091] An immunoglobulin is a tetrameric molecule, normally composed of two identical pairs of polypeptide chains, each pair having one "light" (about 25 kDa) and one "heavy" chain (about 50-70 kDa). The amino-terminal portion of each chain includes a variable region of about 100 to 130 or more amino acids primarily responsible for antigen recognition. The carboxy-terminal portion of each chain defines a constant region primarily responsible for effector function. Human light chains are classified as kappa and lambda light chains. Heavy chains are classified as mu, delta, gamma, alpha, or epsilon, and define the antibody's isotype as IgM, IgD, IgG, IgA, or IgE, respectively. Within light and heavy chains, the variable and constant regions are joined by a "J" region of about 12 or more amino acids, with the heavy chain also including a "D" region of about 10 more amino acids. See generally, Berzofsky & Berkower, in Fundamental Immunology (Paul, (ed), Lippincott Williams & Wilkins (2012). The variable regions of each light/heavy chain pair form the antibody binding site such that an intact immunoglobulin has two primary binding sites.

[0092] Naturally occurring immunoglobulin chains exhibit the same general structure of relatively conserved framework regions (FR) joined by three hypervariable regions, also

Date Reçue/Date Received 2020-04-16

called complementarity determining regions or "CDRs." From N-terminus to C-terminus, both light and heavy chains comprise the domains FR1, CDR1, FR2, CDR2, FR3, CDR3 and FR4. The assignment of amino acids to each domain can be done in accordance with the definitions of Kabat (*see*, *e.g.*, Kabat *et al.* in Sequences of Proteins of Immunological Interest, 5th Ed., NIH Publication 91-3242, Bethesda MD (1991)) or Chothia (Chothia, used herein, (*see*, *e.g.*, Chothia & Lesk (1987), *J. Mol. Biol.* 196:901-917; Chothia *et al.*, 1989, *Nature* 342:878-883 or Honegger & Pluckthun (2001), *J Mol Biol* 309:657-670). The Kabat, Chothia and Abm (Oxford Molecular) numbering systems are described more fully herein.

[0093] As used herein, the term "*in vitro* cell" refers to any cell that is cultured *ex vivo*. An *in vitro* cell can include a human cell such as a T cell or dendritic cell, or it can include CHO, sP2/0, rabbit and other non-human cells.

[0094] As used herein, the term "light chain" when used in reference to an antibody can refer to any distinct type, *e.g.*, kappa (κ) or lambda (λ) based on the amino acid sequence of the constant domains. Light chain amino acid sequences are known in the art. In specific embodiments, the light chain is a human light chain.

[0095] The term "neutralizing" refers to an antigen binding molecule, scFv, antibody, or a fragment thereof, that binds to a ligand (*e.g.*, a moiety comprising SEQ ID NOs: 1, 2, 3, 499 and/or 500) and prevents or reduces the biological effect of that ligand. In some embodiments, the antigen binding molecule, scFv, antibody, or a fragment thereof, directly blocking a binding site on the ligand or otherwise alters the ligand's ability to bind through indirect means (such as structural or energetic alterations in the ligand). In some embodiments, the antigen binding molecule, scFv, antibody, or a fragment thereof prevents the protein to which it is bound from performing a biological function.

[0096] As used herein, the term "patient" means any human who is being treated for an abnormal physiological condition, such as cancer or has been formally diagnosed with a disorder, those without formally recognized disorders, those receiving medical attention, those at risk of developing the disorders, etc. The terms "subject" and "patient" are used interchangeably herein and include both human and non-human animal subjects.

[0097] As used herein, the terms "peptide," "polypeptide," and "protein" are used interchangeably herein, and mean a compound comprised of amino acid residues covalently linked by peptide bonds. A polypeptide, protein or peptide must contain at least two amino acids, but no limitation is placed on the maximum number of amino acids that can comprise a protein's or peptide's amino acid sequence. As used herein, the term refers to both short

chains, which also commonly are referred to as peptides, oligopeptides and oligomers, and to longer chains, which generally are referred to as proteins. "Polypeptides" include, for example, biologically active fragments, substantially homologous polypeptides, oligopeptides, homodimers, heterodimers, variants of polypeptides, modified polypeptides, derivatives, analogs, fusion proteins, among others. The term "polypeptide" includes natural peptides, recombinant peptides, synthetic peptides, or a combination thereof.

[0098] In some aspects, the polypeptides and/or proteins have deletions from, additions to, and/or substitutions of one or more amino acids of antigen binding molecule. Useful polypeptide fragments may include immunologically functional fragments of antigen binding molecules, including not limited to one or more CDR regions, variable domains of a heavy and/or light chain, a portion of other portions of an antibody chain, and the like. Moieties that can be substituted for one or more amino acids of an antigen binding molecule include, *e.g.*, D or L forms of amino acids, an amino acid different from the amino acid normally found in the same position of an antigen binding molecule (relative to those sequences provided in FIGURES 6 and 8, and their recited SEQ ID NOs), deletions, non-naturally occurring amino acids, and chemical analogs of amino acids.

[0099] Peptide analogs are commonly used in the pharmaceutical industry as non-peptide drugs with properties analogous to those of the template peptide and form an aspect of the instant disclosure. These types of non-peptide compound are termed "peptide mimetics" or "peptidomimetics." *See, e.g.*, Fauchere, (1986) *Adv. Drug Res.* (Testa, ed.) 15:29-69; Veber & Freidinger, (1985) *TINS*, p.392; and Evans *et al.*, (1987) *J. Med. Chem*, 30:1229-39.

[0100] Polypeptides, peptides, proteins and analogous molecules comprising SEQ ID NOs: 1, 2, 3, 499 and/or 500, molecules comprising these sequences and cells presenting such molecules, are specifically encompassed by the terms.

[0101] As used herein, the term "percent identity" means the percent of identical residues between the amino acids or nucleotides in the compared molecules. For these calculations, gaps in alignments (if any) must be addressed by a particular mathematical model or computer program (*i.e.*, an "algorithm"). Methods that can be used to calculate the identity of the aligned nucleic acids or polypeptides include those described in Computational Molecular Biology, (Lesk, ed.), (1988) New York: Oxford University Press; Biocomputing Informatics and Genome Projects, (Smith, ed.), 1993, New York: Academic Press; Computer Analysis of Sequence Data, Part I, (Griffin and Griffin, eds.), 1994, New Jersey: Humana

Date Reçue/Date Received 2020-04-16

Press; von Heinje, (1987) Sequence Analysis in Molecular Biology, New York: Academic Press; Sequence Analysis Primer, (Gribskov and Devereux, eds.), 1991, New York: M. Stockton Press; and Carillo et al., (1988) *J. Applied Math.* 48:1073.

[0102] In calculating percent identity, the sequences being compared are aligned in a way that gives the largest match between the sequences. The computer program used to determine percent identity can be, *e.g.*, MOE (Chemical Computing Group) or DNASTAR (University of Wisconsin, Madison, WI). The computer algorithm GAP can be used to align the two polypeptides or polynucleotides for which the percent sequence identity is to be determined. The sequences are aligned for optimal matching of their respective amino acid or nucleotide (the "matched span," as determined by the algorithm). A gap opening penalty (which is calculated as 3x the average diagonal, wherein the "average diagonal" is the average of the diagonal of the comparison matrix being used; the "diagonal" is the score or number assigned to each perfect amino acid match by the particular comparison matrix) and a gap extension penalty (which is usually 1/10 times the gap opening penalty), as well as a comparison matrix such as PAM 250 or BLOSUM 62 are used in conjunction with the algorithm. In certain embodiments, a standard comparison matrix (see, *e.g.*, Dayhoff et al., (1978) Atlas of Protein Sequence and Structure 5:345-352 for the PAM 250 comparison matrix; Henikoff et al., (1992) *Proc. Natl. Acad. Sci. U.S.A.* 89: 10915-10919 for the BLOSUM 62 comparison matrix) is also used by the algorithm.

[0103] Certain alignment schemes for aligning two amino acid sequences can result in matching of only a short region of the two sequences, and this small aligned region can have very high sequence identity even though there is no significant relationship between the two full-length sequences. Accordingly, the selected alignment method (*e.g.*, the GAP program) can be adjusted if desired to result in an alignment that spans at least 50 contiguous amino acids of the target polypeptide.

[0104] As used herein, the terms "single-chain antibody" and "single chain fragment variable (scFv)" are used interchangeably and mean an antigen binding molecule in which a VL and a VH region are joined via a linker to form a continuous protein chain wherein the linker is long enough to allow the protein chain to fold back on itself and form a monovalent antigen binding site (*see, e.g.*, Bird *et al.*, (1988) *Science* 242:423-26 and Huston *et al.*, (1988) *Proc. Natl. Acad. Sci. U.S.A.* 85:5879-83 (1988). FMC63 (Nicholson *et al.*, (1997) *Mol. Immunol.* 34:(16-17) 1157-65) is a specific example of a scFv, and is specific for CD19.

[0105] A "therapeutically effective amount," "effective dose," "effective amount," or "therapeutically effective dosage" of a therapeutic agent, (*e.g.*, a moiety comprising SEQ ID NOs: 1, 2, 3, 499 and/or 500, molecules comprising these sequences and cells presenting such molecules), is any amount that, when used alone or in combination with another therapeutic agent, protects a subject against the onset of a disease or promotes disease regression evidenced by a decrease in severity of disease symptoms, an increase in frequency and duration of disease symptom-free periods, or a prevention of impairment or disability due to the disease affliction. The ability of a therapeutic agent to promote disease regression can be evaluated using a variety of methods known to the skilled practitioner, such as in human subjects during clinical trials, in animal model systems predictive of efficacy in humans, or by assaying the activity of the agent in *in vitro* assays.

[0106] The terms "transduction" and "transduced" refer to the process whereby foreign DNA is introduced into a cell via viral vector (*see* Hartl and Jones (1997) Genetics: Principles and Analysis, 4th ed, Jones & Bartlett). In some embodiments, the vector is a retroviral vector, a DNA vector, a RNA vector, an adenoviral vector, a baculoviral vector, an Epstein Barr viral vector, a papovaviral vector, a vaccinia viral vector, a herpes simplex viral vector, an adenovirus associated vector, a lentiviral vector, or any combination thereof.

[0107] As used herein, the terms "variable region" or "variable domain" are used interchangeably and mean a portion of an antibody, generally, a portion of a light or heavy chain, typically the amino-terminal end of the antibody, and comprising about 100-130 amino acids in the heavy chain and about 90 to 115 amino acids in the light chain, which differ extensively in sequence among antibodies and are used in the binding and specificity of a particular antibody for a particular antigen. The variability in sequence is concentrated in those regions called complementarity determining regions (CDRs) while the more highly conserved regions in the variable domain are called framework regions (FR). The CDRs of the light and heavy chains are primarily responsible for the interaction and specificity of the antibody with antigen.

[0108] In certain embodiments, the variable region of an antigen binding molecule is a human variable region. In further embodiments, the variable region comprises rodent, human or murine CDRs and human framework regions (FRs). In further embodiments, the variable region is a primate (*e.g.*, a non-human primate) variable region. In yet further embodiments, the variable region is a rabbit variable region. In other embodiments, the variable region comprises human CDRs and non-human (*e.g.*, rabbit, murine, rat or non-

human primate) framework regions (FRs). In other embodiments, the variable region comprises non-human (*e.g.*, rabbit, murine, rat or non-human primate) CDRs and human framework regions (FRs).

[0109] The terms "VH," "VH domain" and "VH chain" are used interchangeably and mean the heavy chain variable region of an antigen binding molecule, antibody or an antigen binding fragment thereof.

[0110] The terms "VL," "VL domain" and "VL chain" are used interchangeably and mean the light chain variable region of an antigen binding molecule, antibody or an antigen binding fragment thereof.

[0111] Various aspects of the invention are described in further detail in the following subsections.

II. Antigen Binding Molecules and Polynucleotides Encoding the Same

[0112] The present disclosure is directed to antigen binding molecules, including antibodies, that specifically bind GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising these sequences and cells presenting such molecules, and/or antigen binding molecules which cross compete with one or more antigen binding molecules described herein (*i.e.*, one or more of those described in FIGURES 6 and 8 and/or disclosed in the appended Sequence Listing). Polynucleotides encoding the antigen binding molecules are also provided, and form an aspect of the instant disclosure.

[0113] An antibody or antigen binding molecule encoded of the present invention can be single chained or double chained. In some embodiments, the antibody or antigen binding molecule is single chained. In certain embodiments, the antigen binding molecule is selected from the group consisting of an scFv, a Fab, a Fab', a Fv, a $F(ab')_2$, a dAb, and any combination thereof. In one particular embodiment, the antibody or antigen binding molecule comprises an scFv.

[0114] In certain embodiments, an antigen binding molecule such as an antibody comprises a single chain, wherein the heavy chain variable region and the light chain variable region are connected by a linker (an scFv). In some embodiments, the VH is located at the N terminus of the linker and the VL is located at the C terminus of the linker. In other embodiments, the VL is located at the N terminus of the linker and the VH is located at the C

terminus of the linker. In some embodiments, the linker comprises at least about 5, at least about 8, at least about 10, at least about 13, at least about 15, at least about 18, at least about 20, at least about 25, at least about 30, at least about 35, at least about 40, at least about 45, at least about 50, at least about 60, at least about 70, at least about 80, at least about 90, or at least about 100 amino acids. In some embodiments, the linker comprises between about 8 amino acids and about 18 amino acids (*e.g.*, 10 amino acids).

[0115] In some embodiments, the antigen binding molecules of the present invention specifically bind to GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising these sequences and cells presenting such molecules. In certain embodiments, an antigen binding molecule of the present disclosure specifically binds SEQ ID NOs: 1, 2, 3, 499 and/or 500, as well as molecules comprising these sequences and cells presenting such molecules, with a K_D of less than 1×10^{-6} M, less than 1×10^{-7} M, less than 1×10^{-8} M, or less than 1×10^{-9} M. In one particular embodiment, an antigen binding molecule specifically binds to SEQ ID NOs: 1, 2, 3, 499 and/or 500, as well as molecules comprising these sequences and cells presenting such molecules, with a K_D of less than 1×10^{-7} M. In another embodiment, an antigen binding molecule specifically binds SEQ ID NOs: 1, 2, 3, 499 and/or 500, as well as molecules comprising these sequences and cells presenting such molecules, with a K_D of less than 1×10^{-8} M. In some embodiments, an antigen binding molecule binds the scFv FMC63, as well as molecules comprising this sequence and cells presenting such molecules, with a K_D of about 1×10^{-7} M, about 2×10^{-7} M, about 3×10^{-7} M, about 4×10^{-7} M, about 5×10^{-7} M, about 6×10^{-7} M, about 7×10^{-7} M, about 8×10^{-7} M, about 9×10^{-7} M, about 1×10^{-8} M, about 2×10^{-8} M, about 3×10^{-8} M, about 4×10^{-8} M, about 5×10^{-8} M, about 6×10^{-8} M, about 7×10^{-8} M, about 8×10^{-8} M, about 9×10^{-8} M, about 1×10^{-9} M, about 2×10^{-9} M, about 3×10^{-9} M, about 4×10^{-9} M, about 5×10^{-9} M, about 6×10^{-9} M, about 7×10^{-9} M, about 8×10^{-9} M, about 9×10^{-9} M, about 1×10^{-10} M, or about 5×10^{-10} M. K_D can be calculated using standard methodologies, as described herein.

[0116] In specific embodiments, an antigen binding molecule of the instant disclosure is an antibody identified herein as Clone 8 or Clone 16 and each comprises the following heavy and light chain amino acid, coding, variable, and CDR sequences, as provided and labeled:

Clone 8 VH DNA Coding Sequence
ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGTCCAG
TGTCAGTCGGTGGAGGAGTCCGGGGGTCGCCTGGTCACGCCTGGGACACCCCTG
ACACTCACCTGCACAGCCTCTGGATTCACCATCAGTAACCTTGCAATAATCTGG
GTCCGCCAGGCTCCAGGGAAGGGGCTGGAATATATCGGAGACATTGATGGTCG
TGGTGACATATACTGTGCGACCTGGGCGAAAGGCCGATTCACCATCTCCAAAAC
CTCGACCACACTGGATCTGAGATTCACCAGCCCGACAACCGAGGACACGGCCA
CCTACTTCTGTGCCGTAGATGGTGATGGTAGTGGTTGGGGTGACTTTAACTTTTG
GGGCCCAGGCACCCTGGTCACCGTCTCCTCA (SEQ ID NO: 4)

Clone 8 VH AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQSVEESGGRLVTPGTPLTLTCTASGFTISNLAIIWVR
QAPGKGLEYIGDIDGRGDIYCATWAKGRFTISKTSTTLDLRFTSPTTEDTATYFCAV
DGDGSGWGDFNFWGPGTLVTVSS (SEQ ID NO: 5)

Clone 8 HC AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQSVEESGGRLVTPGTPLTLTCTASGFTISNLAIIWVR
QAPGKGLEYIGDIDGRGDIYCATWAKGRFTISKTSTTLDLRFTSPTTEDTATYFCAV
DGDGSGWGDFNFWGPGTLVTVSSGQPKAPSVFPLAPCCGDTPSSTVTLGCLVKGY
LPEPVTVTWNSGTLTNGVRTFPSVRQSSGLYSLSSVVSVTSSSQPVTCNVAHPATNT
KVDKTVAPSTCSKPTCPPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVVVDVSQDDP
EVQFTWYINNEQVRTARPPLREQQFNSTIRVVSTLPIAHQDWLRGKEFKCKVHNKA
LPAPIEKTISKARGQPLEPKVYTMGPPREELSSRSVSLTCMINGFYPSDISVEWEKNG
KAEDNYKTTPAVLDSDGSYFLYSKLSVPTSEWQRGDVFTCSVMHEALHNHYTQKS
ISRSPGK (SEQ ID NO: 6)

Clone 8 VH CDR1 AA
GFTISNL (SEQ ID NO: 7)

Clone 8 VH CDR2 AA
DIDGRGDIYCATWAK (SEQ ID NO: 8)

Clone 8 VH CDR3 AA
DGDGSGWGDFNF (SEQ ID NO: 9)

Clone 8 VL DNA Coding Sequence
ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCTCCCA
GGTGCCAGATGTGCCTATGATATGACCCAGACTCCAGCCTCTGTGGAGGTAGCT
GTGGGAGGCACAGTCAGCATCAAGTGCCAGGCCAGTCAGAGCATTAGCACTGC
ATTAGCCTGGTATCAGCAGAAACCAGGACAGCCTCCCAAGCTCCTGATCTACAG
GGCATCCACTCTGGCATCTGGGGTCTCATCGCGGTTCAAAGGCAGTGGATCTGG
GACACAGTTCACTCTCACCATCAGCGGCGTGGAGTGTGACGATGCTGCCACTTA
CTACTGTCAACAGGGTTGGAGTACTGTGAATGTTGATAATGTTTTCGGCGGAGG
GACCGAGGTGGTGGTCAGA (SEQ ID NO: 10)

Clone 8 VL AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGARCAYDMTQTPASVEVAVGGTVSIKCQASQSISTALA
WYQQKPGQPPKLLIYRASTLASGVSSRFKGSGSGTQFTLTISGVECDDAATYYCQQ
GWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 11)

Clone 8 LC AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGARCAYDMTQTPASVEVAVGGTVSIKCQASQSISTALA
WYQQKPGQPPKLLIYRASTLASGVSSRFKGSGSGTQFTLTISGVECDDAATYYCQQ
GWSTVNVDNVFGGGTEVVVRDPVAPTVLIFPPAADQVATGTVTIVCVANKYFPDV
TVTWEVDGTTQTTGIENSKTPQNSADCTYNLSSTLTLTSTQYNSHKEYTCKVTQGT
TSVVQSFNRGDC (SEQ ID NO: 12)

Clone 8 VL CDR1 AA
QASQSISTALA (SEQ ID NO: 13)

Clone 8 VL CDR2 AA
RASTLAS (SEQ ID NO: 14)

Clone 8 VL CDR3 AA
QQGWSTVNVDNV (SEQ ID NO: 15)

Clone 16 VH DNA Coding Sequence
ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGTCCAG
TGTCAGTCGCTGGAGGAGTCCGGGGGTCGCCTGGTCACGCCTGGGACACCCCTG
ACACTCACCTGCACAGTCTCTGGATCCGACATCAGTAGCTACCACATGGGCTGG
GTCCGCCAGGCTCCAGGGAAGGGGCTGGAATACATCGGAATCATTGTTAGTAG
TGGTAGCGCATACTACGCGACCTGGGCAAAAGGCCGATTCACCATCTCCAGGA
CCTCGACCACGGTGGATCTGAAAATCACCAGTCCGACAACCGAGGACTCGGCC
ACCTATTTCTGTGCCAGAAATCAATATAGTGGTTATGGCTTTAGCTTCTGGGGCC
CAGGCACCCTGGTCACCGTCTCCTCA (SEQ ID NO: 16)

Clone 16 VH AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWV
RQAPGKGLEYIGIIVSSGSAYYATWAKGRFTISRTSTTVDLKITSPTTEDSATYFCAR
NQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 17)

Clone 16 HC AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWV
RQAPGKGLEYIGIIVSSGSAYYATWAKGRFTISRTSTTVDLKITSPTTEDSATYFCAR
NQYSGYGFSFWGPGTLVTVSSGQPKAPSVFPLAPCCGDTPSSTVTLGCLVKGYLPEP
VTVTWNSGTLTNGVRTFPSVRQSSGLYSLSSVVSVTSSSQPVTCNVAHPATNTKVD
KTVAPSTCSKPTCPPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVVVDVSQDDPEVQ
FTWYINNEQVRTARPPLREQQFNSTIRVVSTLPIAHQDWLRGKEFKCKVHNKALPA
PIEKTISKARGQPLEPKVYTMGPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAE
DNYKTTPAVLDSDGSYFLYSKLSVPTSEWQRGDVFTCSVMHEALHNHYTQKSISRS
PGK (SEQ ID NO: 18)

Clone 16 VH CDR1 AA
GSDISSY (SEQ ID NO: 19)

Clone 16 VH CDR2 AA
IIVSSGSAYYATWAK (SEQ ID NO: 20)

Clone 16 VH CDR3 AA
NQYSGYGFSF (SEQ ID NO: 21)

Clone 16 VL DNA Coding Sequence
ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCTCCCA
GGTGCCACATTTGCCGTCGTGCTGACCCAGACTCCATCCCCAGTGTCTACAGCT
GTAGGAGGCACAGTCACCATCAATTGCCAGTCCAGTCACAGTGTTTATTATGGC
GACTGGTTAGCCTGGTATCAGCAGAAACCAGGGCAGCCTCCTAAGCTCCTGATC
TACAGGGCATCCAATCTGGCATCTGGTGTCCCATCGCGGTTCAAAGGCAGTGGA

TCTGGGACACAGTTCACTCTCACCATCAGCGGCGTGCAGTGTGACGATGCTGCC
ACTTACTACTGTCTAGGCGGTTATGATGATGATGGTGAGACTGCTTTCGGCGGA
GGGACCGAGGTGGTGGTCAAA (SEQ ID NO: 22)

Clone 16 VL AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGATFAVVLTQTPSPVSTAVGGTVTINCQSSHSVYYGD
WLAWYQQKPGQPPKLLIYRASNLASGVPSRFKGSGSGTQFTLTISGVQCDDAATYY
CLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 23)

Clone 16 LC AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGATFAVVLTQTPSPVSTAVGGTVTINCQSSHSVYYGD
WLAWYQQKPGQPPKLLIYRASNLASGVPSRFKGSGSGTQFTLTISGVQCDDAATYY
CLGGYDDDGETAFGGGTEVVVKDPVAPTVLIFPPAADQVATGTVTIVCVANKYFP
DVTVTWEVDGTTQTTGIENSKTPQNSADCTYNLSSTLTLTSTQYNSHKEYTCKVTQ
GTTSVVQSFNRGDC (SEQ ID NO: 24)

Clone 16 VL CDR1 AA
QSSHSVYYGDWLA (SEQ ID NO: 25)

Clone 16 VL CDR2 AA
RASNLAS (SEQ ID NO: 26)

Clone 16 VL CDR3 AA
LGGYDDDGETA (SEQ ID NO: 27)

[0117] In one embodiment, the antigen binding molecules of the present disclosure are antibodies and antigen binding fragments thereof. In one embodiment, the antibodies of the present disclosure comprise at least one CDR set forth in FIGURES 6 and 8. In another aspect, the present disclosure provides hybridomas capable of producing the antibodies disclosed herein and methods of producing antibodies from hybridomas, as described herein and as known in the art.

[0118] Humanized antibodies are described herein and may be prepared by known techniques. In one embodiment, a humanized monoclonal antibody comprises the variable domain of a murine or rabbit antibody (or all or part of the antigen binding site thereof) and a constant domain derived from a human antibody. Alternatively, a humanized antibody fragment may comprise an antigen binding site of a murine or rabbit monoclonal antibody and a variable domain fragment (lacking the antigen binding site) derived from a human antibody. Procedures for the production of engineered monoclonal antibodies include those

described in Riechmann *et al.*, (1988) *Nature* 332:323, Liu *et al.*, (1987) *Proc. Nat. Acad. Sci. USA* 84:3439, Larrick *et al.*, (1989) *Bio/Technology* 7:934, and Winter *et al.*, (1993) *TIPS* 14:139. In one embodiment, the chimeric antibody is a CDR grafted antibody. Techniques for humanizing antibodies are discussed in, *e.g.*, U.S. Pat. Nos. 5,869,619; 5,225,539; 5,821,337; 5,859,205; 6,881,557; Padlan et al., (1995) *FASEB J.* 9:133-39; Tamura et al., (2000) *J. Immunol.* 164:1432-41; Zhang *et al.*, (2005) *Mol. Immunol.* 42(12):1445-1451; Hwang *et al.*, *Methods.* (2005) 36(1):35-42; Dall'Acqua *et al.*, (2005) *Methods* 36(1):43-60; and Clark, (2000) *Immunology Today* 21(8):397-402.

[0119] An antigen binding molecule of the present invention can also be a fully human monoclonal antibody. Fully human monoclonal antibodies can be generated by any number of techniques with which those having ordinary skill in the art will be familiar. Such methods include, but are not limited to, Epstein Barr Virus (EBV) transformation of human peripheral blood cells (*e.g.*, containing B lymphocytes), *in vitro* immunization of human B-cells, fusion of spleen cells from immunized transgenic mice carrying inserted human immunoglobulin genes, isolation from human immunoglobulin V region phage libraries, or other procedures as known in the art and based on the disclosure herein.

[0120] Procedures have been developed for generating human monoclonal antibodies in non-human animals. For example, mice in which one or more endogenous immunoglobulin genes have been inactivated by various means have been prepared. Human immunoglobulin genes have been introduced into the mice to replace the inactivated mouse genes. In this technique, elements of the human heavy and light chain locus are introduced into strains of mice derived from embryonic stem cell lines that contain targeted disruptions of the endogenous heavy chain and light chain loci (see also Bruggemann *et al.*, (1997) *Curr. Opin. Biotechnol.* 8:455-58).

[0121] Examples of techniques for production and use of transgenic animals for the production of human or partially human antibodies are described in U.S. Pat. Nos. 5,814,318, 5,569,825, and 5,545,806; Davis *et al.*, Antibody Engineering: Methods and Protocols, (Lo, ed) Humana Press, NJ, 191-200 (2003); Kellermann *et al.*, (2002) *Curr Opin Biotechnol.* 13:593-97; Russel *et al.*, (2000) *Infect Immun.* 68:1820-26; Gallo *et al.*, (2000) *Eur J. Immun.* 30:534-40; Davis *et al.*, (1999) *Cancer Metastasis Rev.* 18:421-25; Green, (1999) *J Immunol Methods* 231:11-23; Jakobovits, (1998) *Advanced Drug Delivery Reviews* 31:33-42; Green *et al.*, (1998) *J Exp Med.* 188:483-95; Jakobovits, (1998) *Exp. Opin. Invest. Drugs.* 7:607-14; Tsuda *et al.*, (1997) *Genomics*, 42:413-21; Mendez *et al.*, (1997) *Nat. Genet.* 15:146-56;

Jakobovits, (1994) *Curr Biol.* 4:761-63; Arbones *et al.*, (1994) *Immunity* 1:247-60; Green *et al.*, (1994) *Nat. Genet.* 7:13-21; Jakobovits *et al.*, (1993) *Nature* 362:255-58; Jakobovits *et al.*, (1993) *Proc Natl Acad Sci USA* 90:2551-55; Chen *et al.*, (1993) *Intl Immunol* 5:647-656; Choi *et al.*, (1993) *Nature Genetics* 4:117-23; Fishwild *et al.*, (1996) *Nature Biotechnology* 14:845-51; Lonberg *et al.*, (1994) *Nature* 368: 856-59; Lonberg, (1994) Handbook of Experimental Pharmacology 113: 49-101; Neuberger, (1996) *Nature Biotech* 14:826; Taylor *et al.*, (1992) *Nucleic Acids Research* 20:6287-95; Taylor et al., (1994) *Intl Immunol* 6:579-91; Tomizuka *et al.*, (1997) *Nature Genetics* 16:133-43; Tomizuka *et al.*, (2000) *Proc Nat Acad Sci USA* 97:722-27; Tuaillon *et al.*, (1993) *Proc Nat Acad Sci USA* 90:3720-24; Tuaillon *et al.*, (1994) *J Immunol* 152:2912-20.; Lonberg *et al.*, (1994) *Nature* 368:856; Taylor *et al.*, (1994) *Intl Immunol* 6:579; U.S. Pat. No. 5,877,397; Bruggemann *et al.*, (1997) *Curr. Opin. Biotechnol.* 8:455-58; Jakobovits *et al.*, (1995) *Ann. N.Y. Acad. Sci.* 764:525-35.

[0122] An additional method for obtaining antigen binding molecules of the invention is by the use of phage display, which is well-established for this purpose. *See, e.g.*, Winter *et al.*, (1994) *Ann. Rev. Immunol.* 12:433-55; Burton *et al.*, (1994) *Adv. Immunol* 57:191-280. Human or murine immunoglobulin variable region gene combinatorial libraries can be created in phage vectors that can be screened to select Ig fragments (Fab, Fv, sFv, or multimers thereof) that bind the scFv FMC63, as well as molecules comprising this sequence and cells presenting such molecules. *See*, e.g., U.S. Pat. No. 5,223,409; Huse *et al.*, (1989) *Science* 246:1275-81; Sastry et al., (1989) *Proc. Natl. Acad. Sci. USA* 86:5728-32; Alting-Mees *et al.*, (1990) *Strategies in Molecular Biology* 3:1-9; Kang *et al.*, (1991) *Proc. Natl. Acad. Sci. USA* 88:4363-66; Hoogenboom *et al.*, (1992) *J. Mol. Biol.* 227:381-388; Schlebusch *et al.*, (1997) *Hybridoma* 16:47-52 and references cited therein. For example, a library containing a plurality of polynucleotide sequences encoding Ig variable region fragments can be inserted into the genome of a filamentous bacteriophage, such as M13 or lambda phage (λImmunoZap™(H) and λImmunoZap™(L) vectors (Stratagene, La Jolla, Calif) can also be used in this approach) or a variant thereof, in frame with the sequence encoding a phage coat protein.

[0123] Briefly, mRNA is isolated from a B-cell population, and used to create heavy and light chain immunoglobulin cDNA expression libraries in the λImmunoZap™(H) and λImmunoZap™(L) and similar vectors. These vectors can be screened individually or co-expressed to form Fab fragments or antibodies. Positive plaques can subsequently be

converted to a non-lytic plasmid that allows high level expression of monoclonal antibody fragments from *E. coli*.

[0124] In one embodiment, in a hybridoma the variable regions of a gene expressing a monoclonal antibody of interest are amplified using nucleotide primers. These primers can be synthesized by one of ordinary skill in the art, or can be purchased from commercial sources, which also sell primers for mouse and human variable regions including, among others, primers for V_H, V_L, C_H and C_L regions). These primers can be used to amplify heavy or light chain variable regions, which can then be inserted into vectors. These vectors can then be introduced into *E. coli*, yeast, or mammalian-based systems for expression. Large amounts of a single-chain protein containing a fusion of the V_H and V_L domains can be produced using these methods.

[0125] Once cells producing the antigen binding molecules provided herein have been obtained using any of the above-described immunization and other techniques, the specific antibody genes can be cloned by isolating and amplifying DNA or mRNA therefrom according to standard procedures as described herein. The antibodies produced therefrom can be sequenced and the CDRs identified and the DNA coding for the CDRs can be manipulated as described previously to generate other antibodies according to the invention.

[0126] It will be understood by those of skill in the art that some proteins, such as antibodies, can undergo a variety of posttranslational modifications. The type and extent of these modifications often depends on the host cell line used to express the protein as well as the culture conditions. Such modifications can include variations in glycosylation, methionine oxidation, diketopiperizine formation, aspartate isomerization and asparagine deamidation. A frequent modification is the loss of a carboxy-terminal basic residue (such as lysine or arginine) due to the action of carboxypeptidases (as described in, *e.g.*, Harris, (1995) *J Chromatog* 705:129-34).

[0127] An alternative method for production of a murine monoclonal antibody is to inject the hybridoma cells into the peritoneal cavity of a syngeneic mouse, for example, a mouse that has been treated (*e.g.*, pristane-primed) to promote formation of ascites fluid containing the monoclonal antibody. Monoclonal antibodies can be isolated and purified by a variety of well-established techniques. Such isolation techniques include affinity chromatography with Protein-A Sepharose, size-exclusion chromatography, and ion-exchange chromatography (see, *e.g.*, Baines and Thorpe, (1992) in Methods in Molecular Biology, 10:79-104 (The Humana Press). Monoclonal antibodies can be purified by affinity

chromatography using an appropriate ligand selected based on particular properties of the antibody (*e.g.*, heavy or light chain isotype, binding specificity, etc.). Examples of a suitable ligand, immobilized on a solid support, include Protein A, Protein G, an anti-constant region (light chain or heavy chain) antibody, and an anti-idiotype antibody.

[0128] Although the disclosed antigen binding molecules were produced in a rabbit system, human, partially human, or humanized antibodies may be suitable for many applications, particularly those involving administration of the antibody to a human subject, other types of antigen binding molecules will be suitable for certain applications. Such antibodies can be prepared as described herein and form an aspect of the instant disclosure.

[0129] The instant disclosure provides antigen binding molecules that specifically bind to GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules. Antigen binding molecules that cross compete with the antigen binding molecules disclosed herein form another aspect of the instant disclosure.

[0130] In certain embodiments, the antigen binding molecule cross competes with a reference antibody comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 5, 11, 17 and 23. In certain embodiments, the antigen binding molecule cross competes with a reference antibody, wherein the reference antibody comprises a VH CDR1 comprising an amino acid sequence of SEQ ID NOs: 13 or 19. In certain embodiments, the antigen binding molecule cross competes with a reference antibody, wherein the reference antibody comprises a VH CDR2 comprising an amino acid sequence of SEQ ID NOs: 14 or 20. In certain embodiments, the antigen binding molecule cross competes with a reference antibody, wherein the reference antibody comprises a VH CDR3 comprising an amino acid sequence of SEQ ID NOs: 15 or 21.

[0131] In other embodiments, the antigen binding molecule cross competes with a reference antibody, wherein the reference antibody comprises a VL CDR1 comprising an amino acid sequence of SEQ ID NO: 13 or 25. In certain embodiments, the antigen binding molecule cross competes with a reference antibody, wherein the reference antibody comprises a VL CDR2 comprising an amino acid sequence of SEQ ID NO: 14 or 26. In certain embodiments, the antigen binding molecule cross competes with a reference antibody, wherein the reference antibody comprises a VL CDR3 comprising an amino acid sequence of SEQ ID NO: 15 or 27.

[0132] In some embodiments, the antibody or antigen binding molecule that specifically binds SEQ ID NOs: 1, 2, 3, 499 and/or 500 binds the same or an overlapping epitope as a reference antibody disclosed herein (*e.g.*, those comprising sequences presented in FIGURES 6 and 8). In certain embodiments, the antibody or antigen binding molecule binds the same or an overlapping epitope as a reference antibody.

IIa. Clone 8

[0133] In some embodiments, an antigen binding molecule or antibody that specifically binds to GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence GFTISNL (SEQ ID NO: 7).

[0134] In some embodiments, an antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence DIDGRGDIYCATWAK (SEQ ID NO: 8).

[0135] In some embodiments, an antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence DGDGSGWGDFNF (SEQ ID NO: 9).

[0136] In some embodiments, an antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a heavy chain VH comprising: (a) a VH CDR1 comprising, consisting of, or consisting essentially of the amino acid

sequence GFTISNL (SEQ ID NO: 7); and/or (b) a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence DIDGRGDIYCATWAK (SEQ ID NO: 8); and/or (c) a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence DGDGSGWGDFNF (SEQ ID NO: 9).

[0137] In some embodiments, the antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR1, a VH CDR2, and VH CDR3, wherein the VH CDR1, VH CDR2, and VH CDR3 comprise the amino acid sequence of the VH CDR1, VH CDR2, and VH CDR3 sequences presented in FIGURES 6 and 8.

[0138] In some embodiments, the antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a heavy chain variable region sequence comprising an amino acid sequence of FIGURES 6 and 8 (*e.g.*, (SEQ ID NO: 5)).

[0139] In some embodiments, the antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises the VH framework regions (FRs) described herein. In specific embodiments, the antibody or antigen binding molecule comprises the VH FRs as set forth in, or derivable from, the sequences presented in FIGURES 6 and 8 (*e.g.*, one, two, three, or four of the FRs in one sequence of FIGURES 6 or 8).

[0140] In some embodiments, the antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a heavy chain sequence disclosed herein (*e.g.*, SEQ ID NO: 6 in FIGURE 6). In one embodiment, the antibody or

antigen binding molecule comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 5.

[0141] In various embodiments, the heavy chain variable region is 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to the heavy chain variable region sequence of SEQ ID NO:5.

[0142] In some embodiments, an antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QASQSISTALA (SEQ ID NO: 13).

[0143] In some embodiments, an antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence RASTLAS (SEQ ID NO: 14).

[0144] In some embodiments, an antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence QQGWSTVNVDNV (SEQ ID NO: 15).

[0145] In some embodiments, an antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a light chain VL comprising: (a) a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QASQSISTALA (SEQ ID NO: 13); and/or (b) a VL CDR2 comprising, consisting of, or

consisting essentially of the amino acid sequence RASTLAS (SEQ ID NO: 14); and/or (c) a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence QQGWSTVNVDNV (SEQ ID NO: 15).

[0146] In some embodiments, the antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1, a VL CDR2, and VL CDR3, wherein the VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of the VL CDR1, VL CDR2, and VL CDR3 sequences presented in FIGURES 6 and 8.

[0147] In some embodiments, the antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a light chain variable region sequence comprising an amino acid sequence of FIGURE 6 or FIGURE 8 (*e.g.*, SEQ ID NO: 11).

[0148] In some embodiments, the antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises the VL framework regions (FRs) described herein. In specific embodiments, the antibody or antigen binding molecule comprises the VL FRs as set forth in, or derivable from, the sequences presented in FIGURES 6 and 8 (*e.g.*, one, two, three, or four of the FRs in one sequence of FIGURE 6 or 8).

[0149] In some embodiments, the antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a light chain sequence disclosed herein (*e.g.*, SEQ ID NO: 12 in FIGURE 6, or in FIGURE 8). In one embodiment, the

antibody or antigen binding molecule comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 11.

[0150] In various embodiments, the light chain variable region is 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to the light chain variable region sequence of SEQ ID NO: 11.

[0151] In some embodiments, the antibody or antigen binding molecule that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises any one, two, and/or three VH CDR sequences disclosed herein. In certain embodiments, the antibody or antigen binding molecule comprises a VH CDR1, a VH CDR2, and a VH CDR3 having the amino acid sequence of any VH CDR1, VH CDR2, and VH CDR3 disclosed herein, respectively. In some embodiments, the antibody or antigen binding molecule comprises any one, two, and/or three VL CDR sequences disclosed herein. In certain embodiments, the antibody or antigen binding molecule comprises a VL CDR1, a VL CDR2, and a VL CDR3 having the amino acid sequence of any VL CDR1, VL CDR2, and VL CDR3 disclosed herein, respectively.

[0152] In one embodiment, the antibody or antigen binding molecule that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises: (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 7; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 8; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 9; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 13; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 14; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 15.

[0153] In one embodiment, the antibody or antigen binding molecule that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises: (a) a VH CDR1 region; (b) a VH CDR2 region;

(c) a VH CDR3 region; (d) a VL CDR1 region; (e) a VL CDR2 region; and (f) a VL CDR3 region, wherein the VH and VL CDRs are shown in FIGURES 6 and 8.

[0154] In some embodiments, the antibody or antigen binding molecule that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a heavy chain variable region sequence disclosed herein (*e.g.*, in FIGURES 6 and 8) and a light chain variable region sequence disclosed herein (*e.g.*, in FIGURES 6 and 8).

[0155] In one embodiment, the antibody or antigen binding molecule comprises: (a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 5; and (b) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 11. Nucleotide sequences encoding the heavy chain variable region and the light chain variable region are provided in FIGURE 6.

[0156] In some embodiments, the antibody or antigen binding molecule that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a heavy chain sequence disclosed herein (*e.g.*, in FIGURES 6 and 8) and a light chain sequence disclosed herein (*e.g.*, in FIGURES 6 and 8).

[0157] In one embodiment, the antibody or antigen binding molecule comprises: (a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 6; and (b) a light chain comprising the amino acid sequence of SEQ ID NO: 12.

[0158] In one embodiment, the antibody or antigen binding molecule comprises: (a) a heavy chain comprising an amino acid sequence that is 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to the amino acid sequence of SEQ ID NO: 6; and (b) a light chain comprising an amino acid sequence that is 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to the amino acid sequence of SEQ ID NO: 12.

IIb. Clone 16

[0159] In some embodiments, an antigen binding molecule or antibody that specifically binds to GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence GSDISSY (SEQ ID NO: 19).

[0160] In some embodiments, an antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence IIVSSGSAYYATWAK (SEQ ID NO: 20).

[0161] In some embodiments, an antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence NQYSGYGFSF (SEQ ID NO: 21).

[0162] In some embodiments, an antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a heavy chain VH comprising: (a) a VH CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence GSDISSY (SEQ ID NO: 19); and/or (b) a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence IIVSSGSAYYATWAK (SEQ ID NO: 20); and/or (c) a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence NQYSGYGFSF (SEQ ID NO: 21).

[0163] In some embodiments, the antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences

thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR1, a VH CDR2, and VH CDR3, wherein the VH CDR1, VH CDR2, and VH CDR3 comprise the amino acid sequence of the VH CDR1, VH CDR2, and VH CDR3 sequences presented in FIGURES 6 and 8.

[0164] In some embodiments, the antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a heavy chain variable region sequence comprising an amino acid sequence of FIGURE 6 or 8 (*e.g.*, SEQ ID NO: 17).

[0165] In some embodiments, the antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises the VH framework regions (FRs) described herein. In specific embodiments, the antibody or antigen binding molecule comprises the VH FRs as set forth in, or derivable from, the sequences presented in FIGURE 6 (*e.g.*, one, two, three, or four of the FRs in one sequence of FIGURE 6 or 8 (*e.g.*, SEQ ID NO: 17).

[0166] In some embodiments, the antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a heavy chain sequence disclosed herein (*e.g.*, SEQ ID NO: 18 in FIGURE 6). In one embodiment, the antibody or antigen binding molecule comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 17.

[0167] In various embodiments, the heavy chain variable region is 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to the heavy chain variable region sequence of SEQ ID NO: 17.

[0168] In some embodiments, an antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QSSHSVYYGDWLA (SEQ ID NO: 25).

[0169] In some embodiments, an antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence RASNLAS (SEQ ID NO: 26).

[0170] In some embodiments, an antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence LGGYDDDGETA (SEQ ID NO: 27).

[0171] In some embodiments, an antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a light chain VL comprising: (a) a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QSSHSVYYGDWLA (SEQ ID NO: 25); and/or (b) a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence RASTLAS (SEQ ID NO: 26); and/or (c) a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence LGGYDDDGETA (SEQ ID NO: 27).

[0172] In some embodiments, the antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences

thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1, a VL CDR2, and VL CDR3, wherein the VL CDR1, VL CDR2, and VL CDR3 comprise the amino acid sequence of the VL CDR1, VL CDR2, and VL CDR3 sequences presented in FIGURE 6 or 8.

[0173] In some embodiments, the antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a light chain variable region sequence comprising an amino acid sequence of FIGURE 6 or FIGURE 8 (*e.g.*, SEQ ID NO: 23).

[0174] In some embodiments, the antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises the VL framework regions (FRs) described herein. In specific embodiments, the antibody or antigen binding molecule comprises the VL FRs as set forth in, or derivable from, the sequences presented in FIGURES 6 and 8 (*e.g.*, one, two, three, or four of the FRs in one sequence of FIGURE 6 or FIGURE 8).

[0175] In some embodiments, the antigen binding molecule or antibody that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a light chain sequence disclosed herein (*e.g.*, SEQ ID NO: 24 in FIGURE 6, or in FIGURE 8). In one embodiment, the antibody or antigen binding molecule comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 23.

[0176] In various embodiments, the light chain variable region is 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to the light chain variable region sequence of SEQ ID NO: 23.

[0177] In some embodiments, the antibody or antigen binding molecule that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises any one, two, and/or three VH CDR sequences disclosed herein. In certain embodiments, the antibody or antigen binding molecule comprises a VH CDR1, a VH CDR2, and a VH CDR3 having the amino acid sequence of any VH CDR1, VH CDR2, and VH CDR3 disclosed herein, respectively. In some embodiments, the antibody or antigen binding molecule comprises any one, two, and/or three VL CDR sequences disclosed herein. In certain embodiments, the antibody or antigen binding molecule comprises a VL CDR1, a VL CDR2, and a VL CDR3 having the amino acid sequence of any VL CDR1, VL CDR2, and VL CDR3 disclosed herein, respectively.

[0178] In one embodiment, the antibody or antigen binding molecule that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises: (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 19; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 20; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 21; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 25; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 26; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 27.

[0179] In one embodiment, the antibody or antigen binding molecule that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises: (a) a VH CDR1 region; (b) a VH CDR2 region; (c) a VH CDR3 region; (d) a VL CDR1 region; (e) a VL CDR2 region; and (f) a VL CDR3 region, wherein the VH and VL CDRs are shown in FIGURES 6 and 8.

[0180] In some embodiments, the antibody or antigen binding molecule that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3),

SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a heavy chain variable region sequence disclosed herein (*e.g.*, in FIGURES 6 and 8) and a light chain variable region sequence disclosed herein (*e.g.*, in FIGURES 6 and 8).

[0181] In one embodiment, the antibody or antigen binding molecule comprises: (a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 17; and (b) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 23. Nucleotide sequences encoding the heavy chain variable region and the light chain variable region are provided in FIGURE 6.

[0182] In some embodiments, the antibody or antigen binding molecule that specifically binds to the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising this sequence and cells presenting such molecules, comprises a heavy chain sequence disclosed herein (*e.g.*, in FIGURES 6 and 8) and a light chain sequence disclosed herein (*e.g.*, in FIGURES 6 and 8).

[0183] In one embodiment, the antibody or antigen binding molecule comprises: (a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 18; and (b) a light chain comprising the amino acid sequence of SEQ ID NO: 24.

[0184] In one embodiment, the antibody or antigen binding molecule comprises: (a) a heavy chain comprising an amino acid sequence that is 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to the amino acid sequence of SEQ ID NO: 18; and (b) a light chain comprising an amino acid sequence that is 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to the amino acid sequence of SEQ ID NO: 24.

III Polynucleotides Encoding Antibodies and Antigen Binding Molecules

[0185] The present invention is also directed to polynucleotides encoding antibodies and antigen binding molecules that specifically bind to GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising these sequences and cells presenting such molecules.

[0186] In some embodiments, a polynucleotide of the present invention encodes an antigen binding molecule, wherein the antigen binding molecule comprises a heavy chain variable region amino acid sequence that is at least about 75%, at least about 85%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or 100% identical to a heavy chain variable region amino acid sequence selected from the group consisting of SEQ ID NOs: 5 and 17.

[0187] In some embodiments, a polynucleotide of the present invention encodes antigen binding molecule, wherein the antigen binding molecule comprises a light chain variable amino acid sequence that is at least about 75%, at least about 85%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or 100% identical to a light chain variable region amino acid sequence selected from the group consisting of SEQ ID NOs: 11 and 23.

[0188] In certain embodiments, the polynucleotide comprises a heavy chain coding sequence selected from the group consisting of SEQ ID NOs: 4 and 16. In another embodiment, the polynucleotide comprises a light chain coding sequence selected from the group consisting of SEQ ID NOs: 10 and 22.

[0189] As will be appreciated by those of skill in the art, variations of the disclosed polynucleotide sequences are possible due to the degeneracy of the genetic code. Such variants of the disclosed polynucleotide sequences thus form an aspect of the instant disclosure.

IV. Vectors, Cells, and Pharmaceutical Compositions

[0190] In certain aspects, provided herein are vectors comprising a polynucleotide of the present invention. In some embodiments, the present invention is directed to a vector or a set of vectors comprising a polynucleotide encoding an antibody or antigen binding molecule that specifically binds to GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500) and molecules comprising these sequences and cells presenting such molecules, as described herein.

[0191] Any vector known in the art can be suitable for expressing the antibodies and antigen binding molecules of the present invention. In some embodiments, the vector is a viral vector. In some embodiments, the vector is a retroviral vector, a DNA vector, a murine leukemia virus vector, an SFG vector, a plasmid, a RNA vector, an adenoviral vector, a

baculoviral vector, an Epstein Barr viral vector, a papovaviral vector, a vaccinia viral vector, a herpes simplex viral vector, an adenovirus associated vector (AAV), a lentiviral vector, or any combination thereof.

[0192] In other aspects, provided herein are cells comprising a polynucleotide or a vector of the present invention. In some embodiments, the present invention is directed to cells, *in vitro* cells, comprising a polynucleotide encoding an antigen binding molecule, as described herein. In some embodiments, the present invention is directed to cells, *e.g.*, *in vitro* cells, comprising a polynucleotide encoding an antibody or an antigen binding molecule thereof that specifically binds to GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising these sequences and cells presenting such molecules, as disclosed herein.

[0193] Any cell can be used as a host cell for the polynucleotides and vectors encoding all or a fragment of the antibodies and antigen binding molecules of the present invention. In some embodiments, a host cell can be a prokaryotic cell, fungal cell, yeast cell, or higher eukaryotic cells such as a mammalian cell. Suitable prokaryotic cells include, without limitation, eubacteria, such as Gram-negative or Gram-positive organisms, for example, *Enterobacteriaceae* such as *Escherichia*, *e.g.*, *E. coli*; *Bacilli* such as *B. subtilis* and *B. licheniformis*; *Pseudomonas* such as *P. aeruginosa*; and *Streptomyces*. In some embodiments, a host cell is a mammalian cell, such as a human cell. In some embodiments, a host cell is a CHO cell and in other embodiments, a host cell is a sP2/0 or other murine cell. A host cell of the present invention can be obtained through any source known in the art.

[0194] Other aspects of the present invention are directed to compositions comprising a polynucleotide described herein, a vector described herein, an antibody an antigen binding molecule described herein, and/or an *in vitro* cell described herein. In some embodiments, the composition comprises a pharmaceutically acceptable carrier, diluent, solubilizer, emulsifier, preservative and/or adjuvant. In some embodiments, the composition comprises an excipient.

[0195] In one embodiment, the composition comprises a polynucleotide encoding an antibody or antigen binding molecule that specifically binds to that specifically binds to GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), and molecules comprising these sequences and cells presenting such molecules.

In another embodiment, the composition comprises an antigen binding molecule that specifically binds to SEQ ID NOs: 1, 2, 3, 499 and/or 500, and molecules comprising these sequences and cells presenting such molecules. In another embodiment, the composition comprises an *in vitro* cell comprising a polynucleotide encoding an antibody or an antigen binding molecule thereof encoded by a polynucleotide disclosed herein.

[0196] In some embodiments, the composition comprises more than one different antibody or antigen binding molecule that specifically binds to GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), and molecules comprising these sequences and cells presenting such molecules. In some embodiments, the composition includes more than one antibody or antigen binding molecule that specifically binds to SEQ ID NOs: 1, 2, 3, 499 and/or 500, and molecules comprising these sequences and cells presenting such molecules, wherein the antibodies or antigen binding molecules bind more than one epitope. In some embodiments, the antibodies or antigen binding molecules will not compete with one another for binding to that epitope. In some embodiments, two or more of the antibodies or antigen binding molecules provided herein are combined together in a pharmaceutical composition. Preferably such a composition will be suitable for administration to a subject, including a human.

V. Exemplary Methods

[0197] The following section describes various exemplary methods of using the disclosed antigen binding molecules herein. Any of the antigen binding molecules, and fragments thereof, disclosed herein (including those provided by the Figures and the attached Sequence Listing) can be employed in the disclosed methods.

[0198] In some of the disclosed methods T cells can be employed. Such T cells can come from any source known in the art. For example, T cells can be differentiated *in vitro* from a hematopoietic stem cell population, or T cells can be obtained from a subject. T cells can be obtained from, *e.g.*, peripheral blood mononuclear cells (PBMCs), bone marrow, lymph node tissue, cord blood, thymus tissue, tissue from a site of infection, ascites, pleural effusion, spleen tissue, and tumors. In addition, the T cells can be derived from one or more T cell lines available in the art. T cells can also be obtained from a unit of blood collected from a subject using any number of techniques known to the skilled artisan, such as FICOLL™ separation and/or apheresis. Additional methods of isolating T cells for a T cell

therapy are disclosed in U.S. Patent Publication No. 2013/0287748.

[0199] In various embodiments, the antigen binding molecule specifically binds to a molecule comprising the amino acid sequence GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) or a subsequence comprising the amino acid sequence GSGKPGSGEG (SEQ ID NO: 2) or SGKPGSGE (SEQ ID NO: 499), molecules comprising these sequences and cells presenting such sequences. In further embodiments, the antigen binding molecule comprises one or more of (a) a light chain CDR1, (b) a light chain CDR2, (c) a light chain CDR3, (d) a heavy chain CDR1, (e) a heavy chain CDR2, and (f) a heavy chain CDR3. In additional embodiments, the antigen binding molecule comprises a heavy chain CDR3 of SEQ ID NO: 9 or 21, or a light chain CDR3 of SEQ ID NO: 15 or 27, or both the heavy and light chains. In other embodiments, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 7 or 19, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 8 or 20, or a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 13 or 25, or a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 14 or 26. In various embodiments, the antigen binding molecule comprises a heavy chain CDR1, a heavy chain CDR2, a heavy chain CDR3, a light chain CDR1, a light chain CDR2, and a light chain CDR3, each CDR comprising an amino acid sequence shown in FIGURE 6.

[0200] In various embodiments, an antigen binding molecule comprises a heavy chain (HC), and the HC can comprise a heavy chain variable region (VH) sequence comprising SEQ ID NO: 5. In various embodiments, the heavy chain comprises a heavy chain CDR1, a heavy chain CDR2, and a heavy chain CDR3, each CDR comprising an amino acid sequence shown in FIGURES 6 and 8. Moreover, in some embodiments, an antigen binding molecule can be employed which comprises a VH amino acid sequence that is at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or about 100% identical to a VH of an antigen binding molecule of claim disclosed herein (*e.g.*, an antigen binding molecule comprising a variable region (VH) sequence comprising SEQ ID NO: 5).

[0201] In various embodiments, an antigen binding molecule comprises a light chain (LC), and the LC can comprise a light chain variable region (VL) sequence comprising SEQ ID NO: 11. In various embodiments, the light chain comprises a light chain CDR1, a light

Date Reçue/Date Received 2020-04-16

chain CDR2, and a light chain CDR3, each CDR comprising an amino acid sequence shown in FIGURES 6 and 8. Moreover, in some embodiments, an antigen binding molecule can be employed which comprises a VL amino acid sequence that is at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or about 100% identical to a VH of an antigen binding molecule of claim disclosed herein (*e.g.*, an antigen binding molecules comprising a variable region (VL) sequence comprising SEQ ID NO: 11).

[0202] In various embodiments, the antigen binding molecule can specifically bind to a molecule comprising the amino acid sequence GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) or a subsequence comprising the amino acid sequence GKPGSGEG (SEQ ID NO: 3) or KPGSG (SEQ ID NO: 500). In further embodiments of the disclosed methods, the antigen binding molecule comprises one or more of (a) a light chain CDR1, (b) a light chain CDR2, (c) a light chain CDR3, (d) a heavy chain CDR1, (e) a heavy chain CDR2, and (f) a heavy chain CDR3. In additional embodiments of the disclosed methods, the antigen binding molecule comprises a heavy chain CDR3 of SEQ ID NO: 21, or a light chain CDR3 of SEQ ID NO: 27, or both the heavy and light chains. In other embodiments of the disclosed methods, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 19 or a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 20 or a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 25 or a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 26.

[0203] In various embodiments, the antigen binding molecule comprises a heavy chain CDR1, a heavy chain CDR2, a heavy chain CDR3, a light chain CDR1, a light chain CDR2, and a light chain CDR3, each CDR comprising an amino acid sequence shown in FIGURES 6 and 8.

[0204] In various embodiments of the disclosed methods, an antigen binding molecule comprises a heavy chain (HC), and the HC can comprise a heavy chain variable region (VH) sequence comprising SEQ ID NO: 17. Referring to the Figures, in various embodiments of the disclosed methods the heavy chain comprises a heavy chain CDR1, a heavy chain CDR2, and a heavy chain CDR3, each CDR comprising an amino acid sequence shown in Figure 6. Moreover, in embodiments of the disclosed methods, an antigen binding molecule can be employed which comprises a VH amino acid sequence that is at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or

about 100% identical to a VH of an antigen binding molecule of claim disclosed herein (*e.g.*, an antigen binding molecule comprising a variable region (VH) sequence comprising SEQ ID NO: 17).

[0205] In various embodiments of the disclosed methods, an antigen binding molecule comprises a light chain (LC), and the LC can comprise a light chain variable region (LH) sequence comprising SEQ ID NO: 23. Referring to the Figures, in various embodiments of the disclosed methods the light chain comprises a light chain CDR1, a light chain CDR2, and a light chain CDR3, each CDR comprising an amino acid sequence shown in FIGURES 6 and 8. Moreover, in embodiments of the disclosed methods, an antigen binding molecule can be employed which comprises a VL amino acid sequence that is at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or about 100% identical to a VH of an antigen binding molecule of claim disclosed herein (*e.g.*, an antigen binding molecule comprising a variable region (VL) sequence comprising SEQ ID NO: 23).

[0206] In specific embodiments of the disclosed methods, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 19, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 20, a heavy chain CDR3 comprising the amino acid sequence SEQ ID NO: 21, a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 25, a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 26, and a light chain CDR3 comprising the amino acid sequence SEQ ID NO: 27.

[0207] In specific embodiments of the disclosed methods, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 7, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 8, a heavy chain CDR3 comprising the amino acid sequence SEQ ID NO: 9, a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 13, a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 14, and a light chain CDR3 comprising the amino acid sequence SEQ ID NO: 15.

[0208] In view of the above description of antigen binding molecules that can be employed in the disclosed methods, representative methods will now be discussed in more detail.

Va. Method of Administering a Dose of a Medicament to a Subject

[0209] In one aspect, a method of administering a dose of a medicament to a subject, the dose comprising a preselected number of cells presenting a therapeutic molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) is provided.

[0210] In specific embodiments, the dose comprises 0.5 x10^6 cells per kilogram of the subject, 1.0x10^6 cells per kilogram of the subject, 2.0x10^6 cells per kilogram of the subject, 3.0x10^6 cells per kilogram of the subject, 4.0x10^6 cells per kilogram of the subject, or 5.0x10^6 cells per kilogram of the subject, although the method can be employed using any dose. 1.0x10^6 cells per kilogram of the subject is a preferred dose.

[0211] Consistent with the definition provided herein, in various embodiments, a subject is a human or non-human subject. When the subject is a human, the subject can be, *e.g.*, any human who is being treated for an abnormal physiological condition, such as cancer or has been formally diagnosed with a disorder, those without formally recognized disorders, those receiving medical attention, those at risk of developing the disorders, those being studied for the presence or absence of a disorder, etc.

[0212] Initially, a sample comprising a population comprising a known number of cells, the population known or suspected to be expressing a therapeutic molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), is provided.

[0213] In one embodiment, the selected amino acid sequence comprises GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1); in another embodiment, the selected amino acid sequence comprises GSGKPGSGEG (SEQ ID NO: 2); in another embodiment, the selected amino acid sequence comprises GKPGSGEG (SEQ ID NO: 3); in another embodiment, the selected amino acid sequence comprises SGKPGSGE (SEQ ID NO: 499); and in a another embodiment, the selected amino acid sequence comprises KPGSG (SEQ ID NO: 500).

[0214] Consistent with the definition provided herein, in various embodiments, a subject is a human or non-human subject. When the subject is a human, the subject can be,

e.g., any human who is being treated for an abnormal physiological condition, such as cancer or has been formally diagnosed with a disorder, those without formally recognized disorders, those receiving medical attention, those at risk of developing the disorders, those being studied for the presence or absence of a disorder, etc.

[0215] Initially, a sample of known volume comprising a population comprising a known number of cells, which cells are known or suspected to be presenting a molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO:s 1, 2, 3, 499 or 500) is provided. The number of cells can be determined using any known method. In preferred embodiments the population is determined by counting the cells in the sample using an automated apparatus, such as a cell sorter (*e.g.*, a FACS), however traditional non-automated cell counting methods can also be employed.

[0216] The cells of the method can comprise any type of cell, with immune cells (*e.g.*, B lymphocytes, monocytes, dendritic cells, Langerhans cells, keratinocytes, endothelial cells, astrocytes, fibroblasts, and oligodendrocytes) being preferred. T cells (including T cytotoxic, T helper and Treg cells) are especially preferred. In specific embodiments, the cells are T cells, which can be obtained as described herein and by methods known in the art. Any type of cell can be employed in the method, and the cell can be a human or non-human cell (including both prokaryotic and eukaryotic cells). Exemplary cells include, but are not limited to immune cells such as T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells. A T cell can be autologous, allogeneic, or heterologous, or it can be an *in vivo* T cell or an *in vitro* T cell, and can be a CD4+ T cell or a CD8+ T cell. In additional embodiments, the cells are T cells presenting a CAR. Moreover, the cells can be disposed in, or isolated from, any environment capable of maintaining the cells in a viable form, such as blood, tissue or any other sample obtained from a subject, cell culture media, tissue grown *ex vivo*, etc. Gradient purification, cell culture selection and/or cell sorting can be useful in obtaining cells.

[0217] The therapeutic molecule expressed by the cell can comprise any molecule known or suspected to provide a therapeutic benefit to a subject to which is it administered. Thus, a therapeutic molecule can be a peptide or polypeptide of any structure or design. Preferably the portion of the therapeutic molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) is expressed or disposed, at least in part, extracellularly, *i.e.*, to a degree that it can be recognized by an extracellular interaction partner such as the antigen binding molecules of the instant disclosure.

[0218] In specific embodiments, the therapeutic molecule is a CAR. When the therapeutic molecule is a CAR it can comprise a molecule, or fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

[0219] Continuing, an aliquot of the sample comprising a population of cells presenting a molecule comprising the selected amino acid sequence is provided. The aliquot can be obtained using any convenient means, such as by a cell sorter, by a simply pipetting of material out of the sample, etc.

[0220] Further, an antigen binding molecule that specifically binds the selected amino acid sequence and comprises a detectable label is provided. The antigen binding molecule is preferably an antigen binding molecule disclosed herein, *e.g.*, in the Figures, Sequence Listing or the instant disclosure. Any detectable label can be employed in the method, and suitable labels can be selected using a desired set of criteria. Examples of types of detectable labels include a fluorescent dye, which can be selected from the group consisting of an Atto

dye, an Alexafluor dye, quantum dots, Hydroxycoumarin, Aminocoumarin, Methoxycoumarin, Cascade Blue, Pacific Blue, Pacific Orange, Lucifer yellow, NBD, R-Phycoerythrin (PE), PE-Cy5 conjugates, PE-Cy7 conjugates, Red 613, PerCP, TruRed, FluorX, Fluorescein, BODIPY-FL, Cy2, Cy3, Cy3B, Cy3.5, Cy5, Cy5.5, Cy7, TRITC, X-Rhodamine, Lissamine Rhodamine B, Texas Red, Allophycocyanin (APC), APC-Cy7 conjugates, Indo-1, Fluo-3, Fluo-4, DCFH, DHR, SNARF, GFP (Y66H mutation), GFP (Y66F mutation), EBFP, EBFP2, Azurite, GFPuv, T-Sapphire, Cerulean, mCFP, mTurquoise2, ECFP, CyPet, GFP (Y66W mutation), mKeima-Red, TagCFP, AmCyan1, mTFP1, GFP (S65A mutation), Midoriishi Cyan, Wild Type GFP, GFP (S65C mutation), TurboGFP, TagGFP, GFP (S65L mutation), Emerald, GFP (S65T mutation), EGFP, Azami Green, ZsGreen1, TagYFP, EYFP,Topaz, Venus, mCitrine, YPet, TurboYFP, ZsYellow1, Kusabira Orange, mOrange, Allophycocyanin (APC), mKO, TurboRFP, tdTomato, TagRFP, DsRed monomer, DsRed2 ("RFP"), mStrawberry, TurboFP602, AsRed2, mRFP1, J-Red, R-phycoerythrin (RPE), B-phycoerythrin (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry. Other types of detectable labels include optical dyes, which are described in Johnson, Molecular Probes Handbook: A Guide to Fluorescent Probes and Labeling Techniques, 11th Edition, Life Technologies, (2010), radiolabels (*e.g.*, isotope markers such as ^{3}H, ^{11}C, ^{14}C, ^{15}N, ^{18}F, ^{35}S, ^{64}CU, ^{90}Y, ^{99}Tc, ^{111}In, ^{124}I, ^{125}I, ^{131}I), photochromic compounds, magnetic labels (e.g., DYNABEADS), etc. Strategies for the labeling of proteins are known in the art and can be employed in the disclosed method.

[0221] The label can be associated with the antigen binding molecule at any position in the molecule, although it is preferable to associate the label with the molecule at a position (or positions, if multiple labels are employed) at a point such that the binding properties of the molecule are not modified, unless such modified binding activity is desired. Any antigen binding molecule that specifically binds the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) can be employed. Examples of suitable antigen binding molecules and components thereof are provided herein, *e.g.*, in the attached Sequence Listing and in FIGURES 6 and 8. In specific embodiments of the disclosed method, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 19, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 20, a heavy chain CDR3 comprising the amino acid sequence SEQ ID NO: 21, a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 25, a light chain CDR2 comprising the amino acid

Date Reçue/Date Received 2020-04-16

sequence SEQ ID NO: 26, and a light chain CDR3 comprising the amino acid sequence SEQ ID NO: 27. In other specific embodiments of the disclosed methods, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 7, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 8, a heavy chain CDR3 comprising the amino acid sequence SEQ ID NO: 9, a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 13, a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 14, and a light chain CDR3 comprising the amino acid sequence SEQ ID NO: 15.

[0222] The antigen binding molecule can be disposed on any surface, or no surface at all. For example, the antigen binding molecule can be present in a buffer and the buffer-antigen binding molecule can be contacted with the sample. Alternatively, the antigen binding molecule can be associated with a surface. Suitable surfaces include agarose beads, magnetic beads such as DYNABEADS, or a plastic, glass or ceramic plate such as a welled plate, a bag such as a cell culture bag, etc. The surface can itself be disposed in another structure, such as a column.

[0223] Continuing, the aliquot of the sample is contacted with the antigen binding molecule under conditions that permit the formation of a binding complex comprising a cell present in the sample and the antigen binding molecule. Thus, the result of this step of the method is the formation of a binding complex in which the antigen binding molecule, with which a detectable label is associated, is bound to the cell expressing the therapeutic molecule, which comprises the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500). Thus, the binding complex itself is detectable. Conditions that permit the formation of a binding complex will be dependent on a variety of factors, however generally aqueous buffers at physiological pH and ionic strength, such as in phosphate-buffered saline (PBS), will favor formation of binding complexes and are preferred in the disclosed method.

[0224] The fraction of cells present in a binding complex of in the aliquot is determined. This calculation can be performed by comparing the number of cells bearing the detectable label to those that do not, and can be represented as percentage. The number of cells in binding complexes can be determined. The specific method employed to determine the number of cells present in a binding complex will be dependent on the nature of the label selected. For example, FACS can be employed when a fluorescent label is selected; when an isotope label is selected mass spectrometry, NMR or other technique can be employed; magnetic-based cell sorting can be employed when a magnetic label is chosen; microscopy

can also be employed. The number of cells in the sample is know *ab initio* and thus the fraction of cells present in a binding complex can be easily determined.

[0225] Continuing, the concentration of cells in the initial sample expressing a molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) is determined; the determination is based on the fraction of cells determined to be present in the binding complex, and thus expressing the therapeutic protein bearing a detectable label.

[0226] The fraction of cells presenting the therapeutic protein is known, and the volume of the aliquot is known; thus a simple comparison of the number of cells in the sample from which the aliquot was taken that are expressing the therapeutic molecule to the volume of the larger sample provides the fraction of the cells in the sample bearing the therapeutic molecule on a therapeutic molecule/volume basis (*i.e.*, the concentration of cells bearing the therapeutic molecule in the larger sample).

[0227] The volume of the sample that comprises the selected number of cells is determined, by extrapolation based on the concentration of cells bearing therapeutic molecule present in the sample.

[0228] Finally, the volume of sample comprising the desired number of cells is administered to the subject. The administration can comprise an aspect of a therapeutic regimen based on the therapeutic molecule present in the sample and expressed by the cells in the sample.

[0229] Although the administration can be performed one time or more than one time, an advantage of the method is that by administering a dose comprising the preselected number of cells, which number of cells will be determined based on a known or expected efficacy, unnecessary administration of cells presenting the therapeutic molecule is avoided; *i.e.*, the subject receives the correct number of cells to provide a desired therapeutic benefit and is not too many or too few cells.

Vb. Method of Activating Cells

[0230] The disclosed methods of activating an immune cell can be employed in connection with any immune cell presenting a molecule comprising a sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500). In the context of the disclosed methods, T cells (including T cytotoxic,

T helper and Treg cells) presenting such molecules are preferred and will be used to exemplify the disclosed methods, however other immune cells presenting such molecules (*e.g.*, lymphocytes such as tumor infiltrating lymphocytes (TILs), cytotoxic T lymphocytes, tumor infiltrating lymphocytes, neutrophils, basophils, or T helper cells, Treg cells, dendritic cells, B cells, hematopoietic stem cells, macrophages, monocytes, Langerhans cells, keratinocytes, endothelial cells, astrocytes, fibroblasts, and oligodendrocytes and NK cells) can also be employed in the disclosed methods.

[0231] Activation (which term is used interchangeably with the term "stimulation") of T cells is dependent upon signals transferred through antigen-specific T cells receptor recognition and accessory receptors on the T cell. For example, clustering of CD3gamma, CD3delta, CD3epsilon and CD3zeta proteins, further associate with other components of the T cell Receptor (TCR), induces activation of the T cell and makes it immunocompetent. Thus, "activation" or "stimulation" as used herein, refers to a primary response induced by binding of a molecule with a ligand (which may be another copy of the same molecule, *e.g.*, CD3zeta associating with another copy of CD3zeta), wherein the binding mediates a signal transduction event.

[0232] In one embodiment, T cells are activated *in vitro* by means of an antigen binding molecule provided herein, and the T cells activated in accordance with the methods of the instant disclosure can be subsequently expanded *ex vivo* and used in a variety of applications, including those disclosed herein.

[0233] In another embodiment, activation occurs *in vivo*, by means of an antigen binding molecule provided herein, and the T cells activated in accordance with the methods of the instant disclosure; expansion occurs within the organism in which the activated cells are disposed. *In vivo* activation can form a component of a therapeutic regime, examples of which are described herein.

[0234] Prior to activation, immune cells, such as T cells, are obtained from a subject (*e.g.*, a mammal such as a human, dog, cat, mouse, rat, rabbit or transgenic species thereof; cells derived from an artificial system such as an artificial thymic organoid (ATO; see, e.g., Seet et al., Nature Methods 14(5):521 (2017) can also be employed in the disclosed *in vivo* and *in vitro* activation methods). Immune cells, including T cells, can be obtained from a number of sources, as described herein, including PBMCs, bone marrow, lymph node tissue, cord blood, thymus tissue, tissue from a site of infection, spleen tissue, tumors or T cell lines. T cells can also be obtained from a volume of blood

Date Reçue/Date Received 2020-04-16

collected from a subject using any number of techniques known to the skilled artisan, such as FICOLL separation. Gradient purification, cell culture selection and/or cell sorting can also be employed.

[0235] In view thereof, a method of activating an immune cell, such as a T cell, presenting a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), is provided.

[0236] Initially, a sample comprising an immune cell known or suspected to be presenting a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) is provided. In specific embodiments the selected amino acid sequence is GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1); in other embodiments the selected amino acid sequence is GSGKPGSGEG (SEQ ID NO: 2); in other embodiments the selected amino acid sequence is GKPGSGEG (SEQ ID NO: 3); in other embodiments the selected amino acid sequence is SGKPGSGE (SEQ ID NO: 499); and in other embodiments the selected amino acid sequence is KPGSG (SEQ ID NO: 500).

[0237] In specific embodiments, the cells are T cells, which can be obtained as described herein and by methods known in the art. The cell can be a human or non-human cell. The T cells can be autologous, allogeneic, or heterologous. When a T cell is employed in the disclosed methods, the T cell can be an *in vivo* T cell or an *in vitro* T cell. Moreover, the cells can be disposed in, or isolated from, any environment capable of maintaining the cells in a viable form, such as blood, tissue or any other sample obtained from a subject, cell culture media, tissue grown *ex vivo*, a suitable buffer, etc.

[0238] In specific embodiments, the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) is a CAR. When the molecule is a CAR it can comprise a molecule, or fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5),

CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

[0239] An antigen binding molecule is then contacted with the sample, under conditions that permit the formation of a binding complex comprising the antigen binding molecule and two molecules comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500), wherein the molecules comprising the selected amino acid sequence are disposed on two different immune cells. The binding event has the effect of bringing both immune cells into closer proximity to one another, with multiple cells being clustered together following multiple binding events.

[0240] The antigen binding molecule is preferably an antigen binding molecule (or fragment thereof) disclosed herein, *e.g.*, in the Figures, Sequence Listing or the instant section of the disclosure. Any antigen binding molecule that specifically binds the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) can be employed. Multiple examples of suitable antigen binding molecules are provided herein, *e.g.*, those having one or more of the CDRs shown in FIGURES 6 and 8. The molecules comprising the selected sequences that are present on each immune cell of a binding complex can be the same or they can be different, so long as they are specifically recognized by the antigen binding molecule.

[0241] In specific embodiments of the disclosed method, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 19, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 20, a heavy chain

CDR3 comprising the amino acid sequence SEQ ID NO: 21, a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 25, a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 26, and a light chain CDR3 comprising the amino acid sequence SEQ ID NO: 27. In other specific embodiments of the disclosed methods, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 7, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 8, a heavy chain CDR3 comprising the amino acid sequence SEQ ID NO: 9, a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 13, a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 14, and a light chain CDR3 comprising the amino acid sequence SEQ ID NO: 15.

[0242] The antigen binding molecule can be disposed on any surface, or no surface at all. For example, in *in vivo* applications the antigen binding molecule can be present in a buffer and the contacting can be achieved by injecting the antigen binding molecule into the body of a subject, whereupon activation will occur when the antigen binding molecule contacts a cell presenting the molecule comprising the amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500).

[0243] The precise amount of antigen binding molecule that will achieve a desired level of activation can be determined empirically, and will depend on various subject-specific criteria. For in vivo activation, the amount of antigen binding molecule can be, for example, 25 μg/kg/day, 20 μg/kg/day, 15 μg/kg/day, 10 μg/kg/day or 5 μg/kg/day. The antigen binding molecule can administered to a subject for a desired number days, for example 5, 4, 3, 2 or 1 day. Other activating antibodies can be used as a guide when determining how much antigen binding molecule to administer to a subject. For example, the clinical experiences with anti-CD3 activating antibody OKT3 may be illustrative and beneficial when performing the disclosed method.

[0244] Those of skill in the art will recognize that a specific therapeutic regime can be tailored to a given subject, and dosing amounts and conditions can depend on a variety of factors normally considered by clinicians. Examples that can be considered when determining a suitable dose of antigen binding molecule for an *in vivo* activation include the overall health and strength of a subject, the subject's weigh, a desired overall degree of

activation, the efficacy and *in vivo* efficacy of the cells presenting the molecule having the selected sequence,

[0245] In an *in vitro* activation, the antigen binding molecule can be present in a buffer and the buffer-antigen binding molecule can be contacted with the sample. Alternatively, in some embodiments, the antigen binding molecule can be associated with a surface. Suitable surfaces include agarose beads, magnetic beads such as DYNABEADS, or a plastic, glass or ceramic plate such as a welled plate, a bag such as a cell culture bag, etc. The surface can itself be disposed in another structure, such as a column.

[0246] Conditions that permit the formation of a binding complex will be dependent on a variety of factors, however generally aqueous buffers at physiological pH and ionic strength, such as in phosphate-buffered saline (PBS), will favor formation of binding complexes and are preferred in the disclosed method.

[0247] In practice, when the binding of the antigen binding molecule specifically binds to the molecules comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500), one molecule on each of two different immune cells, the two cells are drawn closer to one another. This close proximity, or clustering, has the effect of activating the immune cells.

Vc. Method of Determining a Number of Cells Presenting a Molecule of Interest

[0248] There are situations in which it may be desirable to determine the number of cells present in a sample that are expressing a molecule of interest. For example, it may be desirable to determine the number of immune cells present a sample obtained from a subject that are expressing a molecule of interest. Or it may be desirable to determine the number of cells transfected and expressing a molecule of interest, which can be used as a measure of the level of efficiency of the transfection. The disclosed method can be employed in these and other applications in which it is desirable to determine the number of cells present in a sample that are expressing a molecule of interest.

[0249] Thus, a method of determining a number of cells presenting a molecule in a sample wherein the molecule comprises an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500) is provided.

[0250] In on embodiment, a sample comprising cells known or suspected to be expressing a molecule of interest comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) is provided.

[0251] In specific embodiments the selected amino acid sequence is GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1); in other embodiments the selected amino acid sequence is GSGKPGSGEG (SEQ ID NO: 2); in other embodiments the selected amino acid sequence is GKPGSGEG (SEQ ID NO: 3); in other embodiments the selected amino acid sequence is SGKPGSGE (SEQ ID NO: 499); in other embodiments the selected amino acid sequence is KPGSG (SEQ ID NO: 500).

[0252] The cell can be of any type, and can be human or non-human (*e.g.*, mouse, rate, rabbit, hamster, etc). In a preferred embodiment, the cell is an immune cell. An immune cell of the method can be any type of immune cell (*e.g.*, B lymphocytes, monocytes, dendritic cells, Langerhans cells, keratinocytes, endothelial cells, astrocytes, fibroblasts, and oligodendrocytes). T cells (including T cytotoxic, T helper and Treg cells) are especially preferred. In specific embodiments, the cells are T cells, which can be obtained as described herein and by methods known in the art. Any type of immune cell can be employed in this embodiment of the disclosed method. Exemplary cells include, but are not limited to immune cells such as T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells. The T cells can be autologous, allogeneic, or heterologous. The T cells can be CD4+ T cells or CD8+ T cells. When a T cell is employed in the disclosed methods, the T cell can be an *in vivo* T cell or an *in vitro* T cell. Moreover, the cells can be disposed in, or isolated from, any environment capable of maintaining the cells in a viable form, such as blood, tissue or any other sample obtained from a subject, cell culture media, tissue grown *ex vivo*, a suitable buffer, etc.

[0253] In specific embodiments, the molecule of interest is a CAR. When the molecule is a CAR it can comprise a molecule, or fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e

(CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

[0254] The sample is then contacted with an antigen binding molecule that specifically binds the molecule of interest and comprises a detectable label, under conditions that permit the formation of a binding complex comprising a cell present in the sample and the antigen binding molecule. The antigen binding molecule is preferably an antigen binding molecule (or fragment thereof) disclosed herein, *e.g.*, in the Figures, Sequence Listing or the instant section of the disclosure. Any antigen binding molecule that specifically binds the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) can be employed in the disclosed method. Multiple examples of suitable antigen binding molecules are provided herein, *e.g.*, those having one or more of the CDRs shown in FIGURES 6 and 8.

[0255] Any detectable label can be employed in the method, and suitable labels can be selected using a desired set of criteria. Examples of types of detectable labels include a fluorescent dye, which can be selected from the group consisting of an Atto dye, an Alexafluor dye, quantum dots, Hydroxycoumarin, Aminocoumarin, Methoxycoumarin, Cascade Blue, Pacific Blue, Pacific Orange, Lucifer yellow, NBD, R-Phycoerythrin (PE), PE-Cy5 conjugates, PE-Cy7 conjugates, Red 613, PerCP, TruRed, FluorX, Fluorescein, BODIPY-FL, Cy2, Cy3, Cy3B, Cy3.5, Cy5, Cy5.5, Cy7, TRITC, X-Rhodamine, Lissamine Rhodamine B, Texas Red, Allophycocyanin (APC), APC-Cy7 conjugates, Indo-1, Fluo-3,

Fluo-4, DCFH, DHR, SNARF, GFP (Y66H mutation), GFP (Y66F mutation), EBFP, EBFP2, Azurite, GFPuv, T-Sapphire, Cerulean, mCFP, mTurquoise2, ECFP, CyPet, GFP (Y66W mutation), mKeima-Red, TagCFP, AmCyan1, mTFP1, GFP (S65A mutation), Midoriishi Cyan, Wild Type GFP, GFP (S65C mutation), TurboGFP, TagGFP, GFP (S65L mutation), Emerald, GFP (S65T mutation), EGFP, Azami Green, ZsGreen1, TagYFP, EYFP, Topaz, Venus, mCitrine, YPet, TurboYFP, ZsYellow1, Kusabira Orange, mOrange, Allophycocyanin (APC), mKO, TurboRFP, tdTomato, TagRFP, DsRed monomer, DsRed2 ("RFP"), mStrawberry, TurboFP602, AsRed2, mRFP1, J-Red, R-phycoerythrin (RPE), B-phycoerythrin (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry. Other types of detectable labels include optical dyes, which are described in Johnson, Molecular Probes Handbook: A Guide to Fluorescent Probes and Labeling Techniques, 11th Edition, Life Technologies, (2010), radiolabels (*e.g.*, isotope markers such as ^{3}H, ^{11}C, ^{14}C, ^{15}N, ^{18}F, ^{35}S, ^{64}CU, ^{90}Y, ^{99}Tc, ^{111}In, ^{124}I, ^{125}I, ^{131}I), photochromic compounds, magnetic labels (e.g., DYNABEADS), etc. Strategies for the labeling of proteins are known in the art and can be employed in the disclosed method.

[0256] The label can be associated with the antigen binding molecule at any position in the molecule, although it is preferable to associate the label with the molecule at a position (or positions, if multiple labels are employed) at a point such that the binding properties of the molecule are not modified (unless such modified binding activity is desired). Any antigen binding molecule or fragment thereof that specifically binds the molecule of interest comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) can be employed in the disclosed method.

[0257] In specific embodiments of the disclosed method, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 19, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 20, a heavy chain CDR3 comprising the amino acid sequence SEQ ID NO: 21, a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 25, a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 26, and a light chain CDR3 comprising the amino acid sequence SEQ ID NO: 27. In other specific embodiments of the disclosed methods, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 7, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 8, a heavy chain CDR3 comprising the amino acid sequence SEQ ID NO: 9, a light chain CDR1 comprising

Date Reçue/Date Received 2020-04-16

the amino acid sequence SEQ ID NO: 13, a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 14, and a light chain CDR3 comprising the amino acid sequence SEQ ID NO: 15.

[0258] The antigen binding molecule can be disposed on any surface, or no surface at all. For example, the antigen binding molecule can be present in a buffer and the buffer-antigen binding molecule can be contacted with the sample. Alternatively, the antigen binding molecule can be associated with a surface. Suitable surfaces include agarose beads, magnetic beads such as DYNABEADS, or a plastic, glass or ceramic plate such as a welled plate, a bag such as a cell culture bag, etc. The surface can itself be disposed in another structure, such as a column.

[0259] Conditions that permit the formation of a binding complex will be dependent on a variety of factors, however generally aqueous buffers at physiological pH and ionic strength, such as in phosphate-buffered saline (PBS), will favor formation of binding complexes and are preferred in the disclosed method.

[0260] Continuing, the number of cells present in a binding complex in the sample is determined. The specific method employed to determine the number of cells present in a binding complex will be dependent on the nature of the label selected. For example, FACS can be employed when a fluorescent label is selected; when an isotope label is selected mass spectrometry, NMR or other technique can be employed; magnetic-based cell sorting can be employed when a magnetic label is chosen; microscopy can also be employed. The output of these detection methods can be in the form of a number of cells or the output can be of a form that allows the calculation of the number of cells based on the output.

Vd. Method of Isolating a Molecule

[0261] It is of tremendous value to have the ability to separate populations of different molecules, and particularly biologically-relevant molecules, from one another. Using the antigen binding molecules provided herein, such separation can be achieved and employed in a range of biotechnological, biopharmaceutical and therapeutic applications.

[0262] In one aspect of the instant disclosure, a method of isolating a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) is provided.

[0263] In one embodiment, the method comprises providing a sample known or suspected to comprise a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500).

[0264] In specific embodiments the selected amino acid sequence is GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1); in other embodiments the selected amino acid sequence is GSGKPGSGEG (SEQ ID NO: 2); in other embodiments the selected amino acid sequence is GKPGSGEG (SEQ ID NO: 3); in other embodiments the selected amino acid sequence is SGKPGSGE (SEQ ID NO: 499); in other embodiments the selected amino acid sequence is KPGSG (SEQ ID NO: 500).

[0265] In specific embodiments, the molecule of interest is a CAR. When the molecule is a CAR it can comprise a molecule, or fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine

receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

[0266] An antigen binding molecule that specifically binds the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2 or 3) and optionally comprises a detectable label is provided. When it is decided to employ a detectable label, any detectable label can be employed in the method, as described herein, and suitable labels can be selected using a desired set of criteria. Examples of types of detectable labels include fluorescent labels (*e.g.*, fluorescein, rhodamine, tetramethylrhodamine, eosin, erythrosin, coumarin, methyl-coumarins, pyrene, Malachite green, stilbene, Lucifer Yellow, Cascade Blue, Texas Red, IAEDANS, EDANS, BODIPY FL, LC Red 640, Cy 5, Cy 5.5, LC Red 705, Oregon green, the Alexa-Fluor dyes (Alexa Fluor 350, Alexa Fluor 430, Alexa Fluor 488, Alexa Fluor 546, Alexa Fluor 568, Alexa Fluor 594, Alexa Fluor 633, Alexa Fluor 647, Alexa Fluor 660, Alexa Fluor 680), Cascade Blue, Cas-cade Yellow and R-phycoerythrin (PE) (Molecular Probes), FITC, Rhodamine, and Texas Red (Pierce), Cy5, Cy5.5, Cy7 (Amersham Life Science)). Suitable optical dyes, including fluorophores, are described in Johnson, Molecular Probes Handbook:A Guide to Fluorescent Probes and Labeling Techniques, 11th Edition, Life Technologies, (2010), radiolabels (*e.g.*, isotope markers such as ^{3}H, ^{11}C, ^{14}C, ^{15}N, ^{18}F, ^{35}S, ^{64}CU, ^{90}Y, ^{99}Tc, ^{111}In, ^{124}I, ^{125}I, ^{131}I). Photochromic compounds, a Halo-tag, Atto dyes, Tracy dyes, proteinaceous fluorescent labels (*e.g.*, proteinaceous fluorescent labels also include, but are not limited to, green fluorescent protein, including a Renilla, Ptilosarcus, or Aequorea species of GFP (Chalfie et al., (1994) *Science* 263:802-805), EGFP (Clon-tech Labs., Inc., Genbank Accession Number U55762), blue fluorescent protein (BFP, Quantum Biotechnologies, Inc; Stauber, (1998) *Biotechniques* 24:462-471; Heim et al., (1996) *Curr. Biol.* 6: 178-182), enhanced yellow fluorescent protein (Clontech Labs., Inc.), luciferase (Ichiki et al., (1993) *J. Immunol.* 150:5408-5417), magnetic labels (e.g., DYNABEADS), etc can also be employed. Strategies for the labeling of proteins are well known in the art and can be employed in the disclosed method.

[0267] The label can be associated with the antigen binding molecule at any position in the molecule, although it is preferable to associate the label with the molecule at a position (or positions, if multiple labels are employed) at a point such that the binding properties of the molecule are not modified (unless such modified binding activity is desired). Any antigen binding molecule, or fragment thereof, that specifically binds the selected amino acid

Date Reçue/Date Received 2020-04-16

sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) can be employed, such as those disclosed herein, *e.g.*, those having one or more of the CDRs shown in FIGURES 6 and 8.

[0268] In specific embodiments of the disclosed method, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 19, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 20, a heavy chain CDR3 comprising the amino acid sequence SEQ ID NO: 21, a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 25, a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 26, and a light chain CDR3 comprising the amino acid sequence SEQ ID NO: 27. In other specific embodiments of the disclosed methods, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 7, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 8, a heavy chain CDR3 comprising the amino acid sequence SEQ ID NO: 9, a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 13, a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 14, and a light chain CDR3 comprising the amino acid sequence SEQ ID NO: 15.

[0269] The antigen binding molecule can be disposed on any surface, or no surface at all. For example, the antigen binding molecule can be present in a buffer and the buffer-antigen binding molecule can be contacted with the sample. Alternatively, the antigen binding molecule can be associated with a surface. Suitable surfaces include agarose beads, magnetic beads such as DYNABEADS, or a plastic, glass or ceramic plate such as a welled plate, a bag such as a cell culture bag, etc. The surface can itself be disposed in another structure, such as a column.

[0270] The sample is contacted with the antigen binding molecule, under conditions that permit the formation of a binding complex comprising a molecule comprising the selected amino acid sequence and the antigen binding molecule. Conditions that permit the formation of a binding complex will be dependent on a variety of factors, however generally aqueous buffers at physiological pH and ionic strength, such as in phosphate-buffered saline (PBS), will favor formation of binding complexes and are preferred in the disclosed method. Since the component parts of a binding complex can be disposed on surfaces as described herein, formed binding complexes can also be disposed on surfaces.

[0271] At this stage, no binding complexes may have formed, or a plurality of binding complexes comprising one or more antigen binding molecules bound to a molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) may have

formed. Unbound molecules comprising the selected amino acid sequence and/or unbound antigen binding molecules may also be present in the local environment of any formed binding complexes.

[0272] Any molecules not part of a binding complex are then separated from any formed binding complexes. The method of the removal will depend on the structure and/or local environment of the binding complexes. For example, if the antigen binding molecule is disposed on a bead, plate or bag the unbound components of the reaction mixture can be washed away using a solution that leaves formed binding complexes intact. If a binding complex is disposed on a bead, the bead itself may be situated in a column or other structure and the same approach can be used.

[0273] The solution used to induce the formation of binding complexes can be used, for example, as a wash solution to remove unbound components. Any suitable buffer or solution that does not disrupt formed binding complexes can be used. Typically, buffers having high salt concentrations, non-physiological pH, containing chaotropes or denaturants, are preferably avoided when performing this step of the method.

[0274] A formed binding complex is then separated into (a) a molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500), and (b) an antigen binding molecule. The separation can be achieved using standard methodologies known to those of skill in the art. For example, a solution of suitable pH and composition can be washed over the complexes. A solution that is commonly employed for this purpose is 0.1 M glycine HCl, pH 2.5-3.0, and this solution can be employed to achieve the separation. Other solutions that can be employed include 100 mM citric acid, pH 3.0, 50-100 mM triethylamine or triethanolamine, pH 11.5; 150 mM ammonium hydroxide, pH 10.5; 0.1 M glycine•NaOH, pH 10.0; 5 M lithium chloride, 3.5 M magnesium or potassium chloride, 3.0 M potassium chloride, 2.5 M sodium or potassium iodide, 0.2-3.0 M sodium thiocyanate, 0.1 M Tris-acetate with 2.0 M NaCl, pH 7.7; 2-6 M guanidine HCl, 2-8 M urea, 1.0 M ammonium thiocyanate, 1% sodium deoxycholate 1% SDS; and 10% dioxane 50% ethylene glycol, pH 8-11.5.

[0275] Following the separation, if the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 499 or 500) is of primary interest it can be collected; alternatively, if the antigen binding molecule is of primary interest it can be collected.

Ve. Method of Determining the Presence or Absence of a Molecule

[0276] As disclosed herein, it may sometimes be desirable to isolate a molecule comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 1, 2, 499 or 500. In other cases, simply knowing whether a molecule comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 1, 2, 499 or 500, is present or absent from a sample is enough information. For example, it may be beneficial to know that such a molecule is being expressed, regardless of the level of expression. In other cases it may be desirable to know if a purification process or step designed to remove such a molecule has been effectively. Thus, the qualitative determination of the presence or absence of a molecule comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 1, 2, 499 or 500, can be useful in multiple applications.

[0277] In view thereof, a method of determining the presence or absence in a sample of a molecule comprising an amino acid selected from the Group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), in a sample is provided.

[0278] In one embodiment, the method comprises providing a sample known or suspected to comprise a molecule comprising an amino acid sequence selected from the Group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500).

[0279] In specific embodiments the selected amino acid sequence is GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1); in other embodiments the selected amino acid sequence is GSGKPGSGEG (SEQ ID NO: 2); in other embodiments the selected amino sequence is GKPGSGEG (SEQ ID NO: 3); in other embodiments the selected amino acid sequence is SGKPGSGE (SEQ ID NO: 499); and in other embodiments the selected amino acid sequence is KPGSG (SEQ ID NO: 500).

[0280] In specific embodiments, the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 499 or 500) is a CAR. When the molecule is a CAR it can comprise a molecule, or fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1),

CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

[0281] An antigen binding molecule comprising a detectable label, which antigen binding molecule specifically binds the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 499 or 500) is provided. Suitable labels can be selected using a desired set of criteria. Examples of types of detectable labels include fluorescent labels (*e.g.*, fluorescein, rhodamine, tetramethylrhodamine, eosin, erythrosin, coumarin, methyl-coumarins, pyrene, Malachite green, stilbene, Lucifer Yellow, Cascade Blue, Texas Red, IAEDANS, EDANS, BODIPY FL, LC Red 640, Cy 5, Cy 5.5, LC Red 705, Oregon green, the Alexa-Fluor dyes (Alexa Fluor 350, Alexa Fluor 430, Alexa Fluor 488, Alexa Fluor 546, Alexa Fluor 568, Alexa Fluor 594, Alexa Fluor 633, Alexa Fluor 647, Alexa Fluor 660, Alexa Fluor 680), Cascade Blue, Cas-cade Yellow and R-phycoerythrin (PE) (Molecular Probes), FITC, Rhodamine, and Texas Red (Pierce), Cy5, Cy5.5, Cy7 (Amersham Life Science)). Suitable optical dyes, including fluorophores, are described in Johnson, Molecular Probes Handbook:A Guide to Fluorescent Probes and Labeling Techniques, 11th Edition, Life Technologies, (2010), radiolabels (*e.g.*, isotope markers such as ^{3}H, ^{11}C, ^{14}C, ^{15}N, ^{18}F, ^{35}S, ^{64}CU, ^{90}Y, ^{99}Tc, ^{111}In, ^{124}I, ^{125}I, ^{131}I). Photochromic compounds, a Halo-tag, Atto dyes, Tracy dyes, proteinaceous fluorescent labels (*e.g.*, proteinaceous fluorescent labels also include, but are not limited to, green fluorescent protein,

Date Reçue/Date Received 2020-04-16

including a Renilla, Ptilosarcus, or Aequorea species of GFP (Chalfie et al., (1994) *Science* 263:802-805), EGFP (Clon-tech Labs., Inc., Genbank Accession Number U55762), blue fluorescent protein (BFP, Quantum Biotechnologies, Inc; Stauber, (1998) *Biotechniques* 24:462-471; Heim et al., (1996) *Curr. Biol.* 6: 178-182), enhanced yellow fluorescent protein (Clontech Labs., Inc.), luciferase (Ichiki et al., (1993) *J. Immunol.* 150:5408-5417), magnetic labels (e.g., DYNABEADS), etc can also be employed. Strategies for the labeling of proteins are well known in the art and can be employed in the disclosed method.

[0282] In specific embodiments of the disclosed method, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 19, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 20, a heavy chain CDR3 comprising the amino acid sequence SEQ ID NO: 21, a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 25, a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 26, and a light chain CDR3 comprising the amino acid sequence SEQ ID NO: 27. In other specific embodiments of the disclosed methods, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 7, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 8, a heavy chain CDR3 comprising the amino acid sequence SEQ ID NO: 9, a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 13, a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 14, and a light chain CDR3 comprising the amino acid sequence SEQ ID NO: 15.

[0283] The label can be associated with the antigen binding molecule at any position in the molecule, although it is preferable to associate the label with the molecule at a position (or positions, if multiple labels are employed) at a point such that the binding properties of the molecule are not modified (unless such modified binding activity is desired). Any antigen binding molecule that specifically binds the a molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) can be employed, such as those disclosed herein, *e.g.*, those having one or more of the CDRs shown in FIGURES 6 and 8.

[0284] Continuing, the sample is contacted with the antigen binding molecule under conditions that permit the formation of a binding complex comprising a cell present in the sample and the antigen binding molecule. The antigen binding molecule can be disposed on any surface, or no surface at all. For example, the antigen binding molecule can be present in a buffer and the buffer-antigen binding molecule can be contacted with the sample. Alternatively, the antigen binding molecule can be associated with a surface. Suitable

surfaces include agarose beads, magnetic beads such as DYNABEADS, or a plastic, glass or ceramic plate such as a welled plate, a bag such as a cell culture bag, etc. The surface can itself be disposed in another structure, such as a column.

[0285] The sample is contacted with the antigen binding molecule, under conditions that permit the formation of a binding complex comprising a molecule comprising the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) and the antigen binding molecule. Conditions that permit the formation of a binding complex will be dependent on a variety of factors, however generally aqueous buffers at physiological pH and ionic strength, such as in phosphate-buffered saline (PBS), will favor formation of binding complexes and are preferred in the disclosed method. Since the component parts of a binding complex can be disposed on surfaces as described herein, formed binding complexes can also be disposed on surfaces.

[0286] At this stage, no binding complexes may have formed, or a plurality of binding complexes comprising one or more antigen binding molecules bound to a molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 499 or 500) (or one or more molecules comprising the selected amino acid sequence bound to an antigen binding molecule) may have formed. Unbound molecules comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 499 or 500) and/or unbound antigen binding molecules may also be present in the local environment of any formed binding complexes.

[0287] Any molecules not part of a binding complex are then separated from any formed binding complexes. The method of the removal will depend on the structure and/or local environment of the binding complexes. For example, if the antigen binding molecule is disposed on a bead, plate or bag the unbound components of the reaction mixture can be washed away using a solution that leaves formed binding complexes intact. If a binding complex is disposed on a bead, the bead itself may be situated in a column or other structure and the same approach can be used.

[0288] The solution used to induce the formation of binding complexes can be used, for example, as a wash solution to remove unbound components. Any suitable buffer or solution that does not disrupt formed binding complexes can also be used. Typically, buffers having high salt concentrations, non-physiological pH, containing chaotropes or denaturants, should be avoided when performing this step of the method.

[0289] Lastly, the presence or absence of a binding complex--which will comprise a molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 499 or 500)

and an antigen binding molecule—is detected. The specific method employed to detect the presence or absence of a binding complex will be dependent on the nature of the label selected. For example, FACS can be employed when a fluorescent label is selected; when an isotope label is selected mass spectrometry, NMR or other technique can be employed; magnetic-based cell sorting can be employed when a magnetic label is chosen; microscopy can also be employed. The end result of the method is a qualitative assessment of the presence or absence of the antigen binding molecule comprising the detectable label, and thus, the presence or absence of its binding partner, the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 499 or 500).

[0290] As is the case with all of the disclosed methods, the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 499 or 500) can be disposed in any environment. In preferred embodiments, the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 499 or 500) is expressed on the surface of a cell. In this embodiment, the cell can be of any type, and can be human or non-human (*e.g.*, mouse, rate, rabbit, hamster, etc). In a preferred embodiment, the cell is an immune cell. An immune cell of the method can be any type of immune cell (*e.g.*, B lymphocytes, monocytes, dendritic cells, Langerhans cells, keratinocytes, endothelial cells, astrocytes, fibroblasts, and oligodendrocytes). T cells (including T cytotoxic, T helper and Treg cells) are especially preferred. In specific embodiments, the cells are T cells, which can be obtained as described herein and by methods known in the art. Any type of immune cell can be employed in this embodiment of the disclosed method, and the cell can be a human or non-human cell. Exemplary cells include, but are not limited to immune cells such as T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells. The T cells can be autologous, allogeneic, or heterologous. In additional embodiments, the cells are T cells presenting a CAR. The T cells can be CD4+ T cells or CD8+ T cells. When a T cell is employed in the disclosed methods, the T cell can be an *in vivo* T cell or an *in vitro* T cell.

[0291] In additional embodiment, the cell can be disposed in, or isolated from, any environment capable of maintaining the cell in a viable form, such as blood, tissue or any other sample obtained from a subject, cell culture media, tissue grown *ex vivo*, a suitable buffer, etc.

Vf. Method of Increasing the Concentration of a Molecule

[0292] Very often a molecule of interest is present in a sample in lower-than-desired levels. For example, when a cell is transfected with a foreign gene expression levels of the protein(s) encoded by the foreign gene are low. The same can be true for molecules secreted from a cell; such molecules are often present in low quantities (but can still be detected using the methods provided herein, if the molecule comprises one of the disclosed amino acid sequences of SEQ ID NO: 1, 2 or 3). One solution to the problem of low expression levels is to increase the concentration of the molecule of interest, which can be free in solution, or expressed on the surface of a cell. The concentration of intracellularly-expressed molecules of interest can also be enhanced, however the cells must first be lysed to release the molecule.

[0293] To address this problem, a method of increasing the concentration of cells presenting a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) is provided.

[0294] In one embodiment, the method comprises providing a sample comprising cells known or suspected to comprise a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500).

[0295] In specific embodiments, the selected amino acid sequence is GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1); in other embodiments the selected amino acid sequence is GSGKPGSGEG (SEQ ID NO: 2); in other embodiments the selected amino acid sequence is GKPGSGEG (SEQ ID NO: 3); in other embodiments the selected amino acid sequence is SGKPGSGE (SEQ ID NO: 499); in other embodiments the selected amino acid sequence is KPGSG (SEQ ID NO: 500).

[0296] In specific embodiments, the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) is a CAR. When the molecule is a CAR it can comprise a molecule, or fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1),

CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

[0297] An antigen binding molecule that specifically binds the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) and optionally comprises a detectable label is provided. When it is preferable to employ a detectable label, any detectable label can be employed in the method, as described herein, and suitable labels can be selected using a desired set of criteria. Examples of types of detectable labels include fluorescent labels (*e.g.*, fluorescein, rhodamine, tetramethylrhodamine, eosin, erythrosin, coumarin, methyl-coumarins, pyrene, Malachite green, stilbene, Lucifer Yellow, Cascade Blue, Texas Red, IAEDANS, EDANS, BODIPY FL, LC Red 640, Cy 5, Cy 5.5, LC Red 705, Oregon green, the Alexa-Fluor dyes (Alexa Fluor 350, Alexa Fluor 430, Alexa Fluor 488, Alexa Fluor 546, Alexa Fluor 568, Alexa Fluor 594, Alexa Fluor 633, Alexa Fluor 647, Alexa Fluor 660, Alexa Fluor 680), Cascade Blue, Cas-cade Yellow and R-phycoerythrin (PE) (Molecular Probes), FITC, Rhodamine, and Texas Red (Pierce), Cy5, Cy5.5, Cy7 (Amersham Life Science)). Suitable optical dyes, including fluorophores, are described in Johnson, Molecular Probes Handbook:A Guide to Fluorescent Probes and Labeling Techniques, 11th Edition, Life Technologies, (2010), radiolabels (*e.g.*, isotope markers such as ^{3}H, ^{11}C, ^{14}C, ^{15}N, ^{18}F, ^{35}S, ^{64}CU, ^{90}Y, ^{99}Tc, ^{111}In, ^{124}I, ^{125}I, ^{131}I). Photochromic compounds, a Halo-tag, Atto dyes, Tracy dyes, proteinaceous fluorescent labels (*e.g.*,

Date Reçue/Date Received 2020-04-16

proteinaceous fluorescent labels also include, but are not limited to, green fluorescent protein, including a Renilla, Ptilosarcus, or Aequorea species of GFP (Chalfie et al., (1994) *Science* 263:802-805), EGFP (Clon-tech Labs., Inc., Genbank Accession Number U55762), blue fluorescent protein (BFP, Quantum Biotechnologies, Inc; Stauber, (1998) *Biotechniques* 24:462-471; Heim et al., (1996) *Curr. Biol.* 6: 178-182), enhanced yellow fluorescent protein (Clontech Labs., Inc.), luciferase (Ichiki et al., (1993) *J. Immunol.* 150:5408-5417), magnetic labels (*e.g.*, DYNABEADS), etc can also be employed. Strategies for the labeling of proteins are well known in the art and can be employed in the disclosed method.

[0298] The label can be associated with the antigen binding molecule at any position in the molecule, although it is preferable to associate the label with the molecule at a position (or positions, if multiple labels are employed) at a point such that the binding properties of the molecule are not modified (unless such modified binding activity is desired). Any antigen binding molecule that specifically binds the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500; or one or more molecules comprising the selected amino acid sequence bound to an antigen binding molecule or fragment thereof) can be employed, such as those disclosed herein, *e.g.*, those having one or more of the CDRs shown in FIGURES 6 and 8.

[0299] In specific embodiments of the disclosed methods, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 19, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 20, a heavy chain CDR3 comprising the amino acid sequence SEQ ID NO: 21, a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 25, a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 26, and a light chain CDR3 comprising the amino acid sequence SEQ ID NO: 27. In other specific embodiments of the disclosed methods, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 7, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 8, a heavy chain CDR3 comprising the amino acid sequence SEQ ID NO: 9, a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 13, a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 14, and a light chain CDR3 comprising the amino acid sequence SEQ ID NO: 15.

[0300] The antigen binding molecule can be disposed on any surface, or no surface at all. For example, the antigen binding molecule can be present in a buffer and the buffer-antigen binding molecule can be contacted with the sample. Alternatively, the antigen

binding molecule can be associated with a surface. Suitable surfaces include agarose beads, magnetic beads such as DYNABEADS, or a plastic, glass or ceramic plate such as a welled plate, a bag such as a cell culture bag, etc. The surface can itself be disposed in another structure, such as a column.

[0301] A cell expressing a molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) can be of any type, and can be human or non-human (*e.g.*, mouse, rate, rabbit, hamster, etc). In a preferred embodiment, the cell is an immune cell. An immune cell of the method can be any type of immune cell (*e.g.*, B lymphocytes, monocytes, dendritic cells, Langerhans cells, keratinocytes, endothelial cells, astrocytes, fibroblasts, and oligodendrocytes). T cells (including T cytotoxic, T helper and Treg cells) are especially preferred. In specific embodiments, the cells are T cells, which can be obtained as described herein and by methods known in the art. Any type of immune cell can be employed , and the cell can be a human or non-human cell. Exemplary cells include, but are not limited to immune cells such as T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells. The T cells can be autologous, allogeneic, or heterologous. In additional embodiments, the cells are T cells presenting a CAR. The T cells can be CD4+ T cells or CD8+ T cells. When a T cell is employed in the disclosed methods, the T cell can be an in vivo T cell or an in vitro T cell. Moreover, the cells can be disposed in, or isolated from, any environment capable of maintaining the cells in a viable form, such as blood, tissue or any other sample obtained from a subject, cell culture media, tissue grown *ex vivo*, a suitable buffer, etc.

[0302] The sample comprising cells is contacted with the antigen binding molecule, under conditions that permit the formation of a binding complex comprising a molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) and the antigen binding molecule. Conditions that permit the formation of a binding complex will be dependent on a variety of factors, however generally aqueous buffers at physiological pH and ionic strength, such as in phosphate-buffered saline (PBS), will favor formation of binding complexes and are preferred in the disclosed method. Since the component parts of a binding complex can be disposed on surfaces as described herein, formed binding complexes can also be disposed on surfaces.

[0303] At this stage, no binding complexes may have formed, or a plurality of binding complexes comprising one or more antigen binding molecules bound to a molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) may have

formed. Unbound molecules comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) and/or unbound antigen binding molecules may also be present in the local environment of any formed binding complexes.

[0304] Any molecules or cells not part of a binding complex are then separated from any formed binding complexes. The method of the removal will depend on the structure and/or local environment of the binding complexes. For example, if the antigen binding molecule is disposed on a bead, plate or bag the unbound components of the reaction mixture can be washed away using a solution that leaves formed binding complexes intact. If a binding complex is disposed on a bead, the bead itself may be situated in a column or other structure and the same approach can be used.

[0305] The solution used to induce the formation of binding complexes can be used, for example, as a wash solution to remove unbound components. Any suitable buffer or solution that does not disrupt formed binding complexes can also be used. Typically, buffers having high salt concentrations, non-physiological pH, containing chaotropes or denaturants, should be avoided when performing this step of the method.

[0306] At this stage of the method, a population of cells presenting a molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) will be present. If a detectable label was employed, the concentration of the cells can be easily determined, consistent with the nature of the label. Cells not expressing the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) will be absent, and thus the population (or concentration) of cells presenting a molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) will be increased compared to the levels prior to performing the method.

[0307] If the concentration of the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) is not at a desired level, the above steps can be repeated a desired number of times. In the context of this step of the method, a desired number of times can also be zero, if the desired concentration of cells is already present.

Vg. Method of Depleting a Population of Immune Cells

[0308] When a subject has an immune cell-mediated condition, it can be of significant importance that the condition be controlled in a timely fashion so as to prevent harm to the subject. For example, when a subject has an autoimmune reaction it may be desirable to suppress an immune cell-mediated response by depleting a population of immune cells, in an

effort to prevent harm. In another example, a subject receiving immunotherapy may react too strongly to the therapy and be at risk of harm; depleting the population of immune cells administered to the subject may be an effective approach to mitigating the subject's reaction to the immunotherapy. In view of the need for a method of controlling a subject's immune cell-mediated response, a method of depleting a population of immune cells presenting a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2) and GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), KPGSG (SEQ ID NO: 500) is provided. An antigen binding molecule that specifically recognizes GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and more specifically the subsequence GSGKPGSGEG (SEQ ID NO: 2), the subsequence GKPGSGEG (SEQ ID NO: 3), the subsequence SGKPGSGE (SEQ ID NO: 499), or the subsequence KPGSG (SEQ ID NO: 500) such as those provided herein, *e.g.*, those having one or more of the CDRs shown in FIGURES 6 and 8, can be employed in the disclosed method.

[0309] In specific embodiments of the disclosed method, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 19, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 20, a heavy chain CDR3 comprising the amino acid sequence SEQ ID NO: 21, a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 25, a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 26, and a light chain CDR3 comprising the amino acid sequence SEQ ID NO: 27. In other specific embodiments of the disclosed methods, the antigen binding molecule comprises a heavy chain CDR1 comprising the amino acid sequence SEQ ID NO: 7, a heavy chain CDR2 comprising the amino acid sequence SEQ ID NO: 8, a heavy chain CDR3 comprising the amino acid sequence SEQ ID NO: 9, a light chain CDR1 comprising the amino acid sequence SEQ ID NO: 13, a light chain CDR2 comprising the amino acid sequence SEQ ID NO: 14, and a light chain CDR3 comprising the amino acid sequence SEQ ID NO: 15.

[0310] In one embodiment, the method comprises providing a population of immune cells to be depleted, wherein the cells are known or suspected to be presenting a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500).

[0311] In specific embodiments the selected amino acid sequence is GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1); in other embodiments the selected amino acid sequence is GSGKPGSGEG (SEQ ID NO: 2); in other embodiments the selected amino acid sequence is GKPGSGEG (SEQ ID NO: 3), in other embodiments the selected amino acid sequence is SGKPGSGE (SEQ ID NO: 499), in other embodiments the selected amino acid sequence is KPGSG (SEQ ID NO: 500).

[0312] In specific embodiments, the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) is a CAR. When the molecule is a CAR it can comprise a molecule, or fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

[0313] In some embodiments, it may be beneficial to kill cells expressing a molecule, such as a CAR. As described above, in some embodiments, a therapeutic cell, such as a CAR T-cell may be used therapeutically and, subsequently, need to be depleted in a patient. In one embodiment, the present invention provides a method of removing these T-cells comprising

using T-cells to kill other T-cells that express a CAR. A cell presenting a molecule comprising a specific epitope recognized by a specific antigen binding molecule, such as those disclosed herein (i.e. anti-linker Clone 8 and/or 16, and fragments thereof) can be killed using a diabody, a bispecific molecule comprising a human CD3-binding scFv linked to a specific antigen-binding scFv, such as those composed of fragments of Clone 8 and/or 16, as described herein). In certain embodiments, the diabody binds to a cell expressing a molecule comprising GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500) and to a human T-cell to form an immunological synapse and facilitate cell death.

[0314] An immune cell presenting a molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) can be of any type, and can be human or non-human (*e.g.*, mouse, rate, rabbit, hamster, etc). An immune cell of the method can be any type of immune cell (*e.g.*, B lymphocytes, monocytes, dendritic cells, Langerhans cells, keratinocytes, endothelial cells, astrocytes, fibroblasts, and oligodendrocytes). T cells (including T cytotoxic, T helper and Treg cells) are especially preferred. In specific embodiments, the cells are T cells, which can be obtained as described herein and by methods known in the art. Any type of immune cell can be employed in this embodiment of the disclosed method, and the cell can be a human or non-human cell. Exemplary cells include, but are not limited to immune cells such as T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells. The T cells can be autologous, allogeneic, or heterologous. In additional embodiments, the cells are T cells presenting a CAR. The T cells can be CD4+ T cells or CD8+ T cells. When a T cell is employed in the disclosed methods, the T cell can be an *in vivo* T cell or an *in vitro* T cell. Moreover, the cells can be disposed in, or isolated from, any environment capable of maintaining the cells in a viable form, such as blood, tissue or any other sample obtained from a subject, cell culture media, tissue grown *ex vivo*, a suitable buffer, etc. As the disclosed method can be employed in therapeutic settings, in preferred embodiments the population of immune cells are disposed in a subject, and more preferably a human subject.

[0315] Continuing, immune cells are contacted with an antigen binding molecule that specifically binds to (a) the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2 or 3), and (b) an activating molecule expressed on the surface of the an immune cell not expressing the molecule comprising the selected amino acid sequence, under

conditions that permit the formation of a ternary binding complex comprising the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500), the activating molecule and the antigen binding molecule. The antigen binding molecule can be disposed on any surface, or no surface at all. For example, the antigen binding molecule (which can also comprise the population of immune cells to be depleted and/or can be present in a buffer) and the buffer-antigen binding molecule can be contacted with the sample. Alternatively, the antigen binding molecule can be associated with a surface. Suitable surfaces include agarose beads, magnetic beads such as DYNABEADS, or a plastic, glass or ceramic plate such as a welled plate, a bag such as a cell culture bag, etc. The surface can itself be disposed in another structure, such as a column.

[0316] The immune cells are contacted with the antigen binding molecule, under conditions that permit the formation of a ternary binding complex comprising a molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500), the antigen binding molecule and an activating molecule expressed on the surface of an immune cell not expressing the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500). Conditions that permit the formation of a binding complex will be dependent on a variety of factors, however generally aqueous buffers at physiological pH and ionic strength, such as in phosphate-buffered saline (PBS), will favor formation of binding complexes and are preferred in the disclosed method. Since the component parts of a binding complex can be disposed on surfaces as described herein, formed binding complexes can also be disposed on surfaces.

[0317] In preferred embodiments, the contacting is performed by administering the antigen binding molecule directly to a subject. In this embodiment, the subject will already have a population of cells to be depleted, wherein the cells express a molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500). Thus, these cells, as well as cells presenting an activating molecule, will be present in the subject prior to the administration of the antigen binding molecule to the subject. The human blood, lymph and tissue environment will permit the formation of ternary binding complexes. The binding of the antigen binding molecule with the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) serves to "tag" those cells presenting the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) (*i.e.*, the cells to be depleted). This binding event may or may not lead to depletion on its own. When the antigen binding molecule binds the activating molecule to form the ternary binding

complex, however, this binding event brings both cells (*i.e.*, the cell expressing the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500), and the cell expressing the activating molecule) together into proximity. The physiological result of the binding event is the killing of the cell expressing the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500). Thus, with multiple binding events occurring throughout the subject the population of immune cells bearing the molecule comprising the selected amino acid sequence (*i.e.*, SEQ ID NO: 1, 2, 3, 499 or 500) are depleted and the risk of harm to the subject decreases.

Vh. Method of Monitoring a Molecule in vivo

[0318] Positron emission tomography (PET) imaging is often used in oncology research and patient care. For space-occupying lesions in the head, chest, abdomen and pelvis, one of the best documented applications of PET is in the discrimination of benign from malignant causes. Particularly, ^{18}F-fluorodeoxyglucose (FDG) has been used to image the distribution of glucose uptake in all of these applications. In addition, the development of other radiotracers which image different aspects of tumor metabolism and growth add a further dimension of capabilities. These tracers include ^{11}C-methionine to measure amino acid incorporation, ^{18}F-thymidine to measure nucleotide incorporation (a measure of cell proliferation), and ^{18}F-fluoromisonidazole to measure tissue hypoxia.

[0319] The present invention provides the use of antigen binding molecules in PET analysis to increase specificity of FDG uptake. In particular, the methods provided herein may be used to assess changes early after treatment with CAR cells, in addition to monitoring, detection, stimulalation, activation, or depletion of CAR T-cells. Specifically, the methods provided herein may fascilitate the use of PET for whole-body scans. Using this technique to stage cancer, occult metastatic disease in almost any region of the body can potentially be detected by increased FDG accumulation.

[0320] In some embodiments, the present invention provides an *in vivo* method of detecting a molecule comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 1, 2, 499 or 500. For example, in particular embodiments the antigen binding molecules can be used to follow or monitor the presence or absence of a molecule comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 1, 2, 499 or 500 in a living subject. In some embodiments, the living subject is a human. In some embodiments, the molecule comprising an amino acid sequence selected from the group

consisting of SEQ ID NO: 1, 2, 499 or 500 is provided to a living subject and the presence or absence of said molecule is determined using an antigen binding molecule provided herein and a positron emission tomography (PET) scan.

[0321] In some embodiments, antigen binding molecules provided herein can be used to control CAR T-cells *in vivo*. In some embodiments, the antigen binding molecules provided herein can be used to activate or stimulate CAR T-cells *in vivo*. In some embodiments, the antigen binding molecules provided herein can be used to deplete CAR T-cells *in vivo*. In some embodiments, the antigen binding molecules provided herein can be used to monitor CAR T-cells *in vivo*. Specifically, when combined with PET, antigen binding molecules provided herein (e.g., anti-linker antibodies) can be used to monitor or follow the distribution of cells expressing a molecule comprising a selected amino acid sequence (e.g., SEQ ID NO: 1, 2, 499 or 500) *in vivo*.

INCORPORATION BY REFERENCE

[0322] (Paragraph is left blank).

EXAMPLES

[0323] The present invention is further illustrated by the following examples which should not be construed as further limiting.

Date Reçue/Date Received 2020-04-16

EXAMPLE 1: GENERATION OF ANTIGEN BINDING MOLECULES

[0324] Monoclonal antibodies were generated through immunization of rabbits using the 18mer peptide, GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), conjugated to the carrier protein KLH as immunogen. Titer was determined via screening polyclonal sera by ELISA using the full-length linker peptide, GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), conjugated to ovalbumin. A secondary screen was performed using CAR T cells assayed via flow cytometry (FIGURES 2 and 3). Once titer was achieved, the immunized rabbits were sacrificed and monoclonals were derived using standard hybridoma generation and subcloning techniques. The final screening of the hybridoma subclones was accomplished via additional rounds of flow cytometry and immunohistochemistry (IHC) of proliferating CAR T cells or fixed cell pellets derived from CAR T cells, respectively. The sequences of the final two subclones selected were determined by standard Sanger sequencing of the hybridomas subclones.

EXAMPLE 2: IMMUNOHISTOCHEMISTRY (IHC)

[0325] The candidate antibodies were screened for their utility in immunohistochemistry (IHC; FIGURE 4). To create the fixed cell pellets for IHC staining, ~2e6 CAR T cells were centrifuged and washed with PBS. The cells were resuspended in PBS containing 0.45% paraformaldehyde (PFA) and incubated on a shaking platform for 2 hours at room temperature. After the incubation the cells were washed once more with PBS and resuspended in PBS with 5% BSA. As shown in Figure 4, CAR transduced cells were positively recognized by exemplary anti-linker antibodies provided herein.

EXAMPLE 3: EPITOPE MAPPING

[0326] The antibodies (*i.e.*, antigen binding molecules) were epitope mapped via ELISA using the full length peptide, GSTSGSGKPGSGEGSTKG (SEQ ID NO:1), and variants truncated on either the N- or C-terminus and containing either a biotin moiety on the N-terminus, or a lysine residue with a biotin moiety on the C-terminus. The antibodies were captured in 96-well plate format using plates pre-coated with Protein G (Pierce). The plates were washed 6x in PBST buffer followed by incubation with target peptides. An additional 6x wash was performed with PBST and the antibodies were further incubated with streptavidin-HRP. Upon a final 6x wash in PBST, signal was detected and quantified via enhanced chemiluminescense kit (ECL, from GE Healthcare) and a Varioskan Flash plate

reader (Thermo Fisher). The results of the epitope mapping work are shown in FIGURES 5, 7 and 9.

EXAMPLE 4: GENERATION OF HUMANIZED SEQUENCES FROM RABBIT ANTIBODIES CLONE 8-4 AND CLONE 16-6

[0327] The Molecular Operating Environment (MOE) software developed by Chemical Computing Group (CCG) was used to generate alignments between the rabbit antibody Clones 8-4 and 16-6 and pairs of variable light and heavy chains, VL and VH, respectively from two databases:

(1) The Abysis human database: a database of about 2000 known human VL/VH sequence pairs from IMGT-LigM DB; and

(2) A human germline database: a database of germline sequences.

Humanized models show the best sequence alignments (highest identity to both the VL and VH domains) with fewest gaps. The top 100 antibody pairs from each human database was exported and clustered using kClust (Hauser, Mayer, & Soding, (2013) *BMC Bioinformatics*, 248). Presented below are tables for VL and VH sequences for each of the two antibodies, 8-4 (Tables 1-8) and 8-16 (Tables 9-16), with sequences from each of the two databases clustered at 90% (Tables 1, 2, 5, 6, 9, 10, 13, 14) and 95% (Tables 3, 4, 7, 8, 11, 12, 15, 16). Results are presented herein and in FIGURE 8.

Table 1. 8-4 VH humanized sequences -- IMGT-LigM DB (Abysis) clustered at 90% (18 sequences)

Table 2. 8-4 VL humanized sequences -- IMGT-LigM DB (Abysis) clustered at 90% (39 sequences)

Table 3. 8-4 VH humanized sequences -- IMGT-LigM DB (Abysis) clustered at 95% (47 sequences)

Table 4. 8-4 LC humanized sequences -- IMGT-LigM DB (Abysis) clustered at 95% (99 sequences).

Table 5. 8-4 VH humanized sequences -- germline database clustered at 90% (2 sequences).

Table 6. 8-4 VL humanized sequences -- germline database clustered at 90% (5 sequences).

Table 7. 8-4 VH humanized sequences -- germline database clustered at 95% (7 sequences)

Table 8. 8-4 VL humanized sequences -- germline database clustered at 95% (12 sequences)

Table 9. 16-6 VH humanized sequences -- IMGT-LigM DB (Abysis) clustered at 90% (41 sequences).

Table 10. 16-6 VL humanized sequences -- IMGT-LigM DB (Abysis) clustered at 90% (21 sequences).

Table 11. 16-6 VH humanized sequences -- IMGT-LigM DB (Abysis) clustered at 95% (81 sequences).

Table 12. 16-6 VL humanized sequences -- IMGT-LigM DB (Abysis) clustered at 95% (64 sequences).

Table 13. 16-6 VH humanized sequences -- germline database clustered at 90% (3 sequences).

Table 14. 16-6 VL humanized sequences -- germline database clustered at 90% (1 sequences).

Table 15. 16-6 VH humanized sequences -- germline database clustered at 95% (10 sequences).

Table 16. 16-6 VL humanized sequences -- germline database clustered at 95% (7 sequences).

Table 1. 8-4 VH humanized sequences -- IMGT-LigM DB (Abysis) clustered at 90% (18 sequences)

>8_4_HC_humanized_866
VQLQESGGGVVQPGRSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDI
YCATWAKGRFTISRDNSTLYLQMNSLRADDTAVYYCARDGDGSGWGDFNFWGQ
GTLVTVSS (SEQ ID NO: 28)

>8_4_HC_humanized_673
QSVVESGGVVVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGPEWVSDIDGRGDIY
CATWAKGRFTISRDNSSLYLQMNSLRTEDTAVYYCAKDGDGSGWGDFNFWGQGT
MVTVSS (SEQ ID NO: 29)

>8_4_HC_humanized_631
QSVEESGGRLVTPGATVKISCKVSGFTISNLAIIWVQQAPGKGLEWMGDIDGRGDIY
CATWAQGRVTITADSSTAYMELNGLRYADTAVYYCATDGDGSGWGDFNFWGQG
TLVTVSS (SEQ ID NO: 30)

>8_4_HC_humanized_1002
QSLEESGGGVVQPGKSLRLSCTASGFTISNLAIIWVRQAPGKGLESVADIDGRGDIY
CATWATGRFAISRDNSKLYLHMDNLRAEDTAVYYCARDGDGSGWGDFNFWGQG
TTVIVSS (SEQ ID NO: 31)

>8_4_HC_humanized_771
QSLEQSGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISKSKNTLYLQMNSLRAEDTAVYYCAVDGDGSGWGDFNFWGQG
TLVTVSS (SEQ ID NO: 32)

>8_4_HC_humanized_849
QSVEESGGDLVKPGGSLRLSCAASGFTISNLAIIWIRQAPGKGLEWLSDIDGRGDIYC
ATWAKGRFTISRDNASLNLQMNSLRAEDTAVYYCAVDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 33)

>8_4_HC_humanized_706
VLLLESGGGLAQPGGTLRLSCSASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWARGRFIISRDNSTLYLQMNSLRAEDTAVYYCAKDGDGSGWGDFNFWGQGIL
VTVSS (SEQ ID NO: 34)
>8_4_HC_humanized_703
VQLVESGGTLVQPGGSLRLSCSASGFTISNLAIIWVRQAPGKGLEYVSDIDGRGDIY
CATWAKGRITISRDNSTLSLQMSTLRTEDTAVYYCVRDGDGSGWGDFNFWGQGTL
VTVSS (SEQ ID NO: 35)
>8_4_HC_humanized_278
VQLVQSGGGLVKPGGSLRLSCEASGFTISNLAIIWIRQAPGKGLEWVGDIDGRGDIY
CATWAKGRFTISRDDSTLYLQVNSLKTEDSAVYYCTTDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 36)
>8_4_HC_humanized_800
QSVLESGPGLVKPSETLSLTCTVSGFTISNLAIIWIRQPPGKGLEWIGDIDGRGDIYCA
TWAKSRLTISTSKNQFSLRLTSVTAADTAMYYCAVDGDGSGWGDFNFWGQGTLV
SVSS (SEQ ID NO: 37)
>8_4_HC_humanized_809
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWLSDIDGRGDIY
CATWARGRFAISNARNSLYLQMNSLRDEDTAVYFCARDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 38)
>8_4_HC_humanized_273
VQLVQSGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQASGKGLEWIGDIDGRGDIY
CATWAKGRFTVSRSQNSVFLQMNSLETEDTAVYYCARDGDGSGWGDFNFWGQG
TLVTVSS (SEQ ID NO: 39)
>8_4_HC_humanized_716
QSVLESGGGWVQPGRSLRLSCSASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDNNSLYLQMNSLRPEDTALYYCAKDGDGSGWGDFNFWGQGV
LVTVSS (SEQ ID NO: 40)
>8_4_HC_humanized_202
VQLQESGEGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEYVSDIDGRGDIY
CATWAKGRFTISRDNSTLYLQMGSLRAEDMAVYYCAVDGDGSGWGDFNFWGQG
TMVTVSS (SEQ ID NO: 41)
>8_4_HC_humanized_21
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEFVSDIDGRGDIY
CATWAKDRFTISRDNSTVYLQMDSLRTEDTAMYFCARDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 42)
>8_4_HC_humanized_173
QSVEESGGRLVTPGGSLRLSCTATGFTISNLAIIWFRQAPGKGLEWVGDIDGRGDIY
CATWAKGRFTISRDDNSLYLQMNSLKTEDTAVYYCARDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 43)
>8_4_HC_humanized_23
QSVLESGGDLVQPGGSLRLSCEASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISKSKHTLFLQMHSLRVEDTAVYYCAKDGDGSGWGDFNFWGQGT
TVTVSS (SEQ ID NO: 44)
>8_4_HC_humanized_879
QSVEESGGGLVQPGGSLRLSCTASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDSSTLYLQMNNLRVEDTALYYCAHDGDGSGWGDFNFWGRGT
QVTVSS (SEQ ID NO: 45)

Table 2. 8-4 VL humanized sequences – IMGT-LigM DB (Abysis) clustered at 90% (39 sequences)

>8_4_LC_humanized_866
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKRLIYRASTLASG
VPSRFSGSGSGTEFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 46)
>8_4_LC_humanized_340
DIQMTQSPFSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYFCQQGWSTVNVDNVFGGGTKLEIK (SEQ ID NO: 47)
>8_4_LC_humanized_322
DIQLTQSPSFLSASVGDTVSITCQASQSISTALAWYQQKPGKAPKHLIYRASTLASGV
PSRFSGGGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 48)
>8_4_LC_humanized_305
DIQLTQSPSSLSASVGDRVTITCQASQSISTALAWFQQKPGKAPKSLIYRASTLASGV
PSRFSGSGSGTDFTLTISSLQPEDSATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 49)
>8_4_LC_humanized_303
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTFTISSLQPEDIATYYCQQGWSTVNVDNVFGPGTKVDIK (SEQ ID NO: 50)
>8_4_LC_humanized_291
DIQLTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKGPKLLIYRASTLASGV
PSRFSGSGSGTDFSLTISSLQPEDLATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 51)
>8_4_LC_humanized_217
DIVMTQSPDSLAVSLGERATINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASG
VPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 52)
>8_4_LC_humanized_197
AYDMTQTPATLSLSPGERATLSCQASQSISTALAWYQQKPGQAPRLLIYRASTLASG
IPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQGWSTVNVDNVFGQGTEVVVR (SEQ ID NO: 53)
>8_4_LC_humanized_169
EIVLTQSPSFLSAFVGDRITITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGV
PSRFSGSGSGTEFTLTISGLQPEDFASYYCQQGWSTVNVDNVFGGGTKLEIK (SEQ ID NO: 54)
>8_4_LC_humanized_17
DIQLTQSPSSLSAAVGDRVTIACQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLSISSLQPGDFATYYCQQGWSTVNVDNVFGGGTKVQMK (SEQ ID NO: 55)
>8_4_LC_humanized_13
DIQMTQSPSSLSASVGDSVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTEFTLTINGLQPEDFATYYCQQGWSTVNVDNVFGGGTKLEIK (SEQ ID NO: 56)
>8_4_LC_humanized_791

AYELTQTPLSSPVTLGQPASISCQASQSISTALAWLHQRPGQPPRLLIYRASTLASGV PDRFSGSGAGTAFTLKISRVEVEDVGIYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 57)

>8_4_LC_humanized_673

AYDMTQTPASVEVSPGERATLSCQASQSISTALAWYQHKPGQAPRLLIYRASTLAS GIPARFSGSGSGTEFTLTISSVQSDDFAVYYCQQGWSTVNVDNVFGPGTKVDIK (SEQ ID NO: 58)

>8_4_LC_humanized_678

AYELTQSPSSLSASVGDRVTITCQASQSISTALAWFQQKPGKAPKLLIYRASTLASG VPSRFSGSGSGTDFTLTISSLLPTDFATYFCQQGWSTVNVDNVFGQGTQVEVK (SEQ ID NO: 59)

>8_4_LC_humanized_631

AYDMTQTPASVEVSVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLAS GVPSRFGGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 60)

>8_4_LC_humanized_1002

AYELTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG VSSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ ID NO: 61)

>8_4_LC_humanized_775

AYELTQTPLSSPVTLGQPASISCQASQSISTALAWLQQRPGQPPRLLIYRASTLASGV PDRFSGSGARTDFTLNISRVEAEDAGVYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ ID NO: 62)

>8_4_LC_humanized_771

AYELTQSPATLSLSPGERATLSCQASQSISTALAWYQQKPGQAPRLLIHRASTLASGI PARFSGSGSGTDFTLTISSLEPEDFAVYYCQQGWSTVNVDNVFGGGTRVEIK (SEQ ID NO: 63)

>8_4_LC_humanized_188

DIQLTQSPSTLSASVGDRITITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGV PPRFSGSGSGTEFTLTISSLQPDDFATYYCQQGWSTVNVDNVFGQGTKVVVR (SEQ ID NO: 64)

>8_4_LC_humanized_717

ELVMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPNLLIYRASTLASG IPSRFSGSGSGTYFTLTINGLQPEDFATYYCQQGWSTVNVDNVFGGGTKVDIK (SEQ ID NO: 65)

>8_4_LC_humanized_1048

SYELTQTPPSVSVSPGQTARITCQASQSISTALAWYQQKPGQAPKVLIYRASTLASGI PERFSGSSSGTTVTLTISGVQAEDEADYYCQQGWSTVNVDNVFGGGTKLTVL (SEQ ID NO: 66)

>8_4_LC_humanized_849

AYELTQSPLSLSVTPGQPASISCQASQSISTALAWYLQKPGQPPQLLIYRASTLASGV PDRFSGSGSGTDFTLKISRVEAEDVGVYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 67)

>8_4_LC_humanized_1016

DIELTQSPSSLSASIGDRVSITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVP SRFSGSGSGTDFTLTISSLQPEDFATFYCQQGWSTVNVDNVFGGGTRVEIK (SEQ ID NO: 68)

>8_4_LC_humanized_978

EIVLTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGV
PSRFSGSGSGTDFTLTISNLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 69)
>8_4_LC_humanized_706
DIQMTQYPSSLSASVGDRVTIACQASQSISTALAWYQQKPGKPPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISCLQPEDVATYYCQQGWSTVNVDNVFGQGTRVEFK
(SEQ ID NO: 70)
>8_4_LC_humanized_278
ELVLTQSPSSLSASVGDRVTITCQASQSISTALAWCQQKPGKSPTLLIYRASTLASGV
PSRFSGSGSGTGFTLTISGLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIR (SEQ
ID NO: 71)
>8_4_LC_humanized_129
EIVMTQSPSSLSASVGDRVTITCQASQSISTALAWYQHKPGKAPRLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPDDFATYYCQQGWSTVNVDNVFGQGTKVEVK
(SEQ ID NO: 72)
>8_4_LC_humanized_1133
AYDMTTQPPSVSVSPGQTASITCQASQSISTALAWYQQKPGQSPVLVIYRASTLASG
IPERFSGSNSGNTATLTISGTQAMDEADYYCQQGWSTVNVDNVFGTGTEVVVR
(SEQ ID NO: 73)
>8_4_LC_humanized_881
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPNLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTKVQIK (SEQ
ID NO: 74)
>8_4_LC_humanized_882
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGFGTDFTFTISSLQPEDSATYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ
ID NO: 75)
>8_4_LC_humanized_273
ELVMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGEAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISGLQSEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 76)
>8_4_LC_humanized_716
ELVMTQSPSSLSASEGDRVTITCQASQSISTALAWYQQKPGRAPKLLIHRASTLASG
VPSRFSGSGSGTEFTLTISGLQSEDFATYYCQQGWSTVNVDNVFGGGTTVDVK
(SEQ ID NO: 77)
>8_4_LC_humanized_677
AYDMTQSPSFLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTEFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTRLEIK (SEQ
ID NO: 78)
>8_4_LC_humanized_192
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQAEDFTTYYCQQGWSTVNVDNVFGQGTKVEFK
(SEQ ID NO: 79)
>8_4_LC_humanized_802
AIRMTQSPSSFSASTGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISCLQSEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 80)
>8_4_LC_humanized_54

AYGMTQSPDSLAVSLGERASINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASG
VPDRFSGGGSGTDFTLTISSLQAEDVAVYYCQQGWSTVNVDNVFGGGTKVEIK
(SEQ ID NO: 81)
>8_4_LC_humanized_173
AIQMTQSPFSLSASVGDRVTITCQASQSISTALAWFQQKPGKAPKSLIYRASTLASG
VSSKFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTRLVVR
(SEQ ID NO: 82)
>8_4_LC_humanized_224
AYDMTQTPASVSLSPGERATLSCQASQSISTALAWYQQKPGQAPRLLIYRASTLAS
GIPDRFRGSGSATDFTLTISRLEPEDFAVYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 83)
>8_4_LC_humanized_657
AYDMTQTPASVEVSVGDRVSITCQASQSISTALAWYQQKPGKAPKLLIYRASTLAS
GVPSRFSGSGSGTDFTLTITSLQPVDFATYYCQQGWSTVNVDNVFGPGTTVDAK
(SEQ ID NO: 84)

Table 3. 8-4 VH humanized sequences -- IMGT-LigM DB (Abysis) clustered at 95% (47 sequences)

>cl|CABBABABA|10|117 >8_4_HC_humanized_866 >8_4_HC_humanized_340
>8_4_HC_humanized_336 >8_4_HC_humanized_332 >8_4_HC_humanized_322
VQLVESGGGVVQPGRSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDI
YCATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCAVDGDGSGWGDFNFWGQ
GTLVTVSS (SEQ ID NO: 85)
>cl|KABBABABA|13|117 >8_4_HC_humanized_315 >8_4_HC_humanized_314
>8_4_HC_humanized_305 >8_4_HC_humanized_303 >8_4_HC_humanized_296
VQLVQSGGGVVQPGRSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDI
YCATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCAVDGDGSGWGDFNFWGQ
GTLVTVSS (SEQ ID NO: 86)
>cl|TABBABABA|8|117 >8_4_HC_humanized_217 >8_4_HC_humanized_197
>8_4_HC_humanized_678 >8_4_HC_humanized_978 >8_4_HC_humanized_635
VQLVESGGGLVKPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDNASLYLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGQG
TLVTVSS (SEQ ID NO: 87)
>cl|WABBABABA|7|117 >8_4_HC_humanized_169 >8_4_HC_humanized_122
>8_4_HC_humanized_676 >8_4_HC_humanized_893 >8_4_HC_humanized_57
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCAKDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 88)
>cl|ZABBABABA|1|117 >8_4_HC_humanized_17
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGRGLVWVSDIDGRGDIY
CATWAKGRFTISRDNATLYLQMNNLRAEDTAVYYCARDGDGSGWGDFNFWGQG
TLVTVSS (SEQ ID NO: 89)
>cl|CEBBABABA|1|117 >8_4_HC_humanized_791
QSVLESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWARGRFTISRDNSTLYLQMNSLRAEDTAIYYCAKDGDGSGWGDFNFWGRGT
HVTVSS (SEQ ID NO: 90)
>cl|DEBBABABA|1|117 >8_4_HC_humanized_673

QSVVESGGVVVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGPEWVSDIDGRGDIY
CATWAKGRFTISRDNSSLYLQMNSLRTEDTAVYYCAKDGDGSGWGDFNFWGQGT
MVTVSS (SEQ ID NO: 91)
>cl|GEBBABABA|1|117 >8_4_HC_humanized_631
QSVEESGGRLVTPGATVKISCKVSGFTISNLAIIWVQQAPGKGLEWMGDIDGRGDIY
CATWAQGRVTITADSSTAYMELNGLRYADTAVYYCATDGDGSGWGDFNFWGQG
TLVTVSS (SEQ ID NO: 92)
>cl|HEBBABABA|1|117 >8_4_HC_humanized_1002
QSLEESGGGVVQPGKSLRLSCTASGFTISNLAIIWVRQAPGKGLESVADIDGRGDIY
CATWATGRFAISRDNSKLYLHMDNLRAEDTAVYYCARDGDGSGWGDFNFWGQG
TTVIVSS (SEQ ID NO: 93)
>cl|KEBBABABA|1|117 >8_4_HC_humanized_775
QSLEESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQASGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYSCAVDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 94)
>cl|LEBBABABA|2|117 >8_4_HC_humanized_771 >8_4_HC_humanized_772
QSLEQSGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISKSKNTLYLQMNSLRAEDTAVYYCAVDGDGSGWGDFNFWGQG
TLVTVSS (SEQ ID NO: 95)
>cl|NEBBABABA|1|117 >8_4_HC_humanized_188
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWASDIDGRGDIY
CATWAKGRFTISRDSSTLYLQMNSLRTDDTAVYYCAADGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 96)
>cl|PEBBABABA|9|117 >8_4_HC_humanized_186 >8_4_HC_humanized_292
>8_4_HC_humanized_283 >8_4_HC_humanized_204 >8_4_HC_humanized_201
VQLVESGGGVVQPGRSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDI
YCATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCAKDGDGSGWGDFNFWGQ
GTLVTVSS (SEQ ID NO: 97)
>cl|QEBBABABA|1|117 >8_4_HC_humanized_717
QSVLESGGGWVQPGRSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDI
YCATWAKGRFTISRDNASLYLEMKSLRAEDTAIYYCARDGDGSGWGDFNFWGQG
VLVTVSS (SEQ ID NO: 98)
>cl|REBBABABA|2|117 >8_4_HC_humanized_1048 >8_4_HC_humanized_675
QSVEESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDNASLYLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGQG
TLVTVSS (SEQ ID NO: 99)
>cl|SEBBABABA|1|117 >8_4_HC_humanized_849
QSVEESGGDLVKPGGSLRLSCAASGFTISNLAIIWIRQAPGKGLEWLSDIDGRGDIYC
ATWAKGRFTISRDNASLNLQMNSLRAEDTAVYYCAVDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 100)
>cl|TEBBABABA|3|117 >8_4_HC_humanized_1016 >8_4_HC_humanized_295
>8_4_HC_humanized_319
VQLVQSGGGLVKPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDI
YCATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCAVDGDGSGWGDFNFWGQ
GTLVTVSS (SEQ ID NO: 101)
>cl|XEBBABABA|2|117 >8_4_HC_humanized_868 >8_4_HC_humanized_55
QQLQESGGGLVQPGGSLRLSCSASGFTISNLAIIWVRQAPGKGLEYVSDIDGRGDIY
CATWAKGRFTISRDNSTLYLQMSSLRAEDTAVYYCVKDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 102)
>cl|YEBBABABA|1|117 >8_4_HC_humanized_862

VRLVESGGGVVQPGRSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDI
YCATWAKGRFTISRDNSTLHLQMNSLRAEDTAVYYCAKDGDGSGWGDFNFWGK
GTTVTVSS (SEQ ID NO: 103)
>cl|ZEBBABABA|1|117 >8_4_HC_humanized_715
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRSKNTLYLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGQGT
TVTVSS (SEQ ID NO: 104)
>cl|BIBBABABA|1|117 >8_4_HC_humanized_706
VLLLESGGGLAQPGGTLRLSCSASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWARGRFIISRDNSTLYLQMNSLRAEDTAVYYCAKDGDGSGWGDFNFWGQGIL
VTVSS (SEQ ID NO: 105)
>cl|CIBBABABA|1|117 >8_4_HC_humanized_703
VQLVESGGTLVQPGGSLRLSCSASGFTISNLAIIWVRQAPGKGLEYVSDIDGRGDIY
CATWAKGRITISRDNSTLSLQMSTLRTEDTAVYYCVRDGDGSGWGDFNFWGQGTL
VTVSS (SEQ ID NO: 106)
>cl|FIBBABABA|1|117 >8_4_HC_humanized_341
VQLVQSGGSLVQPGRSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDIY
CATWAKGRFTTSRDNSTLYLQMNSLRADDTAVYFCAVDGDGSGWGDFNFWGQG
TLVTVSS (SEQ ID NO: 107)
>cl|KIBBABABA|1|117 >8_4_HC_humanized_301
VQLVESGGDLVQPGESLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 108)
>cl|QIBBABABA|1|117 >8_4_HC_humanized_278
VQLVQSGGGLVKPGGSLRLSCEASGFTISNLAIIWIRQAPGKGLEWVGDIDGRGDIY
CATWAKGRFTISRDDSTLYLQVNSLKTEDSAVYYCTTDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 109)
>cl|TIBBABABA|1|117 >8_4_HC_humanized_129
MQLVESGGGLVQPGRSLRLSCVTSGFTISNLAIIWVRQVPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDNTSLYLQMNSLRPEDTAVYYCAKDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 110)
>cl|XIBBABABA|1|117 >8_4_HC_humanized_800
QSVLESGPGLVKPSETLSLTCTVSGFTISNLAIIWIRQPPGKGLEWIGDIDGRGDIYCA
TWAKSRLTISTSKNQFSLRLTSVTAADTAMYYCAVDGDGSGWGDFNFWGQGTLV
SVSS (SEQ ID NO: 111)
>cl|YIBBABABA|7|117 >8_4_HC_humanized_1133 >8_4_HC_humanized_881
>8_4_HC_humanized_677 >8_4_HC_humanized_192 >8_4_HC_humanized_65
QSVEESGGGVVQPGRSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDIY
CATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGQGT
TVTVSS (SEQ ID NO: 112)
>cl|FOBBABABA|1|117 >8_4_HC_humanized_882
QSVEESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQPPGKGLEWVGDIDGRGDIY
CATWAKGRFTISRSKSTVYLQMNSLKTEDTAVYYCTADGDGSGWGDFNFWGQG
MLVTVSS (SEQ ID NO: 113)
>cl|GOBBABABA|1|117 >8_4_HC_humanized_660
QSVEESGGGLIQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLECVSDIDGRGDIYC
ATWAKGRFTISRDNSTLYLQMTSLRAEDTAVYYCALDGDGSGWGDFNFWGQGTL
VTVSS (SEQ ID NO: 114)
>cl|HOBBABABA|2|117 >8_4_HC_humanized_1051 >8_4_HC_humanized_1050

VQLVESGGGLVKPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVGDIDGRGDI
YCATWAKGRFTISRSKNTLYLQMNSLKTEDTAVYYCTVDGDGSGWGDFNFWGQG
TLVTVSS (SEQ ID NO: 115)
>cl|MOBBABABA|1|117 >8_4_HC_humanized_809
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWLSDIDGRGDIY
CATWARGRFAISNARNSLYLQMNSLRDEDTAVYFCARDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 116)
>cl|VOBBABABA|1|117 >8_4_HC_humanized_273
VQLVQSGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQASGKGLEWIGDIDGRGDIY
CATWAKGRFTVSRSQNSVFLQMNSLETEDTAVYYCARDGDGSGWGDFNFWGQG
TLVTVSS (SEQ ID NO: 117)
>cl|WOBBABABA|1|117 >8_4_HC_humanized_716
QSVLESGGGWVQPGRSLRLSCSASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDNNSLYLQMNSLRPEDTALYYCAKDGDGSGWGDFNFWGQGV
LVTVSS (SEQ ID NO: 118)
>cl|ZOBBABABA|1|117 >8_4_HC_humanized_202
VQLQESGEGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEYVSDIDGRGDIY
CATWAKGRFTISRDNSTLYLQMGSLRAEDMAVYYCAVDGDGSGWGDFNFWGQG
TMVTVSS (SEQ ID NO: 119)
>cl|GUBBABABA|1|117 >8_4_HC_humanized_54
VQLVESGGGLVQPGGSLRLSCATSGFTISNLAIIWVRQPPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRENATLYLQMNSLRAEDTAVYYCAVDGDGSGWGDFNFWGQG
TLVTVSS (SEQ ID NO: 120)
>cl|HUBBABABA|1|117 >8_4_HC_humanized_21
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEFVSDIDGRGDIY
CATWAKDRFTISRDNSTVYLQMDSLRTEDTAMYFCARDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 121)
>cl|KUBBABABA|1|117 >8_4_HC_humanized_788
QSVLESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDNSTLFLQISSLRAEDTAVYYCAKDGDGSGWGDFNFWGPGTL
VTVSS (SEQ ID NO: 122)
>cl|MUBBABABA|1|117 >8_4_HC_humanized_762
VKLLESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDIY
CATWAKGRFTISRDNSTLYLQMNSLGAEDTAVYYCARDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 123)
>cl|PUBBABABA|1|117 >8_4_HC_humanized_173
QSVEESGGRLVTPGGSLRLSCTATGFTISNLAIIWFRQAPGKGLEWVGDIDGRGDIY
CATWAKGRFTISRDDNSLYLQMNSLKTEDTAVYYCARDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 124)
>cl|RUBBABABA|1|117 >8_4_HC_humanized_224
QSVEESGGGLVKPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVGDIDGRGDIY
CATWAKGRFTISRSKNTLYLQMNSLKTEDTAVYYCATDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 125)
>cl|VUBBABABA|1|117 >8_4_HC_humanized_672
QSVVESGGGLIQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCALDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 126)
>cl|XUBBABABA|1|117 >8_4_HC_humanized_267

QSVEQSGGGLVQPGESLRLSCAGSGFTISNLAIIWVRQAPGKGLEWVADIDGRGDIY
CATWAKGRFTISRDNASLFLQMNSLRVEDTAVYYCARDGDGSGWGDFNFWGQGT
LVTVSS (SEQ ID NO: 127)
>cl|YUBBABABA|1|117 >8_4_HC_humanized_23
QSVLESGGDLVQPGGSLRLSCEASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISKSKHTLFLQMHSLRVEDTAVYYCAKDGDGSGWGDFNFWGQGT
TVTVSS (SEQ ID NO: 128)
>cl|ZUBBABABA|1|117 >8_4_HC_humanized_657
QSVEESGGRLVTPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDNSSLYLQMNSLRTEDSALYYCAIDGDGSGWGDFNFWGQGSL
VTVSS (SEQ ID NO: 129)
>cl|BACBABABA|1|117 >8_4_HC_humanized_879
QSVEESGGGLVQPGGSLRLSCTASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDSSTLYLQMNNLRVEDTALYYCAHDGDGSGWGDFNFWGRGT
QVTVSS (SEQ ID NO: 130)

Table 4. 8-4 LC humanized sequences -- IMGT-LigM DB (Abysis) clustered at 95% (99 sequences).

>cl|CACBABABA|1|110 >8_4_LC_humanized_866
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKRLIYRASTLASG
VPSRFSGSGSGTEFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 131)
>cl|DACBABABA|1|110 >8_4_LC_humanized_340
DIQMTQSPFSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYFCQQGWSTVNVDNVFGGGTKLEIK (SEQ
ID NO: 132)
>cl|FACBABABA|1|110 >8_4_LC_humanized_336
DIQLTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGV
PSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ
ID NO: 133)
>cl|GACBABABA|1|110 >8_4_LC_humanized_332
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLVYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 134)
>cl|HACBABABA|1|110 >8_4_LC_humanized_322
DIQLTQSPSFLSASVGDTVSITCQASQSISTALAWYQQKPGKAPKHLIYRASTLASGV
PSRFSGGGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 135)
>cl|KACBABABA|1|110 >8_4_LC_humanized_315
DIQLTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGV
PSRFSGSGSGTGFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 136)
>cl|LACBABABA|1|110 >8_4_LC_humanized_314
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPNLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 137)
>cl|MACBABABA|1|110 >8_4_LC_humanized_305

DIQLTQSPSSLSASVGDRVTITCQASQSISTALAWFQQKPGKAPKSLIYRASTLASGV
PSRFSGSGSGTDFTLTISSLQPEDSATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 138)
>cl|NACBABABA|1|110 >8_4_LC_humanized_303
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTFTISSLQPEDIATYYCQQGWSTVNVDNVFGPGTKVDIK (SEQ
ID NO: 139)
>cl|PACBABABA|1|110 >8_4_LC_humanized_296
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSTFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 140)
>cl|QACBABABA|1|110 >8_4_LC_humanized_294
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 141)
>cl|RACBABABA|1|110 >8_4_LC_humanized_291
DIQLTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKGPKLLIYRASTLASGV
PSRFSGSGSGTDFSLTISSLQPEDLATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 142)
>cl|SACBABABA|1|110 >8_4_LC_humanized_284
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKSLIYRASTLASG
VPSKFSGSGSGTEFTLTISSLQPDDFATYYCQQGWSTVNVDNVFGQGTRLEIK (SEQ
ID NO: 143)
>cl|TACBABABA|1|110 >8_4_LC_humanized_217
DIVMTQSPDSLAVSLGERATINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASG
VPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQGWSTVNVDNVFGQGTKVEIK
(SEQ ID NO: 144)
>cl|VACBABABA|1|110 >8_4_LC_humanized_197
AYDMTQTPATLSLSPGERATLSCQASQSISTALAWYQQKPGQAPRLLIYRASTLASG
IPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQGWSTVNVDNVFGQGTEVVVR (SEQ
ID NO: 145)
>cl|WACBABABA|1|110 >8_4_LC_humanized_169
EIVLTQSPSFLSAFVGDRITITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGV
PSRFSGSGSGTEFTLTISGLQPEDFASYYCQQGWSTVNVDNVFGGGTKLEIK (SEQ
ID NO: 146)
>cl|XACBABABA|1|110 >8_4_LC_humanized_122
DVVMTQSPASLSASVGDRVTIICQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSRTDFTFTISSLQPEDIATYYCQQGWSTVNVDNVFGPGTKVDIK (SEQ
ID NO: 147)
>cl|YACBABABA|1|110 >8_4_LC_humanized_44
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKRLIYRASTLASG
VPSRFSGSGSGTEFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 148)
>cl|ZACBABABA|1|110 >8_4_LC_humanized_17
DIQLTQSPSSLSAAVGDRVTIACQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLSISSLQPGDFATYYCQQGWSTVNVDNVFGGGTKVQMK
(SEQ ID NO: 149)
>cl|BECBABABA|1|110 >8_4_LC_humanized_13

DIQMTQSPSSLSASVGDSVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTEFTLTINGLQPEDFATYYCQQGWSTVNVDNVFGGGTKLEIK (SEQ
ID NO: 150)
>cl|CECBABABA|1|110 >8_4_LC_humanized_791
AYELTQTPLSSPVTLGQPASISCQASQSISTALAWLHQRPGQPPRLLIYRASTLASGV
PDRFSGSGAGTAFTLKISRVEVEDVGIYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 151)
>cl|DECBABABA|1|110 >8_4_LC_humanized_673
AYDMTQTPASVEVSPGERATLSCQASQSISTALAWYQHKPGQAPRLLIYRASTLAS
GIPARFSGSGSGTEFTLTISSVQSDDFAVYYCQQGWSTVNVDNVFGPGTKVDIK
(SEQ ID NO: 152)
>cl|FECBABABA|1|110 >8_4_LC_humanized_678
AYELTQSPSSLSASVGDRVTITCQASQSISTALAWFQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLLPTDFATYFCQQGWSTVNVDNVFGQGTQVEVK (SEQ
ID NO: 153)
>cl|GECBABABA|1|110 >8_4_LC_humanized_631
AYDMTQTPASVEVSVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLAS
GVPSRFGGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK
(SEQ ID NO: 154)
>cl|HECBABABA|1|110 >8_4_LC_humanized_1002
AYELTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VSSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ
ID NO: 155)
>cl|KECBABABA|1|110 >8_4_LC_humanized_775
AYELTQTPLSSPVTLGQPASISCQASQSISTALAWLQQRPGQPPRLLIYRASTLASGV
PDRFSGSGARTDFTLNISRVEAEDAGVYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ
ID NO: 156)
>cl|LECBABABA|2|110 >8_4_LC_humanized_771 >8_4_LC_humanized_772
AYELTQSPATLSLSPGERATLSCQASQSISTALAWYQQKPGQAPRLLIHRASTLASGI
PARFSGSGSGTDFTLTISSLEPEDFAVYYCQQGWSTVNVDNVFGGGTRVEIK (SEQ
ID NO: 157)
>cl|MECBABABA|1|110 >8_4_LC_humanized_676
AYDMTQSPATLSLSPGERATLSCQASQSISTALAWYQQKPGQAPRLLIYRASTLASG
IPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 158)
>cl|NECBABABA|1|110 >8_4_LC_humanized_188
DIQLTQSPSTLSASVGDRITITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGV
PPRFSGSGSGTEFTLTISSLQPDDFATYYCQQGWSTVNVDNVFGQGTKVVVR (SEQ
ID NO: 159)
>cl|PECBABABA|1|110 >8_4_LC_humanized_186
DIQLTQSPSTLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQGWSTVNVDNVFGQGTKVVVR
(SEQ ID NO: 160)
>cl|QECBABABA|1|110 >8_4_LC_humanized_717
ELVMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPNLLIYRASTLASG
IPSRFSGSGSGTYFTLTINGLQPEDFATYYCQQGWSTVNVDNVFGGGTKVDIK (SEQ
ID NO: 161)
>cl|RECBABABA|1|110 >8_4_LC_humanized_1048

SYELTQTPPSVSVSPGQTARITCQASQSISTALAWYQQKPGQAPKVLIYRASTLASGI
PERFSGSSSGTTVTLTISGVQAEDEADYYCQQGWSTVNVDNVFGGGTKLTVL (SEQ
ID NO: 162)
>cl|SECBABABA|1|110 >8_4_LC_humanized_849
AYELTQSPLSLSVTPGQPASISCQASQSISTALAWYLQKPGQPPQLLIYRASTLASGV
PDRFSGSGSGTDFTLKISRVEAEDVGVYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 163)
>cl|TECBABABA|1|110 >8_4_LC_humanized_1016
DIELTQSPSSLSASIGDRVSITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVP
SRFSGSGSGTDFTLTISSLQPEDFATFYCQQGWSTVNVDNVFGGGTRVEIK (SEQ ID
NO: 164)
>cl|VECBABABA|1|110 >8_4_LC_humanized_978
EIVLTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGV
PSRFSGSGSGTDFTLTISNLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 165)
>cl|WECBABABA|1|110 >8_4_LC_humanized_893
DIEMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKRLIQRASTLASG
VPSRFSGSGSGTEFTLTISSLQPEDFATYHCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 166)
>cl|XECBABABA|1|110 >8_4_LC_humanized_868
DIVMTQSPDSLAVSLGERATINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASG
VPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQGWSTVNVDNVFGQGTKLEIK
(SEQ ID NO: 167)
>cl|YECBABABA|1|110 >8_4_LC_humanized_862
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 168)
>cl|ZECBABABA|1|110 >8_4_LC_humanized_715
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKFLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 169)
>cl|BICBABABA|1|110 >8_4_LC_humanized_706
DIQMTQYPSSLSASVGDRVTIACQASQSISTALAWYQQKPGKPPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISCLQPEDVATYYCQQGWSTVNVDNVFGQGTRVEFK
(SEQ ID NO: 170)
>cl|CICBABABA|1|110 >8_4_LC_humanized_703
DIVMTQSPDSLAVSLGERATINCQASQSISTALAWYQQKAGQPPKLLIYRASTLASG
VPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQGWSTVNVDNVFGGGTKVEIK
(SEQ ID NO: 171)
>cl|DICBABABA|1|110 >8_4_LC_humanized_635
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKVPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDVATYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ
ID NO: 172)
>cl|FICBABABA|1|110 >8_4_LC_humanized_341
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTKLEIK (SEQ
ID NO: 173)
>cl|GICBABABA|1|110 >8_4_LC_humanized_328

DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGRGTKVEIK (SEQ
ID NO: 174)
>cl|HICBABABA|1|110 >8_4_LC_humanized_324
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGNAPKSLIYRASTLASG
VPSKFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 175)
>cl|KICBABABA|1|110 >8_4_LC_humanized_301
DIQMTQSPDSLAVSLGERATINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASG
VPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQGWSTVNVDNVFGQGTKLEIK
(SEQ ID NO: 176)
>cl|LICBABABA|1|110 >8_4_LC_humanized_295
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTRLEIK (SEQ
ID NO: 177)
>cl|MICBABABA|1|110 >8_4_LC_humanized_292
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPNLLIYRASTLASG
VPSRFSGSVSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 178)
>cl|NICBABABA|1|110 >8_4_LC_humanized_283
DIQLTQSPSSVSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTRLEIK (SEQ
ID NO: 179)
>cl|PICBABABA|1|110 >8_4_LC_humanized_282
DIQMTQSPSSVSASVGDRVTITCQASQSISTALAWYQQKLGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 180)
>cl|QICBABABA|1|110 >8_4_LC_humanized_278
ELVLTQSPSSLSASVGDRVTITCQASQSISTALAWCQQKPGKSPTLLIYRASTLASGV
PSRFSGSGSGTGFTLTISGLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIR (SEQ
ID NO: 181)
>cl|RICBABABA|1|110 >8_4_LC_humanized_204
DIQLTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGV
PSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 182)
>cl|SICBABABA|1|110 >8_4_LC_humanized_201
DIRVTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTFTISSLQPEDIATYYCQQGWSTVNVDNVFGGGTKVDIK (SEQ
ID NO: 183)
>cl|TICBABABA|1|110 >8_4_LC_humanized_129
EIVMTQSPSSLSASVGDRVTITCQASQSISTALAWYQHKPGKAPRLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPDDFATYYCQQGWSTVNVDNVFGQGTKVEVK
(SEQ ID NO: 184)
>cl|VICBABABA|1|110 >8_4_LC_humanized_108
DVVMTQSPSSVSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLAS
GVPSRFSGSGSGTDFTLTITSLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK
(SEQ ID NO: 185)
>cl|WICBABABA|1|110 >8_4_LC_humanized_57

DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKRLIYRASTLASG
VPSRFSGSGSGTEFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTRLEIK (SEQ
ID NO: 186)
>cl|XICBABABA|1|110 >8_4_LC_humanized_800
AYELTQTPPSLSVTPGQPASISCQASQSISTALAWYLQKPGQPPQLLIYRASTLASGV
PDRFSGSGSGTDFTLKISRVEAEDVGVYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 187)
>cl|YICBABABA|1|110 >8_4_LC_humanized_1133
AYDMTTQPPSVSVSPGQTASITCQASQSISTALAWYQQKPGQSPVLVIYRASTLASG
IPERFSGSNSGNTATLTISGTQAMDEADYYCQQGWSTVNVDNVFGTGTEVVVR
(SEQ ID NO: 188)
>cl|ZICBABABA|1|110 >8_4_LC_humanized_621
AYELTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 189)
>cl|COCBABABA|1|110 >8_4_LC_humanized_881
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPNLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTKVQIK (SEQ
ID NO: 190)
>cl|DOCBABABA|1|110 >8_4_LC_humanized_55
AYDMTQTPASVEVSPGERATLSCQASQSISTALAWYQQKPGQAPRLLIYRASTLAS
GIPARFSGSGSGTEFTLTISSLQSEDFAVYYCQQGWSTVNVDNVFGQGTEVVVR
(SEQ ID NO: 191)
>cl|FOCBABABA|1|110 >8_4_LC_humanized_882
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGFGTDFTFTISSLQPEDSATYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ
ID NO: 192)
>cl|GOCBABABA|1|110 >8_4_LC_humanized_660
AYVMTQSPATLSLSPGERATLSCQASQSISTALAWYQQRPGQAPRLLIYRASTLASG
IPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 193)
>cl|HOCBABABA|1|110 >8_4_LC_humanized_1051
SYELTQTPPSVSVSPGQTARITCQASQSISTALAWYQQKPGQAPVLVIYRASTLASGI
PERFSGSSSGTTVTLTISGVQAEDEADYYCQQGWSTVNVDNVFGTGTKVTVL (SEQ
ID NO: 194)
>cl|KOCBABABA|1|110 >8_4_LC_humanized_1050
SYELTQTPPSVSVSPGQTARITCQASQSISTALAWYQQKPGQAPVLVIYRASTLASGI
PERFSGSSSGTTVTLTISGVQAEDEADYYCQQGWSTVNVDNVFGTGTKVTVL (SEQ
ID NO: 195)
>cl|LOCBABABA|1|110 >8_4_LC_humanized_860
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 196)
>cl|MOCBABABA|1|110 >8_4_LC_humanized_809
DIQMTQSPSSVSASVRDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGPGTKVDIK (SEQ
ID NO: 197)
>cl|NOCBABABA|1|110 >8_4_LC_humanized_346

DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 198)
>cl|POCBABABA|1|110 >8_4_LC_humanized_345
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTFTISSLQPDDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 199)
>cl|QOCBABABA|1|110 >8_4_LC_humanized_334
DIQMTQSPSFVSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 200)
>cl|ROCBABABA|1|110 >8_4_LC_humanized_319
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 201)
>cl|SOCBABABA|1|110 >8_4_LC_humanized_308
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 202)
>cl|TOCBABABA|1|110 >8_4_LC_humanized_281
DIQLTQSPSSVSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTKVDIK (SEQ
ID NO: 203)
>cl|VOCBABABA|1|110 >8_4_LC_humanized_273
ELVMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGEAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISGLQSEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 204)
>cl|WOCBABABA|1|110 >8_4_LC_humanized_716
ELVMTQSPSSLSASEGDRVTITCQASQSISTALAWYQQKPGRAPKLLIHRASTLASG
VPSRFSGSGSGTEFTLTISGLQSEDFATYYCQQGWSTVNVDNVFGGGTTVDVK
(SEQ ID NO: 205)
>cl|XOCBABABA|1|110 >8_4_LC_humanized_677
AYDMTQSPSFLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTEFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTRLEIK (SEQ
ID NO: 206)
>cl|YOCBABABA|1|110 >8_4_LC_humanized_192
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQAEDFTTYYCQQGWSTVNVDNVFGQGTKVEFK
(SEQ ID NO: 207)
>cl|ZOCBABABA|1|110 >8_4_LC_humanized_202
DIRMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKVPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDVATYYCQQGWSTVNVDNVFGPGTKVVVR
(SEQ ID NO: 208)
>cl|BUCBABABA|1|110 >8_4_LC_humanized_802
AIRMTQSPSSFSASTGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISCLQSEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 209)
>cl|CUCBABABA|1|110 >8_4_LC_humanized_347

DIQMTQSPSSLSASVGDRVSITCQASQSISTALAWYQQKPGKAPKRLIYRASTLASG
VPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 210)
>cl|DUCBABABA|1|110 >8_4_LC_humanized_339
DIQLTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGV
PSRFSGSGSGTEFTLTISSLQPDDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 211)
>cl|FUCBABABA|1|110 >8_4_LC_humanized_168
DIVMTQSPSTLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTEFTLTISGLQPEDFATYYCQQGWSTVNVDNVFGGGTKLEIK (SEQ
ID NO: 212)
>cl|GUCBABABA|1|110 >8_4_LC_humanized_54
AYGMTQSPDSLAVSLGERASINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASG
VPDRFSGGGSGTDFTLTISSLQAEDVAVYYCQQGWSTVNVDNVFGGGTKVEIK
(SEQ ID NO: 213)
>cl|HUCBABABA|1|110 >8_4_LC_humanized_21
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKVLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGPGTKVEVR (SEQ
ID NO: 214)
>cl|KUCBABABA|1|110 >8_4_LC_humanized_788
AYELTQTPLSSPVTLGQPASISCQASQSISTALAWLQQRPGQPPRLLIYRASTLASGV
PDRFSGSGAGTDFTLKISRVEAEDVGIYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 215)
>cl|LUCBABABA|1|110 >8_4_LC_humanized_675
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTEFTLTITSLQPEDFATYYCQQGWSTVNVDNVFGPGTKLEIK (SEQ
ID NO: 216)
>cl|MUCBABABA|1|110 >8_4_LC_humanized_762
AYELTQSPDSLAVSLGERATINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASG
VPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQGWSTVNVDNVFGGGTKVEIK
(SEQ ID NO: 217)
>cl|NUCBABABA|1|110 >8_4_LC_humanized_818
AYDMTQTPSSVSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLAS
GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK
(SEQ ID NO: 218)
>cl|PUCBABABA|1|110 >8_4_LC_humanized_173
AIQMTQSPFSLSASVGDRVTITCQASQSISTALAWFQQKPGKAPKSLIYRASTLASG
VSSKFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTRLVVR
(SEQ ID NO: 219)
>cl|QUCBABABA|1|110 >8_4_LC_humanized_65
DIQMTQSPSTLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ
ID NO: 220)
>cl|RUCBABABA|1|110 >8_4_LC_humanized_224
AYDMTQTPASVSLSPGERATLSCQASQSISTALAWYQQKPGQAPRLLIYRASTLAS
GIPDRFRGSGSATDFTLTISRLEPEDFAVYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 221)
>cl|SUCBABABA|1|110 >8_4_LC_humanized_230

AYDMTQTPASVSASVGDRVTITCQASQSISTALAWYQQKPGKAPKVLIYRASTLAS
GVPSRFSGSGSGTDFTLTISTLQPEDFATYYCQQGWSTVNVDNVFGQGTKLEIK
(SEQ ID NO: 222)
>cl|TUCBABABA|1|110 >8_4_LC_humanized_880
AYDMTQSPSSLSASVGDRVNITCQASQSISTALAWYQQKPGKAPKLLIYRASTLAS
GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGPGTKVDIK
(SEQ ID NO: 223)
>cl|VUCBABABA|1|110 >8_4_LC_humanized_672
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ
ID NO: 224)
>cl|WUCBABABA|1|110 >8_4_LC_humanized_299
DIQMTQSPSSVSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 225)
>cl|XUCBABABA|1|110 >8_4_LC_humanized_267
AYDMTQSPSTLAASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLAS
GVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQGWSTVNVDNVFGQGTKVEVK
(SEQ ID NO: 226)
>cl|YUCBABABA|1|110 >8_4_LC_humanized_23
AYELTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGPGTKVDIK (SEQ
ID NO: 227)
>cl|ZUCBABABA|1|110 >8_4_LC_humanized_657
AYDMTQTPASVEVSVGDRVSITCQASQSISTALAWYQQKPGKAPKLLIYRASTLAS
GVPSRFSGSGSGTDFTLTITSLQPVDFATYYCQQGWSTVNVDNVFGPGTTVDAK
(SEQ ID NO: 228)
>cl|BADBABABA|1|110 >8_4_LC_humanized_879
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYFCQQGWSTVNVDNVFGGGTKVEIK (SEQ
ID NO: 229)

Table 5. 8-4 VH humanized sequences -- germline database clustered at 90% (2 sequences)

>cl|CABBABABA|15|117 >8_4_HC_humanized_356 >8_4_HC_humanized_340
>8_4_HC_humanized_335 >8_4_HC_humanized_303 >8_4_HC_humanized_287
VQLVESGGGVVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDI
YCATWAKGRFTISRDNSSLYLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGPG
TLVTVSS (SEQ ID NO: 230)
>cl|LABBABABA|85|117 >8_4_HC_humanized_2049 >8_4_HC_humanized_2033
>8_4_HC_humanized_1360 >8_4_HC_humanized_1344 >8_4_HC_humanized_777
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGPGT
LVTVSS (SEQ ID NO: 231)

Table 6. 8-4 VL humanized sequences -- germline database clustered at 90% (5 sequences).

>cl|CACBABABA|76|110 >8_4_LC_humanized_356 >8_4_LC_humanized_340 >8_4_LC_humanized_335 >8_4_LC_humanized_303 >8_4_LC_humanized_287
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 232)
>cl|LACBABABA|2|110 >8_4_LC_humanized_2049 >8_4_LC_humanized_2033
AYDMTQSPDSLAVSLGERATINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASG
VPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 233)
>cl|NACBABABA|2|110 >8_4_LC_humanized_1360 >8_4_LC_humanized_1344
AYDMTQTPLSLSVTPGQPASISCQASQSISTALAWYLQKPGQPPQLLIYRASTLASG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 234)
>cl|CECBABABA|5|110 >8_4_LC_humanized_2207 >8_4_LC_humanized_2206 >8_4_LC_humanized_2197 >8_4_LC_humanized_2208 >8_4_LC_humanized_2192
AYDMTQSPAFLSVTPGEKVTITCQASQSISTALAWYQQKPDQAPKLLIKRASTLASG
VPSRFSGSGSGTDFTFTISSLEAEDAATYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 235)
>cl|DICBABABA|15|110 >8_4_LC_humanized_2263 >8_4_LC_humanized_2262 >8_4_LC_humanized_2258 >8_4_LC_humanized_2257 >8_4_LC_humanized_2256
AYDMTQSPASLAVSPGQRATITCQASQSISTALAWYQQKPGQPPKLLIYRASTLASG
VPARFSGSGSGTDFTLTINPVEANDTANYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 236)

Table 7. 8-4 VH humanized sequences -- germline database clustered at 95% (7 sequences)

>cl|CABBABABA|2|117 >8_4_HC_humanized_356 >8_4_HC_humanized_303
VQLVESRGVLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDNSTLHLQMNSLRAEDTAVYYCKKDGDGSGWGDFNFWGPGT
LVTVSS (SEQ ID NO: 237)
>cl|DABBABABA|17|117 >8_4_HC_humanized_340 >8_4_HC_humanized_335 >8_4_HC_humanized_287 >8_4_HC_humanized_282 >8_4_HC_humanized_2207
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDNASLYLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGPGT
LVTVSS (SEQ ID NO: 238)
>cl|LABBABABA|37|117 >8_4_HC_humanized_2049 >8_4_HC_humanized_2033 >8_4_HC_humanized_1360 >8_4_HC_humanized_1344 >8_4_HC_humanized_777
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVGDIDGRGDI
YCATWAKGRFTISRSKNTLYLQMNSLKTEDTAVYYCTRDGDGSGWGDFNFWGPG
TLVTVSS (SEQ ID NO: 239)
>cl|DEBBABABA|22|117 >8_4_HC_humanized_2206 >8_4_HC_humanized_988 >8_4_HC_humanized_987 >8_4_HC_humanized_935 >8_4_HC_humanized_934

VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGPGT
LVTVSS (SEQ ID NO: 240)
>cl|FEBBABABA|16|117 >8_4_HC_humanized_2197 >8_4_HC_humanized_978
>8_4_HC_humanized_925 >8_4_HC_humanized_660 >8_4_HC_humanized_395
VQLLESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIY
CATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCAKDGDGSGWGDFNFWGPGT
LVTVSS (SEQ ID NO: 241)
>cl|HIBBABABA|3|117 >8_4_HC_humanized_2257 >8_4_HC_humanized_349
>8_4_HC_humanized_296
VQLVESGGGLVQPGRSLRLSCTASGFTISNLAIIWFRQAPGKGLEWVGDIDGRGDIY
CATWAKGRFTISRSKSIAYLQMNSLKTEDTAVYYCTRDGDGSGWGDFNFWGPGTL
VTVSS (SEQ ID NO: 242)
>cl|LIBBABABA|3|117 >8_4_HC_humanized_2254 >8_4_HC_humanized_346
>8_4_HC_humanized_293
VQLVESGGVVVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDI
YCATWAKGRFTISRDNSSLYLQMNSLRTEDTALYYCAKDGDGSGWGDFNFWGPG
TLVTVSS (SEQ ID NO: 243)

Table 8. 8-4 VL humanized sequences -- germline database clustered at 95% (12 sequences)

>cl|CACBABABA|1|110 >8_4_LC_humanized_356
AYDMTQSPSSVSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLAS
GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 244)
>cl|LACBABABA|2|110 >8_4_LC_humanized_2049 >8_4_LC_humanized_2033
AYDMTQSPDSLAVSLGERATINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASG
VPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 245)
>cl|NACBABABA|2|110 >8_4_LC_humanized_1360 >8_4_LC_humanized_1344
AYDMTQTPLSLSVTPGQPASISCQASQSISTALAWYLQKPGQPPQLLIYRASTLASG
VPDRFSGSGSGTDFTLKISRVEAEDVGVYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 246)
>cl|QACBABABA|1|110 >8_4_LC_humanized_777
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTFTISSLQPEDIATYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ
ID NO: 247)
>cl|VACBABABA|1|110 >8_4_LC_humanized_565
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKRLIYRASTLASG
VPSRFSGSGSGTEFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 248)
>cl|XACBABABA|2|110 >8_4_LC_humanized_247 >8_4_LC_humanized_231
AYDMTQSPSFLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTEFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 249)
>cl|ZACBABABA|2|110 >8_4_LC_humanized_141 >8_4_LC_humanized_125
AYDMTQSPSSFSASTGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISCLQSEDFATYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 250)

>cl|CECBABABA|1|110 >8_4_LC_humanized_2207
AYDMTQSPAFLSVTPGEKVTITCQASQSISTALAWYQQKPDQAPKLLIKRASTLASG
VPSRFSGSGSGTDFTFTISSLEAEDAATYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 251)
>cl|GECBABABA|1|110 >8_4_LC_humanized_988
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 252)
>cl|PECBABABA|1|110 >8_4_LC_humanized_670
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKVPKLLIYRASTLASG
VPSRFSGSGSGTDFTLTISSLQPEDVATYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 253)
>cl|ZECBABABA|1|110 >8_4_LC_humanized_34
AYDMTQSPSTLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASG
VPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 254)
>cl|DICBABABA|15|110 >8_4_LC_humanized_2263 >8_4_LC_humanized_2262
>8_4_LC_humanized_2258 >8_4_LC_humanized_2257 >8_4_LC_humanized_2256
AYDMTQSPASLAVSPGQRATITCQASQSISTALAWYQQKPGQPPKLLIYRASTLASG
VPARFSGSGSGTDFTLTINPVEANDTANYYCQQGWSTVNVDNVFGGGTEVVVR
(SEQ ID NO: 255)

Table 9. 16-6 VH humanized sequences -- IMGT-LigM DB (Abysis) clustered at 90% (41 sequences)

>cl|CABBABABA|1|115 >16_6_HC_humanized_586
VQLQESGGGVVQPGTSLRLSCVVSGSDISSYHMGWVRQAPGKGLEWLAIIVSSGSA
YYATWAKGRFTVSRSKSTLFLKMNSLRADDTAVYYCARNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 256)
>cl|DABBABABA|2|115 >16_6_HC_humanized_411 >16_6_HC_humanized_213
LQLQESGPRLVKPSETLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYY
ATWAKSRLTISTSKNQFSLRLSSVTAADSAVYYCARNQYSGYGFSFWGQGTLVTVS
S (SEQ ID NO: 257)
>cl|FABBABABA|1|115 >16_6_HC_humanized_372
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEAVAIIVSSGSA
YYATWAKGRFTISRDSSTLFLQLNSLRVEDSGIYYCAKNQYSGYGFSFWGQGTLVT
VSS (SEQ ID NO: 258)
>cl|GABBABABA|7|115 >16_6_HC_humanized_1996 >16_6_HC_humanized_230
>16_6_HC_humanized_2056 >16_6_HC_humanized_672 >16_6_HC_humanized_657
QSLEESGGRLVTPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 259)
>cl|HABBABABA|2|115 >16_6_HC_humanized_1907 >16_6_HC_humanized_716
QSLLESGGGWVQPGRSLRLSCSASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRDNNSLYLQMNSLRPEDTALYYCAKNQYSGYGFSFWGQGVL
VTVSS (SEQ ID NO: 260)
>cl|LABBABABA|3|115 >16_6_HC_humanized_1945 >16_6_HC_humanized_1451
>16_6_HC_humanized_65

QSLEESGGGLVKPGESLRLSCAASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRDDSTVYLEMNSLKTEDTAVYYCATNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 261)
>cl|NABBABABA|1|115 >16_6_HC_humanized_1004
QSLLESGPRLVKPSETLSLTCSVSGSDISSYHMGWVRQPPGQGLEWIGIIVSSGSAYY
ATWARSRVSISTSQNQVSLKLTSVTAADTAVYYCARNQYSGYGFSFWGQGILVTV
SS (SEQ ID NO: 262)
>cl|PABBABABA|13|115 >16_6_HC_humanized_1971 >16_6_HC_humanized_305
>16_6_HC_humanized_1877 >16_6_HC_humanized_860 >16_6_HC_humanized_283
VQLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCAKNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 263)
>cl|QABBABABA|22|115 >16_6_HC_humanized_802 >16_6_HC_humanized_587
>16_6_HC_humanized_1012 >16_6_HC_humanized_988 >16_6_HC_humanized_129
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 264)
>cl|RABBABABA|1|115 >16_6_HC_humanized_609
VQLVESGGGLVQPGGSLRLSCTTSGSDISSYHMGWVRQVPGKGLEWVSIIVSSGSA
YYATWAKGRFTISRDNSTSYLQMTSLTPEDTAVYYCAKNQYSGYGFSFWGQGTVV
SVSS (SEQ ID NO: 265)
>cl|YABBABABA|4|115 >16_6_HC_humanized_910 >16_6_HC_humanized_218
>16_6_HC_humanized_912 >16_6_HC_humanized_917
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYY
ATWAKSRVTISTSKNQLSLKLTSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTV
SS (SEQ ID NO: 266)
>cl|GEBBABABA|1|115 >16_6_HC_humanized_136
VQLQQSGPGLVKTSETLPLTCTVSGSDISSYHMGWIRQPPGKGLEYIGIIVSSGSAYY
ATWAKNRVTISTSKNQFSLKLSSVTAADTALYYCARNQYSGYGFSFWGQGTLVTV
SS (SEQ ID NO: 267)
>cl|KEBBABABA|1|115 >16_6_HC_humanized_109
VQLVESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGKGLEYIGIIVSSGSAYY
ATWAKSRLTMSVDTSNYQLKLSSVTAADTAVYYCARNQYSGYGFSFWGQGTTVT
VSS (SEQ ID NO: 268)
>cl|LEBBABABA|1|115 >16_6_HC_humanized_103
VQLQQSGPGLVKPSGTLSLTCDVSGSDISSYHMGWVRQPPGKGLEWIGIIVSSGSAY
YATWAKSRVTISKSKNQFSLRLTSVTAADTAVYYCARNQYSGYGFSFWGQGTLVT
VSS (SEQ ID NO: 269)
>cl|NEBBABABA|6|115 >16_6_HC_humanized_902 >16_6_HC_humanized_1982
>16_6_HC_humanized_734 >16_6_HC_humanized_920 >16_6_HC_humanized_149
VQLVESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYY
ATWAKSRVTISTSKNQFSLKLSSVTAADTAVYYCARNQYSGYGFSFWGQGTLVTV
SS (SEQ ID NO: 270)
>cl|PEBBABABA|1|115 >16_6_HC_humanized_851
VQLVQSGGGVVQPGGSLRVSCAASGSDISSYHMGWVRQAPGKGLEWMAIIVSSGS
AYYATWAKGRFTISRDNSTVSLQMSSLRAEDTAVYYCAKNQYSGYGFSFWGRGTL
VTVSS (SEQ ID NO: 271)
>cl|SEBBABABA|1|115 >16_6_HC_humanized_926

VQLVESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQHSGKTLEWIGIIVSSGSAY
YATWAESRVTISADTSKISLKLSSVTAADTAVYYCARNQYSGYGFSFWGQGTTVT
VSS (SEQ ID NO: 272)
>cl|VEBBABABA|1|115 >16_6_HC_humanized_904
VQLVESGPGLVKPSQTLSLTCNVSGSDISSYHMGWIRQSPGKGLEWIGIIVSSGSAY
YATWARSRVTISADTSKVSLELSPMTAADTAVYYCARNQYSGYGFSFWGQGTTVT
VSS (SEQ ID NO: 273)
>cl|WEBBABABA|1|115 >16_6_HC_humanized_903
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGTGLEWIGIIVSSGSAYY
ATWAKSRVTISGDTSKFSLMLRSVTAADTAVYYCARNQYSGYGFSFWGQGTMVT
VSS (SEQ ID NO: 274)
>cl|YEBBABABA|1|115 >16_6_HC_humanized_946
VQLVESGGGLIKPGGSLRLSCEVPGSDISSYHMGWVRQGPGRGLEWVGIIVSSGSA
YYATWARGRFTISRSKSTVYLEMNALKTEDTGIYYCVTNQYSGYGFSFWGQGTMV
TVSS (SEQ ID NO: 275)
>cl|ZEBBABABA|1|115 >16_6_HC_humanized_882
QSLEESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQPPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRSKSTVYLQMNSLKTEDTAVYYCTANQYSGYGFSFWGQGML
VTVSS (SEQ ID NO: 276)
>cl|CIBBABABA|1|115 >16_6_HC_humanized_2041
QSLVQSGTEVRKPGASVKVSCKASGSDISSYHMGWVRQAPGQGLEWMGIIVSSGS
AYYATWAQGRVTMSDTSTTVYMELSSLTSEDTAIYYCARNQYSGYGFSFWGPGTL
VTVSS (SEQ ID NO: 277)
>cl|KIBBABABA|1|115 >16_6_HC_humanized_1944
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQPPGKGLEWIGIIVSSGSAY
YATWAKNRVTISTSKNQFSLRLNSVTAADTAVYYCARNQYSGYGFSFWGQGTLVT
VSS (SEQ ID NO: 278)
>cl|LIBBABABA|4|115 >16_6_HC_humanized_1895 >16_6_HC_humanized_1992
>16_6_HC_humanized_1995 >16_6_HC_humanized_1949
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLVWVSIIVSSGSAY
YATWAKGRFTISRDNATLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGPGTLV
TVSS (SEQ ID NO: 279)
>cl|SIBBABABA|2|115 >16_6_HC_humanized_993 >16_6_HC_humanized_994
VQLVESGGGLIQPGRPLRLSCSGSGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRDDSVVHLQMNSLRSEDTAVYYCTRNQYSGYGFSFWGQGTM
VTVSS (SEQ ID NO: 280)
>cl|TIBBABABA|2|115 >16_6_HC_humanized_956 >16_6_HC_humanized_965
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQHPGKGLEWIGIIVSSGSAY
YATWAESRLTISADTSNIQLRLSSVTAADTAVYFCARNQYSGYGFSFWGQGTTVTV
SS (SEQ ID NO: 281)
>cl|WIBBABABA|1|115 >16_6_HC_humanized_278
VQLVQSGGGLVKPGGSLRLSCEASGSDISSYHMGWIRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRDDSTLYLQVNSLKTEDSAVYYCTTNQYSGYGFSFWGQGTLV
TVSS (SEQ ID NO: 282)
>cl|GOBBABABA|1|115 >16_6_HC_humanized_1894
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAY
YATWAKGRFTISRDNASLYLQMNSLRAEDTAVYYCARNQYSGYGFSFFSDYWLVT
VSS (SEQ ID NO: 283)
>cl|MOBBABABA|3|115 >16_6_HC_humanized_1917 >16_6_HC_humanized_677
>16_6_HC_humanized_267

QSLEESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSA
YYATWAKRRFTISRDNSTLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 284)
>cl|POBBABABA|1|115 >16_6_HC_humanized_2038
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAY
YATWAKGRFTISRDNASLYLQMNSLRAEDTAVYYCARNQYSGYGFSFPTSGYYY
MDVS (SEQ ID NO: 285)
>cl|QOBBABABA|1|115 >16_6_HC_humanized_23
QSLLESGGDLVQPGGSLRLSCEASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSA
YYATWAKGRFTISRDKSTLFLQMHSLRVEDTAVYYCAKNQYSGYGFSFWGQGTT
VTVSS (SEQ ID NO: 286)
>cl|VOBBABABA|1|115 >16_6_HC_humanized_1013
VQLVQSGGGVVQPGRSLRLSCEVSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSA
YYATWAKGRFTISRSNNTLYLQMNSLTAEDTALYFCARNQYSGYGFSFWGKGTTV
TVSS (SEQ ID NO: 287)
>cl|YOBBABABA|1|115 >16_6_HC_humanized_113
LQLQESGPGLVKPSQTLSLTCSVSGSDISSYHMGWIRQHPGKGLEWIGIIVSSGSAYY
ATWAKSRITISTSKNQFSLKLTSVTAADTALYYCARNQYSGYGFSFWGRGTLVTVS
S (SEQ ID NO: 288)
>cl|HUBBABABA|1|115 >16_6_HC_humanized_12
VQLVQSGGGVVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGS
AYYATWAQGRVTISRDNSTVHLQITSLKSEDTAVYYCAKNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 289)
>cl|LUBBABABA|1|115 >16_6_HC_humanized_273
VQLVQSGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQASGKGLEWIGIIVSSGSA
YYATWAKGRFTVSRSQNSVFLQMNSLETEDTAVYYCARNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 290)
>cl|NUBBABABA|1|115 >16_6_HC_humanized_879
QSLEESGGGLVQPGGSLRLSCTASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSA
YYATWAKGRFTISRDSSTLYLQMNNLRVEDTALYYCAHNQYSGYGFSFWGRGTQ
VTVSS (SEQ ID NO: 291)
>cl|TUBBABABA|1|115 >16_6_HC_humanized_1934
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAY
YATWAKGRFTISRDNASLYLQMNSLRAEDTAVYYCARNQYSGYGFSFGIFDYWVT
VSS (SEQ ID NO: 292)
>cl|VUBBABABA|1|115 >16_6_HC_humanized_200
VQLQESGPGLVKPSETLSLTCSVSGSDISSYHMGWIRQPAGKGLEWIGIIVSSGSAYY
ATWARSRVTMSMSKNHFSLKLRSVTAADTAVYFCARNQYSGYGFSFWGQGTLVT
VSS (SEQ ID NO: 293)
>cl|WUBBABABA|1|115 >16_6_HC_humanized_1977
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAY
YATWAKGRFTISRSKNTLYLQMNSLRAEDTAVYYCARNQYSGYGFSFTCPYFDYW
VSS (SEQ ID NO: 294)
>cl|XUBBABABA|1|115 >16_6_HC_humanized_2027
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAY
YATWAEGRFTISRDNSTLYLQMYSLRTEDTAVYYCARNQYSGYGFSFYYYGMGV
WVSS (SEQ ID NO: 295)
>cl|YUBBABABA|1|115 >16_6_HC_humanized_1958

VHLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSA
YYATWAEGRFTISRDNSKLYLQMNSLRAEDSATYYCARNQYSGYGFSFFGPPYYY
YYMS (SEQ ID NO: 296)
>cl|BACBABABA|1|115 >16_6_HC_humanized_1905
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAY
YATWAKGRFTISRDNSTLYLQMNSLRAEDTALYYCARNQYSGYGFSFVRGGYFYH
MDS (SEQ ID NO: 297)

Table 10. 16-6 VL humanized sequences – IMGT-LigM DB (Abysis) clustered at 90% (21 sequences)

>cl|CACBABABA|1|110 >16_6_LC_humanized_586
IVLTQTPSSLSASVGDRITITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLAS
GVPSRFSGSRSGTDFTFTISSLRPEDIATYYCLGGYDDDGETAFGGGTKVEIK (SEQ
ID NO: 298)
>cl|DACBABABA|27|110 >16_6_LC_humanized_411 >16_6_LC_humanized_1004
>16_6_LC_humanized_587 >16_6_LC_humanized_305 >16_6_LC_humanized_988
IVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGGGTKVEIK
(SEQ ID NO: 299)
>cl|FACBABABA|15|110 >16_6_LC_humanized_372 >16_6_LC_humanized_1877
>16_6_LC_humanized_1012 >16_6_LC_humanized_860 >16_6_LC_humanized_283
IQLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCLGGYDDDGETAFGQGTKVEIK
(SEQ ID NO: 300)
>cl|GACBABABA|1|110 >16_6_LC_humanized_1996
VVLTQTPSPVSTAVGGTVTLSCQSSHSVYYGDWLAWYQQKPGQAPRLLIYRASNL
ASGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCLGGYDDDGETAKGPGTEVVVK
(SEQ ID NO: 301)
>cl|HACBABABA|2|110 >16_6_LC_humanized_1907 >16_6_LC_humanized_716
LVMTQSPSSLSASEGDRVTITCQSSHSVYYGDWLAWYQQKPGRAPKLLIHRASNLA
SGVPSRFSGSGSGTEFTLTISGLQSEDFATYYCLGGYDDDGETAFGGGTTVDVK
(SEQ ID NO: 302)
>cl|LACBABABA|2|110 >16_6_LC_humanized_1945 >16_6_LC_humanized_1451
VELTQPPSPVSAAPGQKVTISCQSSHSVYYGDWLAWYQQLPGTAPKLLIYRASNLA
SGIPDRFSGSKSGTSATLGITGLQTGDEADYYCLGGYDDDGETAFGGGTRLTVL
(SEQ ID NO: 303)
>cl|PACBABABA|10|110 >16_6_LC_humanized_1971 >16_6_LC_humanized_2041
>16_6_LC_humanized_2038 >16_6_LC_humanized_2008 >16_6_LC_humanized_1992
VVLTQTPSPVSTAVGGTVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNL
ASGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 304)
>cl|QACBABABA|5|110 >16_6_LC_humanized_802 >16_6_LC_humanized_609
>16_6_LC_humanized_851 >16_6_LC_humanized_908 >16_6_LC_humanized_108
VVMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNL
ASGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGGGTKVEIK
(SEQ ID NO: 305)
>cl|CECBABABA|7|110 >16_6_LC_humanized_253 >16_6_LC_humanized_103
>16_6_LC_humanized_882 >16_6_LC_humanized_1982 >16_6_LC_humanized_734

IVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTEFTLTISSLQPEDSATYYCLGGYDDDGETAFGQGTKVEIK (SEQ
ID NO: 306)
>cl|KECBABABA|2|110 >16_6_LC_humanized_109 >16_6_LC_humanized_334
IQLTQSPSFVSASVGDRITITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLAS
GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGQGTKVEIK (SEQ
ID NO: 307)
>cl|RECBABABA|2|110 >16_6_LC_humanized_17 >16_6_LC_humanized_21
IQLTQSPSSLSAAVGDRVTIACQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLSISSLQPEDFATYYCLGGYDDDGETAFGGGTKVQMK
(SEQ ID NO: 308)
>cl|DICBABABA|1|110 >16_6_LC_humanized_202
IRMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKVPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPEDVATYYCLGGYDDDGETAFGPGTKVVVK
(SEQ ID NO: 309)
>cl|FICBABABA|14|110 >16_6_LC_humanized_192 >16_6_LC_humanized_956
>16_6_LC_humanized_230 >16_6_LC_humanized_880 >16_6_LC_humanized_2056
VVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGQGTKVEIK
(SEQ ID NO: 310)
>cl|NICBABABA|2|110 >16_6_LC_humanized_1938 >16_6_LC_humanized_762
VELTQSPDSLAVSLGERATINCQSSHSVYYGDWLAWYQQKPGQPPKLLIYRASNLA
SGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCLGGYDDDGETAFGGGTKVEIK
(SEQ ID NO: 311)
>cl|WICBABABA|1|110 >16_6_LC_humanized_278
LVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWCQQKPGKSPTLLIYRASNLA
SGVPSRFSGSGSGTGFTLTISGLQPEDFATYYCLGGYDDDGETAFGGGTKVEIR
(SEQ ID NO: 312)
>cl|YICBABABA|1|110 >16_6_LC_humanized_169
IVLTQSPSFLSAFVGDRITITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLAS
GVPSRFSGSGSGTEFTLTISGLQPEDFASYYCLGGYDDDGETAFGGGTKLEIK (SEQ
ID NO: 313)
>cl|GOCBABABA|1|110 >16_6_LC_humanized_1894
VVLTQTPSPVSTAVGDRVTITCQSSHSVYYGDWLAWYRQKPGKVPKLLIYRASNL
ASGVPSRFSGSGSGTDFTLTISSLQPEDVATYYGLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 314)
>cl|LOCBABABA|1|110 >16_6_LC_humanized_657
VVLTQTPSPVSTSVGDRVSITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTITSLQPVDFATYYCLGGYDDDGETAFGPGTTVDAK
(SEQ ID NO: 315)
>cl|YOCBABABA|1|110 >16_6_LC_humanized_113
IVLTQSPSSVSASVGDRVTITCQSSHSVYYGDWLAWYQLKPGKAPKLLINRASNLA
SGVPSRFSGSGSGTDFTLTISGLQPEDFATYYCLGGYDDDGETAFGPGTTVDIK
(SEQ ID NO: 316)
>cl|MUCBABABA|3|110 >16_6_LC_humanized_2032 >16_6_LC_humanized_200
>16_6_LC_humanized_1905
VVLTQTPSPVSTAVGGTGTINCQSSHSVYYGDWLAWYQQKPGQPPKLLIYRASNL
ASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCLGGYDDDGETAFGGGTKVVVK
(SEQ ID NO: 317)
>cl|RUCBABABA|1|110 >16_6_LC_humanized_1995

VVLTQTPSPVSTAVGGTVTINCQSSHSVYYGDWLAWYQQKPGQPXKLLIYRASNL
ASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCLGGYDDDGETAFGQGTEVVVK
(SEQ ID NO: 318)

Table 11. 16-6 VH humanized sequences -- IMGT-LigM DB (Abysis) clustered at 95% (81 sequences)

>cl|CABBABABA|1|115 >16_6_HC_humanized_586
VQLQESGGGVVQPGTSLRLSCVVSGSDISSYHMGWVRQAPGKGLEWLAIIVSSGSA
YYATWAKGRFTVSRSKSTLFLKMNSLRADDTAVYYCARNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 319)
>cl|DABBABABA|1|115 >16_6_HC_humanized_411
LQLQESGPRLVKPSETLSLTCTVSGSDISSYHMGWIRQSPGKGLEWIGIIVSSGSAYY
ATWAKSRLTMSTSKNQFSLRLSSVTAADSAVYYCARNQYSGYGFSFWGQGTLVTV
SS (SEQ ID NO: 320)
>cl|FABBABABA|1|115 >16_6_HC_humanized_372
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEAVAIIVSSGSA
YYATWAKGRFTISRDSSTLFLQLNSLRVEDSGIYYCAKNQYSGYGFSFWGQGTLVT
VSS (SEQ ID NO: 321)
>cl|GABBABABA|1|115 >16_6_HC_humanized_1996
QSLEESGGRLVTPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMNSLRVEDTARYYCARNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 322)
>cl|HABBABABA|2|115 >16_6_HC_humanized_1907 >16_6_HC_humanized_716
QSLLESGGGWVQPGRSLRLSCSASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRDNNSLYLQMNSLRPEDTALYYCAKNQYSGYGFSFWGQGVL
VTVSS (SEQ ID NO: 323)
>cl|LABBABABA|2|115 >16_6_HC_humanized_1945 >16_6_HC_humanized_1451
QSLEESGGGLVKPGESLRLSCAASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRDDSTVYLEMNSLKTEDTAVYYCATNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 324)
>cl|NABBABABA|1|115 >16_6_HC_humanized_1004
QSLLESGPRLVKPSETLSLTCSVSGSDISSYHMGWVRQPPGQGLEWIGIIVSSGSAYY
ATWARSRVSISTSQNQVSLKLTSVTAADTAVYYCARNQYSGYGFSFWGQGILVTV
SS (SEQ ID NO: 325)
>cl|PABBABABA|1|115 >16_6_HC_humanized_1971
VQLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWLAIIVSSGSA
YYATWAKGRFTISRDNSSLYLQLSSLRNEDTAVYYCAKNQYSGYGFSFWGPGTLV
TVSS (SEQ ID NO: 326)
>cl|QABBABABA|2|115 >16_6_HC_humanized_802 >16_6_HC_humanized_988
VQLVESGGGLIQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSA
YYATWAKGRFTISRDNASLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 327)
>cl|RABBABABA|1|115 >16_6_HC_humanized_609
VQLVESGGGLVQPGGSLRLSCTTSGSDISSYHMGWVRQVPGKGLEWVSIIVSSGSA
YYATWAKGRFTISRDNSTSYLQMTSLTPEDTAVYYCAKNQYSGYGFSFWGQGTVV
SVSS (SEQ ID NO: 328)
>cl|SABBABABA|1|115 >16_6_HC_humanized_587

VQLVESGGGLVKPGGSLRLSCVVSGSDISSYHMGWVRQAPGKGLEWLSIIVSSGSA
YYATWAKGRFTISRDNASLFLQMNSLRADDTALYFCARNQYSGYGFSFWGQGTLV
TVSS (SEQ ID NO: 329)
>cl|TABBABABA|6|115 >16_6_HC_humanized_305 >16_6_HC_humanized_283
>16_6_HC_humanized_334 >16_6_HC_humanized_281 >16_6_HC_humanized_339
VQLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCAKNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 330)
>cl|VABBABABA|4|115 >16_6_HC_humanized_1877 >16_6_HC_humanized_860
>16_6_HC_humanized_204 >16_6_HC_humanized_818
VQLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 331)
>cl|WABBABABA|1|115 >16_6_HC_humanized_1012
VQLQEWGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGS
AYYATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGT
LVTVSS (SEQ ID NO: 332)
>cl|YABBABABA|1|115 >16_6_HC_humanized_910
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYY
ATWAQSRVLISTSKSQLSLKLTSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTV
SS (SEQ ID NO: 333)
>cl|CEBBABABA|1|115 >16_6_HC_humanized_253
VQLVESGGGLVQPGRSLRLSCATSGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRDNASLYLQMSSLRAEDTALYYCAKNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 334)
>cl|DEBBABABA|1|115 >16_6_HC_humanized_218
VQLQESGPGLVKPSETLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYY
ATWAKSRVTISTSKNQFSLKLSSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTV
SS (SEQ ID NO: 335)
>cl|FEBBABABA|1|115 >16_6_HC_humanized_213
LQLQESGPGLVKPSETLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYY
ATWAKSRVTISTSKNQFSLKLSSVTAADTAVYYCASNQYSGYGFSFWGQGTLVTV
SS (SEQ ID NO: 336)
>cl|GEBBABABA|1|115 >16_6_HC_humanized_136
VQLQQSGPGLVKTSETLPLTCTVSGSDISSYHMGWIRQPPGKGLEYIGIIVSSGSAYY
ATWAKNRVTISTSKNQFSLKLSSVTAADTALYYCARNQYSGYGFSFWGQGTLVTV
SS (SEQ ID NO: 337)
>cl|HEBBABABA|1|115 >16_6_HC_humanized_129
MQLVESGGGLVQPGRSLRLSCVTSGSDISSYHMGWVRQVPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRDNTSLYLQMNSLRPEDTAVYYCAKNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 338)
>cl|KEBBABABA|1|115 >16_6_HC_humanized_109
VQLVESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGKGLEYIGIIVSSGSAYY
ATWAKSRLTMSVDTSNYQLKLSSVTAADTAVYYCARNQYSGYGFSFWGQGTTVT
VSS (SEQ ID NO: 339)
>cl|LEBBABABA|1|115 >16_6_HC_humanized_103
VQLQQSGPGLVKPSGTLSLTCDVSGSDISSYHMGWVRQPPGKGLEWIGIIVSSGSAY
YATWAKSRVTISKSKNQFSLRLTSVTAADTAVYYCARNQYSGYGFSFWGQGTLVT
VSS (SEQ ID NO: 340)
>cl|MEBBABABA|1|115 >16_6_HC_humanized_954

VQLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCAKNQYSGYGFSFWGQGTT
VTVSS (SEQ ID NO: 341)
>cl|NEBBABABA|1|115 >16_6_HC_humanized_902
VQLVESGPGLVKPSQTLSLTCTVSGSDISSYHMGWLRQPPGRGLEWIGIIVSSGSAY
YATWAKSRVTLSTSKNQFSLKLNSVTAADTAVYYCARNQYSGYGFSFWGQGTLV
TVSS (SEQ ID NO: 342)
>cl|PEBBABABA|1|115 >16_6_HC_humanized_851
VQLVQSGGGVVQPGGSLRVSCAASGSDISSYHMGWVRQAPGKGLEWMAIIVSSGS
AYYATWAKGRFTISRDNSTVSLQMSSLRAEDTAVYYCAKNQYSGYGFSFWGRGTL
VTVSS (SEQ ID NO: 343)
>cl|REBBABABA|1|115 >16_6_HC_humanized_17
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGRGLVWVSIIVSSGSA
YYATWAKGRFTISRDNATLYLQMNNLRAEDTAVYYCARNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 344)
>cl|SEBBABABA|1|115 >16_6_HC_humanized_926
VQLVESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQHSGKTLEWIGIIVSSGSAY
YATWAESRVTISADTSKISLKLSSVTAADTAVYYCARNQYSGYGFSFWGQGTTVT
VSS (SEQ ID NO: 345)
>cl|TEBBABABA|1|115 >16_6_HC_humanized_908
VQLVESGGGLVEPGGSLRLSCAASGSDISSYHMGWIRQAPGKGLEWLSIIVSSGSAY
YATWAKGRFTISRDNASLYLQMNSLRAEDTAVYYCVRNQYSGYGFSFWGQGTMV
TVSS (SEQ ID NO: 346)
>cl|VEBBABABA|1|115 >16_6_HC_humanized_904
VQLVESGPGLVKPSQTLSLTCNVSGSDISSYHMGWIRQSPGKGLEWIGIIVSSGSAY
YATWARSRVTISADTSKVSLELSPMTAADTAVYYCARNQYSGYGFSFWGQGTTVT
VSS (SEQ ID NO: 347)
>cl|WEBBABABA|1|115 >16_6_HC_humanized_903
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGTGLEWIGIIVSSGSAYY
ATWAKSRVTISGDTSKFSLMLRSVTAADTAVYYCARNQYSGYGFSFWGQGTMVT
VSS (SEQ ID NO: 348)
>cl|XEBBABABA|1|115 >16_6_HC_humanized_108
VQLVESGGGLVKPGGSLRLSCAASGSDISSYHMGWIRQAPGKGLEWVSIIVSSGSA
YYATWAKGRFTISRDNASLFLQMNSLRAEDTAVYYCAKNQYSGYGFSFWGQGTLI
TVSS (SEQ ID NO: 349)
>cl|YEBBABABA|1|115 >16_6_HC_humanized_946
VQLVESGGGLIKPGGSLRLSCEVPGSDISSYHMGWVRQGPGRGLEWVGIIVSSGSA
YYATWARGRFTISRSKSTVYLEMNALKTEDTGIYYCVTNQYSGYGFSFWGQGTMV
TVSS (SEQ ID NO: 350)
>cl|ZEBBABABA|1|115 >16_6_HC_humanized_882
QSLEESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQPPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRSKSTVYLQMNSLKTEDTAVYYCTANQYSGYGFSFWGQGML
VTVSS (SEQ ID NO: 351)
>cl|BIBBABABA|1|115 >16_6_HC_humanized_186
VQLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLESVAIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 352)
>cl|CIBBABABA|1|115 >16_6_HC_humanized_2041

QSLVQSGTEVRKPGASVKVSCKASGSDISSYHMGWVRQAPGQGLEWMGIIVSSGS
AYYATWAQGRVTMSDTSTTVYMELSSLTSEDTAIYYCARNQYSGYGFSFWGPGTL
VTVSS (SEQ ID NO: 353)
>cl|DIBBABABA|1|115 >16_6_HC_humanized_202
VQLQESGEGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEYVSIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMGSLRAEDMAVYYCARNQYSGYGFSFWGQGT
MVTVSS (SEQ ID NO: 354)
>cl|FIBBABABA|2|115 >16_6_HC_humanized_192 >16_6_HC_humanized_880
QHLEESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTT
VTVSS (SEQ ID NO: 355)
>cl|GIBBABABA|2|115 >16_6_HC_humanized_1982 >16_6_HC_humanized_734
QSLLESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYY
ATWAKSRVTMSTSKNHFSLRLSSVTAADTAVYYCARNQYSGYGFSFWGQGTLVT
VSS (SEQ ID NO: 356)
>cl|KIBBABABA|1|115 >16_6_HC_humanized_1944
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQPPGKGLEWIGIIVSSGSAY
YATWAKNRVTISTSKNQFSLRLNSVTAADTAVYYCARNQYSGYGFSFWGQGTLVT
VSS (SEQ ID NO: 357)
>cl|LIBBABABA|1|115 >16_6_HC_humanized_1895
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLVWVSIIVSSGSAY
YATWAKGRFTISRDNATLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGKGTTV
TVSS (SEQ ID NO: 358)
>cl|MIBBABABA|1|115 >16_6_HC_humanized_65
QSLEESGGGLVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRDNASLYLQMNSLRAEDTALYYCAKNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 359)
>cl|NIBBABABA|2|115 >16_6_HC_humanized_1938 >16_6_HC_humanized_762
VKLLESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMNSLGAEDTAVYYCARNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 360)
>cl|QIBBABABA|2|115 >16_6_HC_humanized_2031 >16_6_HC_humanized_621
VQLVESGGGLVKPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMNNLRAEDTAVYYCARNQYSGYGFSFWGQGTL
VTVLS (SEQ ID NO: 361)
>cl|SIBBABABA|1|115 >16_6_HC_humanized_993
VQLVESGGGLIQPGRPLRLSCSGSGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRDDSVVHLQMNSLKSEDTAVYYCTRNQYSGYGFSFWGQGTT
VTVSS (SEQ ID NO: 362)
>cl|TIBBABABA|1|115 >16_6_HC_humanized_956
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWFRQHPGKGLEWIGIIVSSGSAY
YATWAESRLTISEDTSNIQLRLTSVTAADTAVYFCARNQYSGYGFSFWGQGTTVTV
SS (SEQ ID NO: 363)
>cl|VIBBABABA|1|115 >16_6_HC_humanized_920
VQLVESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQFPGKGLEWIGIIVSSGSAYY
ATWAKSRFTISTSKNQFSLKVDSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTV
SS (SEQ ID NO: 364)
>cl|WIBBABABA|1|115 >16_6_HC_humanized_278

VQLVQSGGGLVKPGGSLRLSCEASGSDISSYHMGWIRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRDDSTLYLQVNSLKTEDSAVYYCTTNQYSGYGFSFWGQGTLV
TVSS (SEQ ID NO: 365)
>cl|YIBBABABA|2|115 >16_6_HC_humanized_169 >16_6_HC_humanized_168
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMDSLRAEDTAIYYCAKNQYSGYGFSFWGQGTLV
TVSS (SEQ ID NO: 366)
>cl|ZIBBABABA|1|115 >16_6_HC_humanized_994
VQLVESGGGLIQPGRSLRLSCSGSGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRDDSVVYLQMNSLRSEDTAVYYCTRNQYSGYGFSFWGQGTM
VTVSS (SEQ ID NO: 367)
>cl|BOBBABABA|2|115 >16_6_HC_humanized_975 >16_6_HC_humanized_978
VQLVESGGGVVRPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRDNASLYLEMNSLRAEDTALYFCARNQYSGYGFSFWGQGTM
VTVSS (SEQ ID NO: 368)
>cl|DOBBABABA|1|115 >16_6_HC_humanized_230
QSLEESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCAKNQYSGYGFSFWGQGTT
VTVSS (SEQ ID NO: 369)
>cl|GOBBABABA|1|115 >16_6_HC_humanized_1894
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAY
YATWAKGRFTISRDNASLYLQMNSLRAEDTAVYYCARNQYSGYGFSFFSDYWLVT
VSS (SEQ ID NO: 370)
>cl|HOBBABABA|2|115 >16_6_HC_humanized_2056 >16_6_HC_humanized_672
QSLVESGGGLIQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAY
YATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTLV
TVSS (SEQ ID NO: 371)
>cl|LOBBABABA|1|115 >16_6_HC_humanized_657
QSLEESGGRLVTPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSA
YYATWAKGRFTISRDNSSLYLQMNSLRTEDSALYYCALNQYSGYGFSFWGQGSLV
TVSS (SEQ ID NO: 372)
>cl|MOBBABABA|2|115 >16_6_HC_humanized_1917 >16_6_HC_humanized_677
QSLEESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSA
YYATWAKRRFTISRDNSTLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 373)
>cl|POBBABABA|1|115 >16_6_HC_humanized_2038
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAY
YATWAKGRFTISRDNASLYLQMNSLRAEDTAVYYCARNQYSGYGFSFPTSGYYY
MDVS (SEQ ID NO: 374)
>cl|QOBBABABA|1|115 >16_6_HC_humanized_23
QSLLESGGDLVQPGGSLRLSCEASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSA
YYATWAKGRFTISRDKSTLFLQMHSLRVEDTAVYYCAKNQYSGYGFSFWGQGTT
VTVSS (SEQ ID NO: 375)
>cl|ROBBABABA|1|115 >16_6_HC_humanized_21
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEFVSIIVSSGSA
YYATWAKDRFTISRDNSTVYLQMDSLRTEDTAMYFCARNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 376)
>cl|SOBBABABA|1|115 >16_6_HC_humanized_469

VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSA
YYATWAKGRFTISRDNTSLFLHMSSLRGEDTAIYYCARNQYSGYGFSFWGQGTLV
TVSS (SEQ ID NO: 377)
>cl|TOBBABABA|1|115 >16_6_HC_humanized_2008
QSLEESGGRLVTPGTSLRLSCAVSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAY
YATWAKGRFTISRDNSTVYLQMNSLRAEDTAVFYCARNQYSGYGFSFWGQGTLV
TVSS (SEQ ID NO: 378)
>cl|VOBBABABA|1|115 >16_6_HC_humanized_1013
VQLVQSGGGVVQPGRSLRLSCEVSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSA
YYATWAKGRFTISRSNNTLYLQMNSLTAEDTALYFCARNQYSGYGFSFWGKGTTV
TVSS (SEQ ID NO: 379)
>cl|XOBBABABA|1|115 >16_6_HC_humanized_149
VQLVQSGPGLVKPSRTLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAY
YATWAQNRLTISTSKNQFSLKLASVTAADTAVYFCARNQYSGYGFSFWGQGTLVT
VSS (SEQ ID NO: 380)
>cl|YOBBABABA|1|115 >16_6_HC_humanized_113
LQLQESGPGLVKPSQTLSLTCSVSGSDISSYHMGWIRQHPGKGLEWIGIIVSSGSAYY
ATWAKSRITISTSKNQFSLKLTSVTAADTALYYCARNQYSGYGFSFWGRGTLVTVS
S (SEQ ID NO: 381)
>cl|BUBBABABA|1|115 >16_6_HC_humanized_965
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQHPGKGLEWIGIIVSSGSAY
YATWAKSRVTISADTSKISLKLSSVTAADTAVYYCARNQYSGYGFSFWGQGTTVT
VSS (SEQ ID NO: 382)
>cl|CUBBABABA|1|115 >16_6_HC_humanized_912
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYY
ATWAKSRVLISTSKNQVSLKLSSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTV
SS (SEQ ID NO: 383)
>cl|HUBBABABA|1|115 >16_6_HC_humanized_12
VQLVQSGGGVVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGS
AYYATWAQGRVTISRDNSTVHLQITSLKSEDTAVYYCAKNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 384)
>cl|KUBBABABA|1|115 >16_6_HC_humanized_924
VQLVESGPGLVKPSQTLSLTCTVSGSDISSYHMGWFRQPPGKGLEWIGIIVSSGSAY
YATWAKSRVTISTSKNQVSLKLSPVTGADTAVYFCARNQYSGYGFSFWGQGTLVT
VSS (SEQ ID NO: 385)
>cl|LUBBABABA|1|115 >16_6_HC_humanized_273
VQLVQSGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQASGKGLEWIGIIVSSGSA
YYATWAKGRFTVSRSQNSVFLQMNSLETEDTAVYYCARNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 386)
>cl|MUBBABABA|1|115 >16_6_HC_humanized_2032
QSLEESGGRLVTPGGSLRLSCAGSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSA
YYATWAEGRFTISRDNATLYLQMNSLRVEDTAVYYCATNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 387)
>cl|NUBBABABA|1|115 >16_6_HC_humanized_879
QSLEESGGGLVQPGGSLRLSCTASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSA
YYATWAKGRFTISRDSSTLYLQMNNLRVEDTALYYCAHNQYSGYGFSFWGRGTQ
VTVSS (SEQ ID NO: 388)
>cl|PUBBABABA|1|115 >16_6_HC_humanized_267

QSLEQSGGGLVQPGESLRLSCAGSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSA
YYATWAKGRFTISRDNASLFLQMNSLRVEDTAVYYCARNQYSGYGFSFWGQGTL
VTVSS (SEQ ID NO: 389)
>cl|QUBBABABA|1|115 >16_6_HC_humanized_1992
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLVWVSIIVSSGSAY
YATWAKGRFTISRDNATLYLQMNSLRVEDTAVYYCARNQYSGYGFSFWGPGTLV
TVSS (SEQ ID NO: 390)
>cl|RUBBABABA|1|115 >16_6_HC_humanized_1995
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAY
YATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCAKNQYSGYGFSFWGPGTLVT
VSS (SEQ ID NO: 391)
>cl|SUBBABABA|1|115 >16_6_HC_humanized_917
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYY
ATWARSRITISETSKNLSLKLTSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTVS
S (SEQ ID NO: 392)
>cl|TUBBABABA|1|115 >16_6_HC_humanized_1934
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAY
YATWAKGRFTISRDNASLYLQMNSLRAEDTAVYYCARNQYSGYGFSFGIFDYWVT
VSS (SEQ ID NO: 393)
>cl|VUBBABABA|1|115 >16_6_HC_humanized_200
VQLQESGPGLVKPSETLSLTCSVSGSDISSYHMGWIRQPAGKGLEWIGIIVSSGSAYY
ATWARSRVTMSMSKNHFSLKLRSVTAADTAVYFCARNQYSGYGFSFWGQGTLVT
VSS (SEQ ID NO: 394)
>cl|WUBBABABA|1|115 >16_6_HC_humanized_1977
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAY
YATWAKGRFTISRSKNTLYLQMNSLRAEDTAVYYCARNQYSGYGFSFTCPYFDYW
VSS (SEQ ID NO: 395)
>cl|XUBBABABA|1|115 >16_6_HC_humanized_2027
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAY
YATWAEGRFTISRDNSTLYLQMYSLRTEDTAVYYCARNQYSGYGFSFYYYGMGV
WVSS (SEQ ID NO: 396)
>cl|YUBBABABA|1|115 >16_6_HC_humanized_1958
VHLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSA
YYATWAEGRFTISRDNSKLYLQMNSLRAEDSATYYCARNQYSGYGFSFFGPPYYY
YYMS (SEQ ID NO: 397)
>cl|ZUBBABABA|1|115 >16_6_HC_humanized_1949
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEYVSIIVSSGSAY
YATWAKGRFTISRDNSTLYLQMSSLRAEDTAVYYCVKNQYSGYGFSFWGPGTLVT
VSS (SEQ ID NO: 398)
>cl|BACBABABA|1|115 >16_6_HC_humanized_1905
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAY
YATWAKGRFTISRDNSTLYLQMNSLRAEDTALYYCARNQYSGYGFSFVRGGYFYH
MDS (SEQ ID NO: 399)

Table 12. 16-6 VL humanized sequences – IMGT-LigM DB (Abysis) clustered at 95% (64 sequences)

>cl|CACBABABA|1|110 >16_6_LC_humanized_586

IVLTQTPSSLSASVGDRITITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLAS
GVPSRFSGSRSGTDFTFTISSLRPEDIATYYCLGGYDDDGETAFGGGTKVEIK (SEQ
ID NO: 400)
>cl|DACBABABA|1|110 >16_6_LC_humanized_411
IVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPNLLIYRASNLA
SGVPSRFSGSGSATDFTLTISSLQPEDFATYYCLGGYDDDGETAFGGGTRVEIK
(SEQ ID NO: 401)
>cl|FACBABABA|1|110 >16_6_LC_humanized_372
IQLTQSPSTLSASVGDRVTITCQSSHSVYYGDWLAWYQQKAGKAPTLLIYRASNLA
SGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCLGGYDDDGETAFGQGTKVDIK
(SEQ ID NO: 402)
>cl|GACBABABA|1|110 >16_6_LC_humanized_1996
VVLTQTPSPVSTAVGGTVTLSCQSSHSVYYGDWLAWYQQKPGQAPRLLIYRASNL
ASGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCLGGYDDDGETAKGPGTEVVVK
(SEQ ID NO: 403)
>cl|HACBABABA|2|110 >16_6_LC_humanized_1907 >16_6_LC_humanized_716
LVMTQSPSSLSASEGDRVTITCQSSHSVYYGDWLAWYQQKPGRAPKLLIHRASNLA
SGVPSRFSGSGSGTEFTLTISGLQSEDFATYYCLGGYDDDGETAFGGGTTVDVK
(SEQ ID NO: 404)
>cl|LACBABABA|2|110 >16_6_LC_humanized_1945 >16_6_LC_humanized_1451
VELTQPPSPVSAAPGQKVTISCQSSHSVYYGDWLAWYQQLPGTAPKLLIYRASNLA
SGIPDRFSGSKSGTSATLGITGLQTGDEADYYCLGGYDDDGETAFGGGTRLTVL
(SEQ ID NO: 405)
>cl|NACBABABA|2|110 >16_6_LC_humanized_1004 >16_6_LC_humanized_283
IQLTQSPSSVSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFALTISSLQPEDFATYYCLGGYDDDGETAFGQGTRLEIK
(SEQ ID NO: 406)
>cl|PACBABABA|1|110 >16_6_LC_humanized_1971
VVLTQTPSPVSTAVGGTVTITCQSSHSVYYGDWLAWYQQKSGKAPKLLIYRASNL
ASGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 407)
>cl|QACBABABA|1|110 >16_6_LC_humanized_802
IRMTQSPSSFSASTGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISCLQSEDFATYYCLGGYDDDGETAFGGGTKVEIK
(SEQ ID NO: 408)
>cl|RACBABABA|1|110 >16_6_LC_humanized_609
IRLTQSPSFLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISTLQPEDFATYYCLGGYDDDGETAFGQGTKLEIK
(SEQ ID NO: 409)
>cl|SACBABABA|1|110 >16_6_LC_humanized_587
VVMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWFQQKPGKAPNLLIYRASNL
ASGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLGGYDDDGETAFGQGTKVEIK
(SEQ ID NO: 410)
>cl|TACBABABA|1|110 >16_6_LC_humanized_305
IQLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWFQQKPGKAPKSLIYRASNLAS
GVPSRFSGSGSGTDFTLTISSLQPEDSATYYCLGGYDDDGETAFGGGTKVEIK (SEQ
ID NO: 411)
>cl|VACBABABA|12|110 >16_6_LC_humanized_1877 >16_6_LC_humanized_860
>16_6_LC_humanized_213 >16_6_LC_humanized_902 >16_6_LC_humanized_334

IQLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGGGTKVEIK
(SEQ ID NO: 412)
>cl|WACBABABA|2|110 >16_6_LC_humanized_1012 >16_6_LC_humanized_65
IQLTQSPSTLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCLGGYDDDGETAFGQGTKLEIK (SEQ
ID NO: 413)
>cl|XACBABABA|6|110 >16_6_LC_humanized_988 >16_6_LC_humanized_910
>16_6_LC_humanized_956 >16_6_LC_humanized_2056 >16_6_LC_humanized_672
IVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGQGTRLEIK (SEQ
ID NO: 414)
>cl|CECBABABA|1|110 >16_6_LC_humanized_253
IVLTQSPSAMSASVGDRVTITCQSSHSVYYGDWLAWFQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTEFTLTISSLQPEDSATYYCLGGYDDDGETAFGQGTKVDIK
(SEQ ID NO: 415)
>cl|DECBABABA|1|110 >16_6_LC_humanized_218
IVMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKVPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPEDVATYYCLGGYDDDGETAFGPGTKVEIK
(SEQ ID NO: 416)
>cl|GECBABABA|1|110 >16_6_LC_humanized_136
VVMTQSPSTLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKVLIYRASNL
ASGVPSRFSGSGSGTEFTLTISSLQPDDFASYYCLGGYDDDGETAFGPGTKVDIK
(SEQ ID NO: 417)
>cl|HECBABABA|1|110 >16_6_LC_humanized_129
IVMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQHKPGKAPRLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPDDFATYYCLGGYDDDGETAFGQGTKVEVK
(SEQ ID NO: 418)
>cl|KECBABABA|1|110 >16_6_LC_humanized_109
IQLTQSPSSVSASVGDTITITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLAS
GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGQGTKVEIK (SEQ
ID NO: 419)
>cl|LECBABABA|1|110 >16_6_LC_humanized_103
IVLTQSPSTLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGQAPKLLIYRASNLA
SGVPSRFSGSGSGTEFTLSINSLQPDDSATYFCLGGYDDDGETAFGQGTKVEIK
(SEQ ID NO: 420)
>cl|MECBABABA|1|110 >16_6_LC_humanized_954
IVLTQSPSTLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCLGGYDDDGETAFGQGTKAEIK
(SEQ ID NO: 421)
>cl|PECBABABA|3|110 >16_6_LC_humanized_851 >16_6_LC_humanized_908
>16_6_LC_humanized_912
VVMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNL
ASGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGGGTKVEIK
(SEQ ID NO: 422)
>cl|RECBABABA|1|110 >16_6_LC_humanized_17
IQLTQSPSSLSAAVGDRVTIACQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLSISSLQPGDFATYYCLGGYDDDGETAFGGGTKVQMK
(SEQ ID NO: 423)
>cl|XECBABABA|2|110 >16_6_LC_humanized_108 >16_6_LC_humanized_946

IVLTQSPSSVSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGGGTKVEIK
(SEQ ID NO: 424)
>cl|ZECBABABA|1|110 >16_6_LC_humanized_882
VVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGFGTDFTFTISSLQPEDSATYYCLGGYDDDGETAFGQGTKLEIK (SEQ
ID NO: 425)
>cl|BICBABABA|1|110 >16_6_LC_humanized_186
IQLTQSPSTLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCLGGYDDDGETAFGQGTKVVVK
(SEQ ID NO: 426)
>cl|CICBABABA|1|110 >16_6_LC_humanized_2041
VVLTQTPSPVSTAVGGTVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNL
ASGVPSRFSGSGSGTDFTLTISCLQSEDFATYYCLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 427)
>cl|DICBABABA|1|110 >16_6_LC_humanized_202
IRMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKVPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPEDVATYYCLGGYDDDGETAFGPGTKVVVK
(SEQ ID NO: 428)
>cl|FICBABABA|1|110 >16_6_LC_humanized_192
VVMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNL
ASGVPSRFSGSGSGTDFTLTISSLQAEDFTTYYCLGGYDDDGETAFGQGTKVEFK
(SEQ ID NO: 429)
>cl|GICBABABA|2|110 >16_6_LC_humanized_1982 >16_6_LC_humanized_734
VELTQSPSSVSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFSLTISSLQPEDSATYYCLGGYDDDGETAFGQGTKVEIK
(SEQ ID NO: 430)
>cl|KICBABABA|2|110 >16_6_LC_humanized_1944 >16_6_LC_humanized_1895
IELTQSPSTLSASVGDRVIISCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLAS
GVPSRFSGSGSGTEFSLTINSLQPDDFATYYCLGGYDDDGETAFGPGTKVDIK (SEQ
ID NO: 431)
>cl|NICBABABA|2|110 >16_6_LC_humanized_1938 >16_6_LC_humanized_762
VELTQSPDSLAVSLGERATINCQSSHSVYYGDWLAWYQQKPGQPPKLLIYRASNLA
SGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCLGGYDDDGETAFGGGTKVEIK
(SEQ ID NO: 432)
>cl|QICBABABA|2|110 >16_6_LC_humanized_2031 >16_6_LC_humanized_621
VELTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGQGTKVEIK
(SEQ ID NO: 433)
>cl|SICBABABA|4|110 >16_6_LC_humanized_993 >16_6_LC_humanized_880
>16_6_LC_humanized_23 >16_6_LC_humanized_917
VVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGPGTKVDIK
(SEQ ID NO: 434)
>cl|VICBABABA|1|110 >16_6_LC_humanized_920
IVMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPEDIATYYCLGGYDDDGETAFGQGTKVEIK (SEQ
ID NO: 435)
>cl|WICBABABA|1|110 >16_6_LC_humanized_278

LVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWCQQKPGKSPTLLIYRASNLA
SGVPSRFSGSGSGTGFTLTISGLQPEDFATYYCLGGYDDDGETAFGGGTKVEIR
(SEQ ID NO: 436)
>cl|YICBABABA|1|110 >16_6_LC_humanized_169
IVLTQSPSFLSAFVGDRITITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLAS
GVPSRFSGSGSGTEFTLTISGLQPEDFASYYCLGGYDDDGETAFGGGTKLEIK (SEQ
ID NO: 437)
>cl|ZICBABABA|1|110 >16_6_LC_humanized_994
IVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKVPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPEDVATYYCLGGYDDDGETAFGQGTKVEIK
(SEQ ID NO: 438)
>cl|BOCBABABA|1|110 >16_6_LC_humanized_975
IVLTQSPSTQSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCLGGYDDDGETAFGQGTKLEIK (SEQ
ID NO: 439)
>cl|DOCBABABA|1|110 >16_6_LC_humanized_230
VVLTQTPSPVSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKVLIYRASNL
ASGVPSRFSGSGSGTDFTLTISTLQPEDFATYYCLGGYDDDGETAFGQGTKLEIK
(SEQ ID NO: 440)
>cl|GOCBABABA|1|110 >16_6_LC_humanized_1894
VVLTQTPSPVSTAVGDRVTITCQSSHSVYYGDWLAWYRQKPGKVPKLLIYRASNL
ASGVPSRFSGSGSGTDFTLTISSLQPEDVATYYGLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 441)
>cl|LOCBABABA|1|110 >16_6_LC_humanized_657
VVLTQTPSPVSTSVGDRVSITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTITSLQPVDFATYYCLGGYDDDGETAFGPGTTVDAK
(SEQ ID NO: 442)
>cl|MOCBABABA|2|110 >16_6_LC_humanized_1917 >16_6_LC_humanized_677
VVLTQSPSFLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTEFTLTISSLQ
PEDFATYYCLGGYDDDGETAFGQGTRLEIK (SEQ ID NO: 443)
>cl|POCBABABA|1|110 >16_6_LC_humanized_2038
VVLTQTPSPVSTAVGGRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNL
ASGVPSRFSGSGSGTEFTLTISSLQDKPFATYYCLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 444)
>cl|ROCBABABA|1|110 >16_6_LC_humanized_21
IQMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKVLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGPGTKVEVK
(SEQ ID NO: 445)
>cl|SOCBABABA|1|110 >16_6_LC_humanized_469
IVLTQSPSLLSASIGDRVTIPCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLAS
GVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLGGYDDDGETAFGGGTKVDIK (SEQ
ID NO: 446)
>cl|TOCBABABA|1|110 >16_6_LC_humanized_2008
VVLTQTPSPVSTAVGGRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNL
ASGVPSRFSGSGSGTDFTLTIGSLQPEDFAAYFCLGGYDDDGETAFGGGTKVEIK
(SEQ ID NO: 447)
>cl|WOCBABABA|1|110 >16_6_LC_humanized_168

IVMTQSPSTLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTEFTLTISGLQPEDFATYYCLGGYDDDGETAFGGGTKLEIK
(SEQ ID NO: 448)
>cl|XOCBABABA|1|110 >16_6_LC_humanized_149
IVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKRLIYRASNLA
SGVPSRFSGSGSGTEFTLTISGLQPEDIATYYCLGGYDDDGETAFGQGTKVEIK (SEQ
ID NO: 449)
>cl|YOCBABABA|1|110 >16_6_LC_humanized_113
IVLTQSPSSVSASVGDRVTITCQSSHSVYYGDWLAWYQLKPGKAPKLLINRASNLA
SGVPSRFSGSGSGTDFTLTISGLQPEDFATYYCLGGYDDDGETAFGPGTTVDIK
(SEQ ID NO: 450)
>cl|ZOCBABABA|4|110 >16_6_LC_humanized_978 >16_6_LC_humanized_965
>16_6_LC_humanized_924 >16_6_LC_humanized_879
IVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGGGTKVEIK
(SEQ ID NO: 451)
>cl|GUCBABABA|1|110 >16_6_LC_humanized_818
VVLTQTPSSVSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNL
ASGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGQGTKVEIK
(SEQ ID NO: 452)
>cl|HUCBABABA|1|110 >16_6_LC_humanized_12
VVMTQSPSTVSASVGDRVTLTCQSSHSVYYGDWLAWYQQKPGQPPKLLIYRASNL
ASGVPDRFSGSGSGTDFTLTISSLQADDFATYYCLGGYDDDGETAFGQGTKVEIK
(SEQ ID NO: 453)
>cl|LUCBABABA|1|110 >16_6_LC_humanized_273
LVMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGEAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISGLQSEDFATYYCLGGYDDDGETAFGQGTKVEIK
(SEQ ID NO: 454)
>cl|MUCBABABA|1|110 >16_6_LC_humanized_2032
VVLTQTPSPVSTAVGGTGPINCQSSHSVYYGDWLAWYQQKPGQPPKLLIYRASNLA
SGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCLGGYDDDGETAFGGGTKLEIK
(SEQ ID NO: 455)
>cl|PUCBABABA|1|110 >16_6_LC_humanized_267
VVLTQSPSTLAASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNL
ASGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCLGGYDDDGETAFGQGTKVEVK
(SEQ ID NO: 456)
>cl|QUCBABABA|1|110 >16_6_LC_humanized_1992
VVLTQTPSPVSTAVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNL
ASGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 457)
>cl|RUCBABABA|1|110 >16_6_LC_humanized_1995
VVLTQTPSPVSTAVGGTVTINCQSSHSVYYGDWLAWYQQKPGQPXKLLIYRASNL
ASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCLGGYDDDGETAFGQGTEVVVK
(SEQ ID NO: 458)
>cl|TUCBABABA|2|110 >16_6_LC_humanized_1934 >16_6_LC_humanized_1977
VVLTQTPSPVSTAVGGTVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNL
ASGVPSRFSGSGSGTDFTFTISSLQPEDIATYYCLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 459)
>cl|VUCBABABA|1|110 >16_6_LC_humanized_200

VVLTQTPSPVSTAVGERATINCQSSHSVYYGDWLAWYQQKPGQPPKLLIYRASNLA
SGVPDRFSGTGSGTDFTLTISSLQAEDVAVYYCLGGYDDDGETAFGGGTKVVVK
(SEQ ID NO: 460)
>cl|XUCBABABA|1|110 >16_6_LC_humanized_2027
VVLTQTPSPVSTAVGGTVTITCQSSHSVYYGDWLAWYQQKPGKAPKRLIYRASNL
ASGVPSRFSGSGSGTEFTLTISSLQPEDFATYYXLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 461)
>cl|YUCBABABA|2|110 >16_6_LC_humanized_1958 >16_6_LC_humanized_1949
VVLTQTPSPVSTAVGGTVTIPCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNL
ASGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 462)
>cl|BADBABABA|1|110 >16_6_LC_humanized_1905
VVLTQTPSPVSTAVGGTVTINCQSSHSVYYGDWLAWYQQKPGQPPKLLIYRASNL
ASGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 463)

Table 13. 16-6 VH humanized sequences -- germline database clustered at 90% (3 sequences)

>cl|CABBABABA|43|115 >16_6_HC_humanized_775 >16_6_HC_humanized_722
>16_6_HC_humanized_563 >16_6_HC_humanized_139 >16_6_HC_humanized_988
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGPGTL
VTVSS (SEQ ID NO: 464)
>cl|DABBABABA|39|115 >16_6_HC_humanized_724 >16_6_HC_humanized_565
>16_6_HC_humanized_141 >16_6_HC_humanized_990 >16_6_HC_humanized_985
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRSKNTLYLQMNSLKTEDTAVYYCTRNQYSGYGFSFWGPGTLV
TVSS (SEQ ID NO: 465)
>cl|REBBABABA|18|115 >16_6_HC_humanized_365 >16_6_HC_humanized_364
>16_6_HC_humanized_363 >16_6_HC_humanized_360 >16_6_HC_humanized_359
VQLQESGPGLVKPSETLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYY
ATWAKSRVTISTSKNQFSLKLSSVTAADTAVYYCARNQYSGYGFSFWGPGTLVTV
SS (SEQ ID NO: 466)

Table 14. 16-6 VL humanized sequences -- germline database clustered at 90% (1 sequences)

>cl|CACBABABA|100|110 >16_6_LC_humanized_775 >16_6_LC_humanized_724
>16_6_LC_humanized_722 >16_6_LC_humanized_565 >16_6_LC_humanized_563
VVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 467)

Table 15. 16-6 VH humanized sequences -- germline database clustered at 95% (10 sequences)

>cl|CABBABABA|13|115 >16_6_HC_humanized_775 >16_6_HC_humanized_722 >16_6_HC_humanized_563 >16_6_HC_humanized_139 >16_6_HC_humanized_987
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEYVSIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMGSLRAEDMAVYYCARNQYSGYGFSFWGPGTL
VTVSS (SEQ ID NO: 468)
>cl|DABBABABA|12|115 >16_6_HC_humanized_724 >16_6_HC_humanized_565 >16_6_HC_humanized_141 >16_6_HC_humanized_989 >16_6_HC_humanized_936
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRSKNSLYLQMNSLKTEDTAVYYCARNQYSGYGFSFWGPGTLV
TVSS (SEQ ID NO: 469)
>cl|MABBABABA|9|115 >16_6_HC_humanized_990 >16_6_HC_humanized_937 >16_6_HC_humanized_672 >16_6_HC_humanized_407 >16_6_HC_humanized_248
VQLVESGGGLVQPGGSLKLSCAASGSDISSYHMGWVRQASGKGLEWVGIIVSSGSA
YYATWAKGRFTISRSKNTAYLQMNSLKTEDTAVYYCTRNQYSGYGFSFWGPGTLV
TVSS (SEQ ID NO: 470)
>cl|NABBABABA|27|115 >16_6_HC_humanized_988 >16_6_HC_humanized_935 >16_6_HC_humanized_670 >16_6_HC_humanized_405 >16_6_HC_humanized_246
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGPGTL
VTVSS (SEQ ID NO: 471)
>cl|PABBABABA|9|115 >16_6_HC_humanized_985 >16_6_HC_humanized_932 >16_6_HC_humanized_667 >16_6_HC_humanized_402 >16_6_HC_humanized_243
VQLVESGGGLVQPGRSLRLSCTASGSDISSYHMGWFRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRSKSIAYLQMNSLKTEDTAVYYCTRNQYSGYGFSFWGPGTLV
TVSS (SEQ ID NO: 472)
>cl|QABBABABA|9|115 >16_6_HC_humanized_973 >16_6_HC_humanized_920 >16_6_HC_humanized_655 >16_6_HC_humanized_390 >16_6_HC_humanized_231
VQLVESGGGLVKPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSA
YYATWAKGRFTISRSKNTLYLQMNSLKTEDTAVYYCTTNQYSGYGFSFWGPGTLV
TVSS (SEQ ID NO: 473)
>cl|REBBABABA|12|115 >16_6_HC_humanized_365 >16_6_HC_humanized_364 >16_6_HC_humanized_363 >16_6_HC_humanized_360 >16_6_HC_humanized_312
VQLQESGPGLVKPSETLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYY
ATWAKSRVTISTSKNQFSLKLSSVTAADTAVYYCARNQYSGYGFSFWGPGTLVTV
SS (SEQ ID NO: 474)
>cl|WEBBABABA|3|115 >16_6_HC_humanized_359 >16_6_HC_humanized_306 >16_6_HC_humanized_41
LQLQESGSGLVKPSQTLSLTCAVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYY
ATWAKSRVTISRSKNQFSLKLSSVTAADTAVYYCARNQYSGYGFSFWGPGTLVTV
SS (SEQ ID NO: 475)
>cl|XEBBABABA|3|115 >16_6_HC_humanized_357 >16_6_HC_humanized_304 >16_6_HC_humanized_39
VQLQESGPGLVKPPGTLSLTCAVSGSDISSYHMGWVRQPPGKGLEWIGIIVSSGSAY
YATWAKSRVTISKSKNQFSLKLSSVTAADTAVYCCARNQYSGYGFSFWGPGTLVT
VSS (SEQ ID NO: 476)
>cl|CIBBABABA|3|115 >16_6_HC_humanized_343 >16_6_HC_humanized_290 >16_6_HC_humanized_25

VQLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSA
YYATWAKGRFTISRDNSTLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGPGTL
VTVSS (SEQ ID NO: 477)

Table 16. 16-6 VL humanized sequences – germline database clustered at 95% (7 sequences)

>cl|CACBABABA|3|110 >16_6_LC_humanized_775 >16_6_LC_humanized_724
>16_6_LC_humanized_722
VVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTFTISSLQPEDIATYYCLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 478)
>cl|GACBABABA|2|110 >16_6_LC_humanized_565 >16_6_LC_humanized_563
VVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKRLIYRASNLA
SGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 479)
>cl|KACBABABA|2|110 >16_6_LC_humanized_141 >16_6_LC_humanized_139
VVLTQSPSSFSASTGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISCLQSEDFATYYCLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 480)
>cl|MACBABABA|62|110 >16_6_LC_humanized_990 >16_6_LC_humanized_988
>16_6_LC_humanized_985 >16_6_LC_humanized_973 >16_6_LC_humanized_937
VVLTQSPSSVSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNL
ASGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 481)
>cl|WACBABABA|6|110 >16_6_LC_humanized_672 >16_6_LC_humanized_670
>16_6_LC_humanized_667 >16_6_LC_humanized_655 >16_6_LC_humanized_671
VVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKVPKLLIYRASNLA
SGVPSRFSGSGSGTDFTLTISSLQPEDVATYYCLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 482)
>cl|GECBABABA|6|110 >16_6_LC_humanized_248 >16_6_LC_humanized_246
>16_6_LC_humanized_243 >16_6_LC_humanized_231 >16_6_LC_humanized_247
VVLTQSPSFLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTEFTLTISSLQPEDFATYYCLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 483)
>cl|YICBABABA|19|110 >16_6_LC_humanized_47 >16_6_LC_humanized_46
>16_6_LC_humanized_45 >16_6_LC_humanized_42 >16_6_LC_humanized_41
VVLTQSPSTLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLA
SGVPSRFSGSGSGTEFTLTISSLQPDDFATYYCLGGYDDDGETAFGGGTEVVVK
(SEQ ID NO: 484)

EXAMPLE 5: USE OF AN ANTI-LINKER ANTIBODY FOR PURIFYING MACROMOLECULES AND CELLS

[0328] The antigen binding molecules disclosed herein are antigen binding molecules, such as antibodies, which specifically bind to the sequence

GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), molecules comprising these sequences and cells presenting such molecules, polynucleotides encoding such antigen binding molecules, as well as humanized forms of the antigen binding molecules. An antigen binding molecule (*e.g.*, an antibody) disclosed herein can thus be used to purify a molecule, such as, macromolecule, polymer, cell, material, etc., displaying an epitope that is recognized by the antigen binding molecules disclosed herein (*e.g.*, GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500)).

[0329] In one embodiment, an antigen binding molecule disclosed herein (*e.g.*, Clones 8 and/or 16 and fragments thereof) can be attached to beads, attached to or associated with a resin, which can be disposed in a column or other structure. A sample comprising a molecule comprising all or a fragment of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500) can then be contacted with the beads, resin, etc. to which the antigen binding molecule was attached or with which an antigen binding molecule was associated. This allows the formation of an association or binding complex comprising the antigen binding molecule and the molecule comprising all or a fragment of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500). The beads or resin can then be washed with a suitable solution, such as a buffer solution (*e.g.*, PBS, HEPES, MOPS, Tris, Tricine, etc) having a pH selected to maintain the stability of the molecule comprising all or a fragment of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500). The washing can remove unwanted and unbound components of the sample. Following the washing step, the molecule comprising all or a fragment of the GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500) can then be eluted from the antigen binding molecules using an elution buffer and conditions selected to disrupt any association or binding complexes formed. Examples of suitable

elution buffers include incubation with peptide epitope in molar excess, 0.1M glycine, pH 2.5-3.0, and 0.1M citric acid, pH 3.0, 50-100mM triethylamine or triethanolamine, pH 11.5, 3.5-4.0M magnesium chloride, pH 7.0 in 10mM Tris, 2-6M guanidine, and 2-8M urea, or a buffer solution around pH 7-8, including, but not limited to, 10 mM Tris, HEPES, or 1X PBS, containing free peptide GSTSGSGKPGSGEGSTKG and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500). . During the elution step, eluted molecules, cells and moieties of interest comprising all or a fragment of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500) is collected, and purity can be subsequently checked by running a sample on an SDS polyacrylamide gel.

[0330] In another embodiment, an antigen binding molecule can be disposed in solution with any molecular entity displaying the epitope, and purified from a mixed population of molecules, cells, etc. and eluted from the beads, resin, or free antibody by washing with 300-500 mM sodium chloride or lowering the pH and neutralizing with 1 M Tris, for proteins, or phosphate buffer, or with buffer containing free peptide, such as GSTSGSGKPGSGEGSTKG and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500). Subsequently, dialysis can be used to return materials to desired buffer conditions.

[0331] In a specific embodiment, cells displaying a molecule comprising all or a fragment of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500) can be incubated with magnetic beads (*e.g.*, DYNABEADS) with which an antigen binding molecule disclosed herein has been associated. Preferably the incubation is performed under conditions that both allow for the formation of binding complexes/associations, such as under physiological conditions, in the presence of a media selected for this purpose (*e.g.*, RPMI-1640).

[0332] Cells bound by the beads (which will be presenting molecules comprising GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500)) are then separated from cells not displaying a

molecule comprising GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500). In one embodiment, the beads can be washed with media, such as RPMI-1640 supplemented with 10% FBS, in the presence of a magnet.

[0333] Selected cells, *i.e.*, those presenting molecules that comprise GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500) can then be separated from the beads: First, selected cells are grown out in media. After growing out cells for 48 hours, the magnetic beads can be separated from cells in solution and discarded, leaving a pure population of cells presenting desired molecule.

[0334] In an alternative embodiment, the beads are not magnetic, and in this embodiment, the above steps can also be followed and adapted to maintain cell integrity, but also to allow separation of bead-bound cells from non-bead bound cells.

[0335] In an alternative embodiment, an antigen binding molecule disclosed herein (*e.g.*, Clones 8 and/or 16 and fragments thereof) can be His-tagged (*i.e.*, labeled with a short polyhistidine sequence), thereby facilitating the separation of cells using a resin comprising a transition metal ion such as Ni^{2+}, Co^{2+}, Cu^{2+} or Zn^{2+}, which are immobilized on the resin. The antigen binding molecules can then be incubated with cells known or suspected to be presenting a molecule comprising GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500) under conditions suitable for the formation of complexes comprising the cells and the antigen binding molecules. Following the incubation, the cells are contacted with the resin, which can be disposed in a solid structure such as a welled plate, column or other structure. The antigen binding molecule-cell complexes can then be separated from one another by washing with imidazole, which will be of a higher concentration than any imidazole included in any solutions used in the formation of the binding complexes. Eluted cells can then be spun down, washed in RPMI or other suitable media, and then resuspended in media.

EXAMPLE 6: SORTING OF CAR-POSITIVE T-CELLS

[0336] PBMCs were isolated from healthy donor leukopaks (Hemacare™) using Ficoll-Paque density centrifugation per manufacturer's instructions. PBMCs were stimulated using OKT3 (50ng/ml, Miltenyi Biotec™) in R10 media + IL-2 (300IU/ml, Proleukin®, Prometheus® Therapeutics and Diagnostics). Two days after stimulation, CAR T cells were generated through viral transduction of these activated primary human T cells. Transduction was performed using either a retro- (pMSVG vector) or lentivirus (pGAR vector) depending upon the origin of the CARs used in the screening. Confirmation of CAR construct expression and viral transduction efficiency was determined using Protein L conjugated to phycoerythrin (PE) or fluorescein isothiocyanate (FITC).

[0337] Cultured CAR T-cells were removed from culture, washed with PBS, and incubated with the anti-linker antibody conjugated to PE for 30 minutes in stain buffer comprising PBS pH 7.4, 0.2% (w/v) bovine serum albumin, and 0.09% sodium azide. Cells were washed two times in stain buffer, resuspended and sorted with a BD Aria cell sorter. Negatively- and positively-gated cells were analyzed post sort for composition (FIGURE 10).

EXAMPLE 7: STIMULATING/ACTIVATING CAR-POSITIVE T CELLS USING AN ANTIGEN BINDING MOLECULE

[0338] T-cells are often stimulated through their T-cell receptors (TCR) using an anti-CD3 antibody, such as clone OKT3, a mouse anti-CD3 antibody, along with an anti-CD28 antibody to provide a second signal or costimulatory signal. CAR T-cells, upon interaction with cognate antigen can provide both signals through their intracellular CD3zeta and costimulatory domain, such as CD28.

[0339] Accordingly, also provided is a method of activating CAR-positive T cells presenting a molecule comprising a specific epitope recognized by a specific antigen binding molecule (*e.g.*, an antigen binding molecule, such as an antibody that recognizes a molecule comprising GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500)), such as those disclosed herein: Clone 8 and/or 16, and fragments thereof). This method can be adapted for any antibody recognizing a protein of interest on a T cell containing an activation domain, such as a chimeric antigen receptor (CAR) comprising GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ

ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500). Activation can be achieved using plate-bound, bead-bound, polymer-bound, or other form of the antibody that specifically recognizes an extracellular component of the CAR or similar molecule.

[0340] In this Example, we show that CAR+ T-cells can be selectively stimulated *in vitro* with an anti-linker antibody, such as those provided herein. For purposes of comparison, OKT3 antibodies, which are commonly used to activate T cells *in vitro* (*see*, *e.g.*, Landegren *et al.*, (1984) *Eur. J. Immunol.* 14(4):325-28) were used to stimulate all T-cells. Bags, flasks, plates, or other vessels for growing T-cells can be used for the stimulation or, as described herein, welled plates can also be used for the stimulation.

[0341] In one instance, CAR-T cells were sorted, as described in EXAMPLE 4 (FIGURE 10), and mixed to form populations of cells at fixed percentages of CAR-positive cells; these cells were then allowed to recover from sort for 24 hours at 37° C in OpTmizer media. 12-well tissue culture treated plates were incubated with either OKT3 or anti-linker antibody at 1.5 μg/mL in HBSS for 2 hours at 37° C, and washed three times with HBSS. 0.5e6 T-cells of defined populations were added in 2 mL of OpTmizer media with IL-2 to the plates pre-coated with antibody and cells were incubated for up to 1 week at 37° C and sampled at various time points.

[0342] Samples were subject to analysis by flow cytometry to check for presence of CAR and various activation markers, including CD25, CD69, and 4-1BB. Over time, we observed that OKT3 antibodies stimulated all T-cells, and the percentage of CAR-positive cells was unchanged. In contrast, when incubated with the anti-linker antibody, T-cells that were CAR-positive received stimulation and proliferated, becoming a larger percentage of the population (FIGURE 11). Additionally, we observed that OKT3 stimulated all T-cells as observed by levels of CD69 and 4-1BB on the surface of T-cells. In contrast, stimulation with the anti-linker antibody selectively stimulated CAR-positive cells (FIGURES 12A and 12B).

[0343] Thus, cells presenting a molecule comprising GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), can be selectively stimulated *in vitro*.

EXAMPLE 8: STIMULATING/ACTIVATING CAR-POSITIVE T CELLS USING AN ANTIGEN BINDING MOLECULE *in vivo*

[0344] In this example, CAR+ T-cells were selectively stimulated *in vivo* with an anti-linker antibody, provided herein. MM1S cells were implanted into female NSG mice. To clear the MM1S cells, CAR-T cells comprising the peptide GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) were injected on Day 6. On Day 13, fludeoxyglucose positron emission tomography (FDG-PET) experiments were performed to assess baseline metabolism. Clone 8 anti-linker antibody was injected into each mouse and the FDG-PET experiment was repeated after 24 hours. As shown in Figure 13, an increase in FDG-PET signal post antibody treatment was best observed in the hind limbs suggesting stimulation of CAR+ T cells *in vivo* responsive to anti-linker injection.

EXAMPLE 9: DEPLETION OF CELLS EXPRESSING MOLECULES CONTAINING SPECIFIC PEPTIDES USING A DIABODY

[0345] In this Example, CAR+ T-cells can be selectively killed *in vitro* with an anti-linker/anti-human CD3 diabody, comprising an anti-linker binding moiety, such as in Clone 8 and 16. T-cells transduced with a CAR containing the specific epitope GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) (CAR1), a CAR not containing the epitope (CAR2), or not transduced (Mock) were grown in 96-well U-bottom in OpTmizer media with T-cell supplements, penicillin, streptomycin, glutamine, and IL-2. Each well contained 20,000 T-cells. The diabody was added to each CAR- and Mock-transduced T-cell samples at concentrations from 1.28 pM to 100 nM. After 16 hours, cells were stained with Live/Dead Violet (Molecular Probes) and recombinant protein L/streptavidin-PE to assess the number of dead cells and percentage of CAR+ T-cells as a function of the concentration of the diabody. As shown in Figure 14A, the amount of dye that binds to cells with ruptured membranes is increased in the CAR1 samples, whereas the expression of a control CAR or no CAR does not lead to a significant increase in dye fluorescence (see CAR2 and Mock, respectively). This can be further observed by a decrease in the percentage of CAR1 T-cells compared to CAR2 T-cells (Figure 14B). CAR1 cells start at approximately 40% positive, but are depleted to about 10% of total T-cells at the highest concentration of the diabody, whereas CAR2 T-cells stay at a constant 20% CAR+. Thus, cells presenting a molecule comprising GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1) and subsequences thereof, particularly GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE

(SEQ ID NO: 499), and/or KPGSG (SEQ ID NO: 500), can be selectively depleted *in vitro* with a diabody specific for T-cells and the specific peptide.

[0345a] In some aspects, described herein are one or more of the following items:

1. An isolated antigen binding molecule that specifically binds to a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and KPGSG (SEQ ID NO: 500), wherein the antigen binding molecule comprises a heavy chain variable region (VH) CDR1, a VH CDR2, and a VH CDR3 from the heavy chain variable region sequence of SEQ ID NO: 5 and a light chain variable region (VL) CDR1, a VL CDR2, and a VL CDR3 from the light chain variable region sequence of SEQ ID NO: 11, or a VH CDR1, a VH CDR2, and a VH CDR3 from the heavy chain variable region sequence of SEQ ID NO: 17 and a VL CDR1 a, VL CDR2, and a VL CDR3 from the VH sequence of SEQ ID NO: 23.
2. The antigen binding molecule of item 1, wherein the antigen binding molecule is selected from the group consisting of an antibody, an scFv, a Fab, a Fab', a Fv, a F(ab')2, a dAb, a human antibody, a humanized antibody, a chimeric antibody, a monoclonal antibody, a polyclonal antibody, a recombinant antibody, an IgE antibody, an IgD antibody, an IgM antibody, an IgG1 antibody, an IgG1 antibody having at least one mutation in the hinge region, an IgG2 antibody, an IgG2 antibody having at least one mutation in the hinge region, an IgG3 antibody, an IgG4 antibody, an IgG4 antibody having at least one mutation in the hinge region, an antibody comprising at least one non-naturally occurring amino acid, and any combination thereof.
3. The antigen binding molecule of item 1 or 2, wherein the antigen binding molecule comprises an antibody.
4. The antigen binding molecule of any one of items 1-3, wherein the antigen binding molecule comprises a heavy chain (HC).
5. The antigen binding molecule of item 4, wherein the HC comprises a heavy chain variable region (VH) sequence that is at least 70% identical to a VH selected from the group consisting of SEQ ID NOs: 5 and 17, relative to its full length.
6. The antigen binding molecule of item 4, wherein the HC comprises a heavy chain variable region (VH) sequence that is at least 80% identical to a VH selected from the group consisting of SEQ ID NOs: 5 and 17, relative to its full length.

Date Reçue/Date Received 2023-05-24

7. The antigen binding molecule of item 4, wherein the HC comprises a heavy chain variable region (VH) sequence that is at least 85% identical to a VH selected from the group consisting of SEQ ID NOs: 5 and 17, relative to its full length.

8. The antigen binding molecule of item 4, wherein the HC comprises a heavy chain variable region (VH) sequence that is at least 90% identical to a VH selected from the group consisting of SEQ ID NOs: 5 and 17, relative to its full length.

9. The antigen binding molecule of item 4, wherein the HC comprises a heavy chain variable region (VH) sequence that is at least 95% identical to a VH selected from the group consisting of SEQ ID NOs: 5 and 17, relative to its full length.

10. The antigen binding molecule of item 4, wherein the HC comprises a heavy chain variable region (VH) sequence that is identical to a VH selected from the group consisting of SEQ ID NOs: 5 and 17.

11. The antigen binding molecule of any one of items 1-10, wherein:
the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 7;
the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 8;
the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 9;
the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 13;
the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 14; and
the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 15;
or
the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 19;
the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 20;
the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 21;
the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 25;
the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 26; and
the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 27.

Date Reçue/Date Received 2023-05-24

12. The antigen binding molecule of any one of items 1-11, wherein the antigen binding molecule comprises a light chain (LC).

13. The antigen binding molecule of item 12, wherein the LC comprises a light chain variable region (VL) sequence that is at least 70% identical to a VL selected from the group consisting of SEQ ID NOs: 11 and 23, relative to its full length.

14. The antigen binding molecule of item 12, wherein the LC comprises a light chain variable region (VL) sequence that is at least 80% identical to a VL selected from the group consisting of SEQ ID NOs: 11 and 23, relative to its full length.

15. The antigen binding molecule of item 12, wherein the LC comprises a light chain variable region (VL) sequence that is at least 85% identical to a VL selected from the group consisting of SEQ ID NOs: 11 and 23, relative to its full length.

16. The antigen binding molecule of item 12, wherein the LC comprises a light chain variable region (VL) sequence that is at least 90% identical to a VL selected from the group consisting of SEQ ID NOs: 11 and 23, relative to its full length.

17. The antigen binding molecule of item 12, wherein the LC comprises a light chain variable region (VL) sequence that is at least 95% identical to a VL selected from the group consisting of SEQ ID NOs: 11 and 23, relative to its full length.

18. The antigen binding molecule of item 12, wherein the LC comprises a light chain variable region (VL) sequence that is identical to a VL selected from the group consisting of SEQ ID NOs: 11 and 23.

19. The antigen binding molecule of any one of items 1-18, wherein the antigen binding molecule comprises:

    (a) a VH comprising the amino acid sequence of SEQ ID NO: 5; and

    (b) a VL comprising the amino acid sequence of SEQ ID NO: 11.

20. The antigen binding molecule of any one of items 1-18, wherein the antigen binding molecule comprises:

    (a) a VH comprising the amino acid sequence of SEQ ID NO: 17; and

    (b) a VL comprising the amino acid sequence of SEQ ID NO: 23.

21. The antigen binding molecule of any one of items 1-20, wherein the antigen binding molecule further comprises a detectable label.

Date Reçue/Date Received 2023-05-24

22. The antigen binding molecule of item 21, wherein the detectable label is selected from the group consisting of a fluorescent label, a photochromic compound, a proteinaceous fluorescent label, a magnetic label, a radiolabel, and a hapten.

23. The antigen binding molecule of item 22, wherein the fluorescent label is selected from the group consisting of an Atto™ dye, an Alexa Fluor™ dye, quantum dots, Hydroxycoumarin, Aminocouramin, Methoxycourmarin, Cascade Blue™, Pacific Blue™, Pacific Orange™, Lucifer Yellow™, NBD, R-Phycoerythrin (PE), PE-Cy™5 conjugates, PE-Cy7 conjugates, Red 613, PerCP, TruRed™, FluorX, Fluorescein, BODIPY-FL, Cy2, Cy3, Cy3B, Cy3.5, Cy5, Cy5.5, Cy7, TRITC, X-Rhodamine, Lissamine, Rhodamine B, Texas Red, Allophycocyanin (APC), APC-Cy7 conjugates, Indo-1, Fluo-3, Fluo-4, DCFH, DHR, SNARF™, GFP (Y66H mutation), GFP (Y66F mutation), EBFP, EBFP2, Azurite, GFPuv, T-Sapphire, Cerulean, mCFP, mTurquoise2, ECFP, CyPet, GFP (Y66W mutation), mKeima-Red, TagCFP, AmCyan1, mTFP1, GFP (S65A mutation), Midorishi Cyan, Wild Type GFP, GFP (S65C mutation), TurboGFP, TagGFP, GFP (S65L mutation), Emerald, GFP (S65T mutation), EGFP, Azami Green, ZsGreen1, TagYFP, EYFP,Topaz, Venus, mCitrine, YPet, TurboYFP, ZsYellow1, Kusabira Orange, mOrange, Allophycocyanin (APC), mKO, TurboRFP, tdTomato, TagRFP, DsRed monomer, DsRed2 ("RFP"), mStrawberry, TurboFP602, AsRed2, mRFP1, J-Red, R-phycoerythrin (RPE), B-phycoerythrin (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

24. A composition comprising the antigen binding molecule of any one of items 1-23 and a carrier, diluent, solubilizer, emulsifier, preservative, adjuvant, excipient, or any combination thereof.

25. A polynucleotide encoding the heavy chain of an antigen binding molecule of any one of items 1-23.

26. A polynucleotide encoding the light chain of an antigen binding molecule of any one of items 1-23.

27. A vector comprising the polynucleotide of item 25 and/or item 26.

28. A cell comprising one or both of the vectors of item 27.

29. The cell of item 28, wherein the cell comprises a cell selected from the group consisting of a CHO cell, a Sp2/0 cell, a rabbit cell and an *E. coli* cell.

Date Reçue/Date Received 2023-05-24

30. A method of making an antigen binding molecule of any one of items 1-23 comprising incubating the cell of item 28 or 29 under suitable conditions.

31. Use of a dose of immune cells expressing a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) for the treatment of a subject with a cancer.

32. Use of a dose of immune cells expressing a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) for the manufacture of a medicament for the treatment of a subject with a cancer.

33. The use of item 31 or 32, wherein the chimeric antigen receptor (CAR) comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS

Date Reçue/Date Received 2023-05-24

(GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

34. The use of any one of items 31-33, wherein the immune cells are selected from the group consisting of CD8+ T cells, CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells.

35. The use of any one of items 31-34, wherein the immune cells are T cells.

36. The use of item 34 or 35, wherein the T cells are expressed *in vitro*.

37. The use of item 34 or 35, wherein the T cells are expressed *in vivo*.

38. The use of any one of items 34-37, wherein the T cells are in one of blood, extracted tissue, tissue grown *ex vivo*, or cell culture media.

39. The use of any one of items 34-38, wherein the T cells are autologous T cells.

40. The use of any one of items 34-38, wherein the T cells are allogeneic T cells.

41. The use of any one of items 33-40, wherein the dose comprises 1.0×10^6 cells per kg of the subject.

42. A method of activating an immune cell expressing a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), the method comprising:

    (a) providing a sample comprising an immune cell known or suspected to be expressing said CAR comprising the selected amino acid sequence; and

    (b) contacting the antigen binding molecule of any one of items 1-23 with the sample, under conditions that permit the formation of a binding complex comprising the antigen binding molecule and two CARs comprising the selected amino acid sequence, wherein the CARs comprising the selected amino acid sequences are expressed on two different immune cells.

43. The method of item 42, wherein the chimeric antigen receptor (CAR) comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM),

Date Reçue/Date Received 2023-05-24

CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

44. The method of item 42 or 43, wherein the immune cell is selected from the group consisting of CD8+ T cells, CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells.

45. The method of any one of items 42-44, wherein the immune cell is a T cell.

46. The method of item 44 or 45, wherein the T cell is expressed *in vitro*.

47. The method of any one of items 44-46, wherein the T cell is isolated from blood or extracted tissue of a subject, or from tissue grown *ex vivo,* or cell culture media.

48. The method of item 47, wherein the T cell is an autologous T cell.

49. The method of item 47, wherein the T cell is an allogeneic T cell.

50. An immune cell expressing a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG

Date Reçue/Date Received 2023-05-24

(SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), wherein the immune cell is activated by the method as defined in any one of items 42-49.

51. The immune cell of item 50, for use in the treatment of a subject with a cancer.

52. Use of the immune cell of item 50, for the treatment of a subject with a cancer.

53. Use of the immune cell of item 50, for the manufacture of a medicament for the treatment of a subject with a cancer.

54. A method of determining a number of cells expressing a chimeric antigen receptor (CAR) in a sample, wherein the CAR comprises an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), the method comprising:

    (a) providing a sample comprising cells known or suspected to be expressing said CAR comprising the selected amino acid sequence;

    (b) contacting the sample of (a) with the antigen binding molecule of any one of items 1-23 that specifically binds the CAR comprising the selected amino acid sequence, under conditions that permit the formation of a binding complex comprising the cell present in the sample and the antigen binding molecule; and

    (c) determining the number of cells present in the binding complex of (b) in the sample.

55. The method of item 54, wherein the chimeric antigen receptor (CAR) comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B),

Date Reçue/Date Received 2023-05-24

CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

56. The method of item 54 or 55, wherein the cell expressing the chimeric antigen receptor (CAR) comprising the selected amino acid sequence is an immune cell selected from the group consisting of CD8+ T cells, CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells.

57. The method of item 56, wherein the immune cell is a T cell.

58. The method of item 56 or 57, wherein the T cell is expressed *in vitro*.

59. The method of any one of items 56-58, wherein the T cell is isolated from blood or extracted tissue of a subject, or from tissue grown *ex vivo,* or cell culture media.

60. The method of item 59, wherein the T cell is an autologous T cell.

61. The method of item 59, wherein the T cell is an allogeneic T cell.

62. A method of isolating a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), the method comprising:

    (a) providing a sample known or suspected to comprise said CAR comprising the selected amino acid sequence;

    (b) providing the antigen binding molecule of any one of items 1-23 that specifically binds the CAR comprising the selected amino acid sequence;

Date Reçue/Date Received 2023-05-24

(c) contacting the sample with the antigen binding molecule, under conditions that permit the formation of a binding complex comprising said CAR comprising the selected amino acid sequence and the antigen binding molecule;

(d) separating any molecules not part of the binding complex from formed binding complexes; and

(e) separating the formed binding complex into: (1) said CAR comprising the selected amino acid sequence, and (2) the antigen binding molecule.

63. The method of item 62, wherein the chimeric antigen receptor (CAR) comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

Date Reçue/Date Received 2023-05-24

64. The method of item 62 or 63, wherein the antigen binding molecule is expressed on a surface selected from the group consisting of an agarose bead, a magnetic bead, a plastic welled plate, a glass welled plate, a ceramic welled plate and a cell culture bag.

65. A method of determining the presence or absence of a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), the method comprising:

(a) providing a sample known or suspected to comprise said CAR comprising the selected amino acid sequence;

(b) providing the antigen binding molecule of any one of items 1-23 that specifically binds the CAR comprising the selected amino acid sequence ;

(c) contacting the sample with the antigen binding molecule under conditions that permit the formation of a binding complex;

(d) separating any molecules not part of the binding complex from formed binding complexes; and

(e) detecting the presence or absence of the binding complex.

66. The method of item 65, wherein the chimeric antigen receptor (CAR) comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR),

Date Reçue/Date Received 2023-05-24

CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

67. The method of item 65 or 66, wherein the antigen binding molecule is expressed on a surface selected from the group consisting of an agarose bead, a magnetic bead, a plastic welled plate, a glass welled plate, a ceramic welled plate and a cell culture bag.

68. A method of increasing the concentration of cells expressing a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), the method comprising:

(a) providing the antigen binding molecule of any one of items 1-23 that specifically binds the selected amino acid sequence;

(b) contacting the cells with the antigen binding molecule under conditions that permit the formation of a binding complex comprising the CAR comprising the selected amino acid sequence and the antigen binding molecule;

(c) removing any components not part of the binding complex; and

(d) repeating steps (a)-(c) a desired number of times.

69. The method of item 68, wherein the chimeric antigen receptor (CAR) comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2),

Date Reçue/Date Received 2023-05-24

CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

70. The method of item 68 or 69, wherein the cells are immune cells selected from the group consisting of CD8+ T cells, CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells.

71. The method of item 70, wherein the immune cells are T cells.

72. The method of item 70 or 71, wherein the T cells are expressed *in vitro*.

73. The method of any one of items 70-72, wherein the T cells are isolated from blood or extracted tissue of a subject, or from tissue grown *ex vivo,* or cell culture media.

74. The method of item 73, wherein the T cells are autologous T cells.

75. The method of item 73, wherein the T cells are allogeneic T cells.

76. A method of depleting a population of immune cells expressing a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), the method comprising:

Date Reçue/Date Received 2023-05-24

(a) contacting the immune cells with the antigen binding molecule of any one of items 1-23 that specifically binds to (1) the CAR comprising the selected amino acid sequence, and (2) an activating molecule expressed on the surface of that immune cell that does not comprise the selected amino acid sequence, under conditions that permit the formation of a ternary binding complex comprising the CAR comprising the selected amino acid sequence, the activating molecule, and the antigen binding molecule.

77. The method of item 76, wherein the chimeric antigen receptor (CAR) comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

Date Reçue/Date Received 2023-05-24

78. The method of item 76 or 77, wherein the immune cells are selected from the group consisting of CD8+ T cells, CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells.

79. The method of any one of items 76-78, wherein the immune cells are T cells.

80. The method of item 78 or 79, wherein the T cells are expressed *in vitro*.

81. The method of any one of items 78-80, wherein the T cells are from blood or extracted tissue of a subject, or from tissue grown *ex vivo,* or cell culture media.

82. The method of item 81, wherein the T cells are an autologous T cell.

83. The method of item 81, wherein the T cells are an allogeneic T cell.

84. A method of monitoring distribution *in vivo* of a population of cells expressing a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), comprising:

    (a) providing the antigen binding molecule of any one of items 1-23; and

    (b) performing a positron emission tomography (PET) scan.

85. The antigen binding molecule of any one of items 1-23, for use in stimulating or depleting a population of cells expressing a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500).

86. Use of the antigen binding molecule of any one of items 1-23, for stimulating or depleting a population of cells expressing a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500).

Date Reçue/Date Received 2023-05-24

1. An isolated antigen binding molecule that specifically binds to a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499), and KPGSG (SEQ ID NO: 500), wherein the antigen binding molecule comprises a heavy chain variable region (VH) CDR1, a VH CDR2, and a VH CDR3 from the heavy chain variable region sequence of SEQ ID NO: 5 and a light chain variable region (VL) CDR1, a VL CDR2, and a VL CDR3 from the light chain variable region sequence of SEQ ID NO: 11, or a VH CDR1, a VH CDR2, and a VH CDR3 from the heavy chain variable region sequence of SEQ ID NO: 17 and a VL CDR1 a, VL CDR2, and a VL CDR3 from the VH sequence of SEQ ID NO: 23.
2. The antigen binding molecule of claim 1, wherein the antigen binding molecule is selected from the group consisting of an antibody, an scFv, a Fab, a Fab', a Fv, a F(ab')2, a dAb, a human antibody, a humanized antibody, a chimeric antibody, a monoclonal antibody, a polyclonal antibody, a recombinant antibody, an IgE antibody, an IgD antibody, an IgM antibody, an IgG1 antibody, an IgG1 antibody having at least one mutation in the hinge region, an IgG2 antibody, an IgG2 antibody having at least one mutation in the hinge region, an IgG3 antibody, an IgG4 antibody, an IgG4 antibody having at least one mutation in the hinge region, an antibody comprising at least one non-naturally occurring amino acid, and any combination thereof.
3. The antigen binding molecule of claim 1 or 2, wherein the antigen binding molecule comprises an antibody.
4. The antigen binding molecule of any one of claims 1-3, wherein the antigen binding molecule comprises a heavy chain (HC).
5. The antigen binding molecule of claim 4, wherein the HC comprises a heavy chain variable region (VH) sequence that is at least 70% identical to a VH selected from the group consisting of SEQ ID NOs: 5 and 17, relative to its full length.
6. The antigen binding molecule of claim 4, wherein the HC comprises a heavy chain variable region (VH) sequence that is at least 80% identical to a VH selected from the group consisting of SEQ ID NOs: 5 and 17, relative to its full length.

Date Reçue/Date Received 2022-05-11

7. The antigen binding molecule of claim 4, wherein the HC comprises a heavy chain variable region (VH) sequence that is at least 85% identical to a VH selected from the group consisting of SEQ ID NOs: 5 and 17, relative to its full length.

8. The antigen binding molecule of claim 4, wherein the HC comprises a heavy chain variable region (VH) sequence that is at least 90% identical to a VH selected from the group consisting of SEQ ID NOs: 5 and 17, relative to its full length.

9. The antigen binding molecule of claim 4, wherein the HC comprises a heavy chain variable region (VH) sequence that is at least 95% identical to a VH selected from the group consisting of SEQ ID NOs: 5 and 17, relative to its full length.

10. The antigen binding molecule of claim 4, wherein the HC comprises a heavy chain variable region (VH) sequence that is identical to a VH selected from the group consisting of SEQ ID NOs: 5 and 17.

11. The antigen binding molecule of any one of claims 1-10, wherein:
the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 7;
the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 8;
the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 9;
the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 13;
the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 14; and
the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 15;
or
the VH CDR1 comprises the amino acid sequence of SEQ ID NO: 19;
the VH CDR2 comprises the amino acid sequence of SEQ ID NO: 20;
the VH CDR3 comprises the amino acid sequence of SEQ ID NO: 21;
the VL CDR1 comprises the amino acid sequence of SEQ ID NO: 25;
the VL CDR2 comprises the amino acid sequence of SEQ ID NO: 26; and
the VL CDR3 comprises the amino acid sequence of SEQ ID NO: 27.

Date Reçue/Date Received 2022-05-11

12. The antigen binding molecule of any one of claims 1-11, wherein the antigen binding molecule comprises a light chain (LC).

13. The antigen binding molecule of claim 12, wherein the LC comprises a light chain variable region (VL) sequence that is at least 70% identical to a VL selected from the group consisting of SEQ ID NOs: 11 and 23, relative to its full length.

14. The antigen binding molecule of claim 12, wherein the LC comprises a light chain variable region (VL) sequence that is at least 80% identical to a VL selected from the group consisting of SEQ ID NOs: 11 and 23, relative to its full length.

15. The antigen binding molecule of claim 12, wherein the LC comprises a light chain variable region (VL) sequence that is at least 85% identical to a VL selected from the group consisting of SEQ ID NOs: 11 and 23, relative to its full length.

16. The antigen binding molecule of claim 12, wherein the LC comprises a light chain variable region (VL) sequence that is at least 90% identical to a VL selected from the group consisting of SEQ ID NOs: 11 and 23, relative to its full length.

17. The antigen binding molecule of claim 12, wherein the LC comprises a light chain variable region (VL) sequence that is at least 95% identical to a VL selected from the group consisting of SEQ ID NOs: 11 and 23, relative to its full length.

18. The antigen binding molecule of claim 12, wherein the LC comprises a light chain variable region (VL) sequence that is identical to a VL selected from the group consisting of SEQ ID NOs: 11 and 23.

19. The antigen binding molecule of any one of claims 1-18, wherein the antigen binding molecule comprises:

    (a) a VH comprising the amino acid sequence of SEQ ID NO: 5; and

    (b) a VL comprising the amino acid sequence of SEQ ID NO: 11.

20. The antigen binding molecule of any one of claims 1-18, wherein the antigen binding molecule comprises:

    (a) a VH comprising the amino acid sequence of SEQ ID NO: 17; and

    (b) a VL comprising the amino acid sequence of SEQ ID NO: 23.

21. The antigen binding molecule of any one of claims 1-20, wherein the antigen binding molecule further comprises a detectable label.

Date Reçue/Date Received 2022-05-11

22. The antigen binding molecule of claim 21, wherein the detectable label is selected from the group consisting of a fluorescent label, a photochromic compound, a proteinaceous fluorescent label, a magnetic label, a radiolabel, and a hapten.

23. The antigen binding molecule of claim 22, wherein the fluorescent label is selected from the group consisting of an Atto™ dye, an Alexa Fluor™ dye, quantum dots, Hydroxycoumarin, Aminocouramin, Methoxycourmarin, Cascade Blue™, Pacific Blue™, Pacific Orange™, Lucifer Yellow™, NBD, R-Phycoerythrin (PE), PE-Cy™5 conjugates, PE-Cy7 conjugates, Red 613, PerCP, TruRed™, FluorX, Fluorescein, BODIPY-FL, Cy2, Cy3, Cy3B, Cy3.5, Cy5, Cy5.5, Cy7, TRITC, X-Rhodamine, Lissamine, Rhodamine B, Texas Red, Allophycocyanin (APC), APC-Cy7 conjugates, Indo-1, Fluo-3, Fluo-4, DCFH, DHR, SNARF™, GFP (Y66H mutation), GFP (Y66F mutation), EBFP, EBFP2, Azurite, GFPuv, T-Sapphire, Cerulean, mCFP, mTurquoise2, ECFP, CyPet, GFP (Y66W mutation), mKeima-Red, TagCFP, AmCyan1, mTFP1, GFP (S65A mutation), Midorishi Cyan, Wild Type GFP, GFP (S65C mutation), TurboGFP, TagGFP, GFP (S65L mutation), Emerald, GFP (S65T mutation), EGFP, Azami Green, ZsGreen1, TagYFP, EYFP,Topaz, Venus, mCitrine, YPet, TurboYFP, ZsYellow1, Kusabira Orange, mOrange, Allophycocyanin (APC), mKO, TurboRFP, tdTomato, TagRFP, DsRed monomer, DsRed2 ("RFP"), mStrawberry, TurboFP602, AsRed2, mRFP1, J-Red, R-phycoerythrin (RPE), B-phycoerythrin (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

24. A composition comprising the antigen binding molecule of any one of claims 1-23 and a carrier, diluent, solubilizer, emulsifier, preservative, adjuvant, excipient, or any combination thereof.

25. A polynucleotide encoding the heavy chain of an antigen binding molecule of any one of claims 1-23.

26. A polynucleotide encoding the light chain of an antigen binding molecule of any one of claims 1-23.

27. A vector comprising the polynucleotide of claim 25 and/or claim 26.

28. A cell comprising one or both of the vectors of claim 27.

29. The cell of claim 28, wherein the cell comprises a cell selected from the group consisting of a CHO cell, a Sp2/0 cell, a rabbit cell and an *E. coli* cell.

Date Reçue/Date Received 2022-05-11

30. A method of making an antigen binding molecule of any one of claims 1-23 comprising incubating the cell of claim 28 or 29 under suitable conditions.

31. Use of a dose of immune cells expressing a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) for the treatment of a subject with a cancer.

32. Use of a dose of immune cells expressing a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500) for the manufacture of a medicament for the treatment of a subject with a cancer.

33. The use of claim 31 or 32, wherein the chimeric antigen receptor (CAR) comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS

Date Reçue/Date Received 2022-05-11

(GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

34. The use of any one of claims 31-33, wherein the immune cells are selected from the group consisting of CD8+ T cells, CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells.

35. The use of any one of claims 31-34, wherein the immune cells are T cells.

36. The use of claim 34 or 35, wherein the T cells are expressed *in vitro*.

37. The use of claim 34 or 35, wherein the T cells are expressed *in vivo*.

38. The use of any one of claims 34-37, wherein the T cells are in one of blood, extracted tissue, tissue grown *ex vivo*, or cell culture media.

39. The use of any one of claims 34-38, wherein the T cells are autologous T cells.

40. The use of any one of claims 34-38, wherein the T cells are allogeneic T cells.

41. The use of any one of claims 33-40, wherein the dose comprises 1.0×10^6 cells per kg of the subject.

42. A method of activating an immune cell expressing a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), the method comprising:

    (a) providing a sample comprising an immune cell known or suspected to be expressing said CAR comprising the selected amino acid sequence; and

    (b) contacting the antigen binding molecule of any one of claims 1-23 with the sample, under conditions that permit the formation of a binding complex comprising the antigen binding molecule and two CARs comprising the selected amino acid sequence, wherein the CARs comprising the selected amino acid sequences are expressed on two different immune cells.

43. The method of claim 42, wherein the chimeric antigen receptor (CAR) comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM),

Date Reçue/Date Received 2022-05-11

CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

44. The method of claim 42 or 43, wherein the immune cell is selected from the group consisting of CD8+ T cells, CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells.

45. The method of any one of claims 42-44, wherein the immune cell is a T cell.

46. The method of claim 44 or 45, wherein the T cell is expressed *in vitro*.

47. The method of any one of claims 44-46, wherein the T cell is isolated from blood or extracted tissue of a subject, or from tissue grown *ex vivo*, or cell culture media.

48. The method of claim 47, wherein the T cell is an autologous T cell.

49. The method of claim 47, wherein the T cell is an allogeneic T cell.

50. An immune cell expressing a molecule comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG

Date Reçue/Date Received 2022-05-11

(SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), wherein the immune cell is activated by the method as defined in any one of claims 42-49.

51. The immune cell of claim 50, for use in the treatment of a subject with a cancer.

52. Use of the immune cell of claim 50, for the treatment of a subject with a cancer.

53. Use of the immune cell of claim 50, for the manufacture of a medicament for the treatment of a subject with a cancer.

54. A method of determining a number of cells expressing a chimeric antigen receptor (CAR) in a sample, wherein the CAR comprises an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), the method comprising:

(a) providing a sample comprising cells known or suspected to be expressing said CAR comprising the selected amino acid sequence;

(b) contacting the sample of (a) with the antigen binding molecule of any one of claims 1-23 that specifically binds the CAR comprising the selected amino acid sequence, under conditions that permit the formation of a binding complex comprising the cell present in the sample and the antigen binding molecule; and

(c) determining the number of cells present in the binding complex of (b) in the sample.

55. The method of claim 54, wherein the chimeric antigen receptor (CAR) comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B),

Date Reçue/Date Received 2022-05-11

CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

56. The method of claim 54 or 55, wherein the cell expressing the chimeric antigen receptor (CAR) comprising the selected amino acid sequence is an immune cell selected from the group consisting of CD8+ T cells, CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells.

57. The method of claim 56, wherein the immune cell is a T cell.

58. The method of claim 56 or 57, wherein the T cell is expressed *in vitro*.

59. The method of any one of claims 56-58, wherein the T cell is isolated from blood or extracted tissue of a subject, or from tissue grown *ex vivo,* or cell culture media.

60. The method of claim 59, wherein the T cell is an autologous T cell.

61. The method of claim 59, wherein the T cell is an allogeneic T cell.

62. A method of isolating a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), the method comprising:

(a) providing a sample known or suspected to comprise said CAR comprising the selected amino acid sequence;

(b) providing the antigen binding molecule of any one of claims 1-23 that specifically binds the CAR comprising the selected amino acid sequence;

Date Reçue/Date Received 2022-05-11

(c) contacting the sample with the antigen binding molecule, under conditions that permit the formation of a binding complex comprising said CAR comprising the selected amino acid sequence and the antigen binding molecule;

(d) separating any molecules not part of the binding complex from formed binding complexes; and

(e) separating the formed binding complex into: (1) said CAR comprising the selected amino acid sequence, and (2) the antigen binding molecule.

63. The method of claim 62, wherein the chimeric antigen receptor (CAR) comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

Date Reçue/Date Received 2022-05-11

64. The method of claim 62 or 63, wherein the antigen binding molecule is expressed on a surface selected from the group consisting of an agarose bead, a magnetic bead, a plastic welled plate, a glass welled plate, a ceramic welled plate and a cell culture bag.

65. A method of determining the presence or absence of a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), the method comprising:

(a) providing a sample known or suspected to comprise said CAR comprising the selected amino acid sequence;

(b) providing the antigen binding molecule of any one of claims 1-23 that specifically binds the CAR comprising the selected amino acid sequence ;

(c) contacting the sample with the antigen binding molecule under conditions that permit the formation of a binding complex;

(d) separating any molecules not part of the binding complex from formed binding complexes; and

(e) detecting the presence or absence of the binding complex.

66. The method of claim 65, wherein the chimeric antigen receptor (CAR) comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR),

Date Reçue/Date Received 2022-05-11

CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

67. The method of claim 65 or 66, wherein the antigen binding molecule is expressed on a surface selected from the group consisting of an agarose bead, a magnetic bead, a plastic welled plate, a glass welled plate, a ceramic welled plate and a cell culture bag.

68. A method of increasing the concentration of cells expressing a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), the method comprising:

(a) providing the antigen binding molecule of any one of claims 1-23 that specifically binds the selected amino acid sequence;

(b) contacting the cells with the antigen binding molecule under conditions that permit the formation of a binding complex comprising the CAR comprising the selected amino acid sequence and the antigen binding molecule;

(c) removing any components not part of the binding complex; and

(d) repeating steps (a)-(c) a desired number of times.

69. The method of claim 68, wherein the chimeric antigen receptor (CAR) comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2),

Date Reçue/Date Received 2022-05-11

CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

70. The method of claim 68 or 69, wherein the cells are immune cells selected from the group consisting of CD8+ T cells, CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells.

71. The method of claim 70, wherein the immune cells are T cells.

72. The method of claim 70 or 71, wherein the T cells are expressed *in vitro*.

73. The method of any one of claims 70-72, wherein the T cells are isolated from blood or extracted tissue of a subject, or from tissue grown *ex vivo*, or cell culture media.

74. The method of claim 73, wherein the T cells are autologous T cells.

75. The method of claim 73, wherein the T cells are allogeneic T cells.

76. A method of depleting a population of immune cells expressing a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), the method comprising:

Date Reçue/Date Received 2022-05-11

(a) contacting the immune cells with the antigen binding molecule of any one of claims 1-23 that specifically binds to (1) the CAR comprising the selected amino acid sequence, and (2) an activating molecule expressed on the surface of that immune cell that does not comprise the selected amino acid sequence, under conditions that permit the formation of a ternary binding complex comprising the CAR comprising the selected amino acid sequence, the activating molecule, and the antigen binding molecule.

77. The method of claim 76, wherein the chimeric antigen receptor (CAR) comprises a molecule, or a fragment thereof, selected from the group consisting of CD2, CD3 delta, CD3 epsilon, CD3 gamma, CD4, CD7, CD8α, CD8β, CD11a (ITGAL), CD11b (ITGAM), CD11c (ITGAX), CD11d (ITGAD), CD18 (ITGB2), CD19 (B4), CD27 (TNFRSF7), CD28, CD29 (ITGB1), CD30 (TNFRSF8), CD40 (TNFRSF5), CD48 (SLAMF2), CD49a (ITGA1), CD49d (ITGA4), CD49f (ITGA6), CD66a (CEACAM1), CD66b (CEACAM8), CD66c (CEACAM6), CD66d (CEACAM3), CD66e (CEACAM5), CD69 (CLEC2), CD79A (B-cell antigen receptor complex-associated alpha chain), CD79B (B-cell antigen receptor complex-associated beta chain), CD84 (SLAMF5), CD96 (Tactile), CD100 (SEMA4D), CD103 (ITGAE), CD134 (OX40), CD137 (4-1BB), CD150 (SLAMF1), CD158A (KIR2DL1), CD158B1 (KIR2DL2), CD158B2 (KIR2DL3), CD158C (KIR3DP1), CD158D (KIRDL4), CD158F1 (KIR2DL5A), CD158F2 (KIR2DL5B), CD158K (KIR3DL2), CD160 (BY55), CD162 (SELPLG), CD226 (DNAM1), CD229 (SLAMF3), CD244 (SLAMF4), CD247 (CD3-zeta), CD258 (LIGHT), CD268 (BAFFR), CD270 (TNFSF14), CD272 (BTLA), CD276 (B7-H3), CD279 (PD-1), CD314 (NKG2D), CD319 (SLAMF7), CD335 (NK-p46), CD336 (NK-p44), CD337 (NK-p30), CD352 (SLAMF6), CD353 (SLAMF8), CD355 (CRTAM), CD357 (TNFRSF18), inducible T cell co-stimulator (ICOS), LFA-1 (CD11a/CD18), NKG2C, DAP-10, ICAM-1, NKp80 (KLRF1), IL-2R beta, IL-2R gamma, IL-7R alpha, LFA-1, SLAMF9, LAT, GADS (GrpL), SLP-76 (LCP2), PAG1/CBP, a CD83 ligand, Fc gamma receptor, MHC class 1 molecule, MHC class 2 molecule, a TNF receptor protein, an immunoglobulin protein, a cytokine receptor, an integrin, activating NK cell receptors, a Toll-like receptor, and combinations thereof.

Date Reçue/Date Received 2022-05-11

78. The method of claim 76 or 77, wherein the immune cells are selected from the group consisting of CD8+ T cells, CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells.

79. The method of any one of claims 76-78, wherein the immune cells are T cells.

80. The method of claim 78 or 79, wherein the T cells are expressed *in vitro*.

81. The method of any one of claims 78-80, wherein the T cells are from blood or extracted tissue of a subject, or from tissue grown *ex vivo*, or cell culture media.

82. The method of claim 81, wherein the T cells are an autologous T cell.

83. The method of claim 81, wherein the T cells are an allogeneic T cell.

84. A method of monitoring distribution *in vivo* of a population of cells expressing a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500), comprising:

    (a) providing the antigen binding molecule of any one of claims 1-23; and

    (b) performing a positron emission tomography (PET) scan.

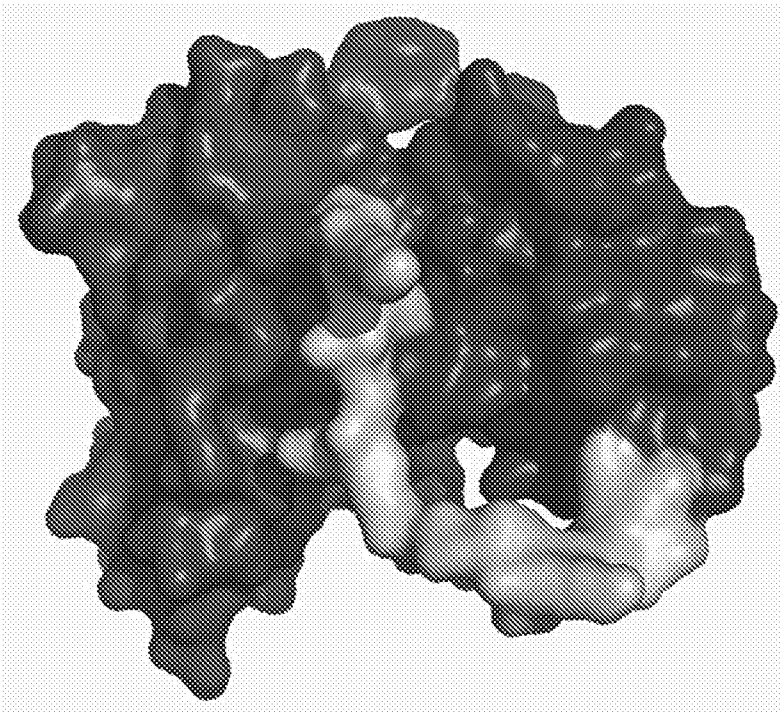
85. The antigen binding molecule of any one of claims 1-23, for use in stimulating or depleting a population of cells expressing a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500).

86. Use of the antigen binding molecule of any one of claims 1-23, for stimulating or depleting a population of cells expressing a chimeric antigen receptor (CAR) comprising an amino acid sequence selected from the group consisting of GSTSGSGKPGSGEGSTKG (SEQ ID NO: 1), GSGKPGSGEG (SEQ ID NO: 2), GKPGSGEG (SEQ ID NO: 3), SGKPGSGE (SEQ ID NO: 499) and KPGSG (SEQ ID NO: 500).

Date Reçue/Date Received 2022-05-11

Figure 1A

Figure 1B



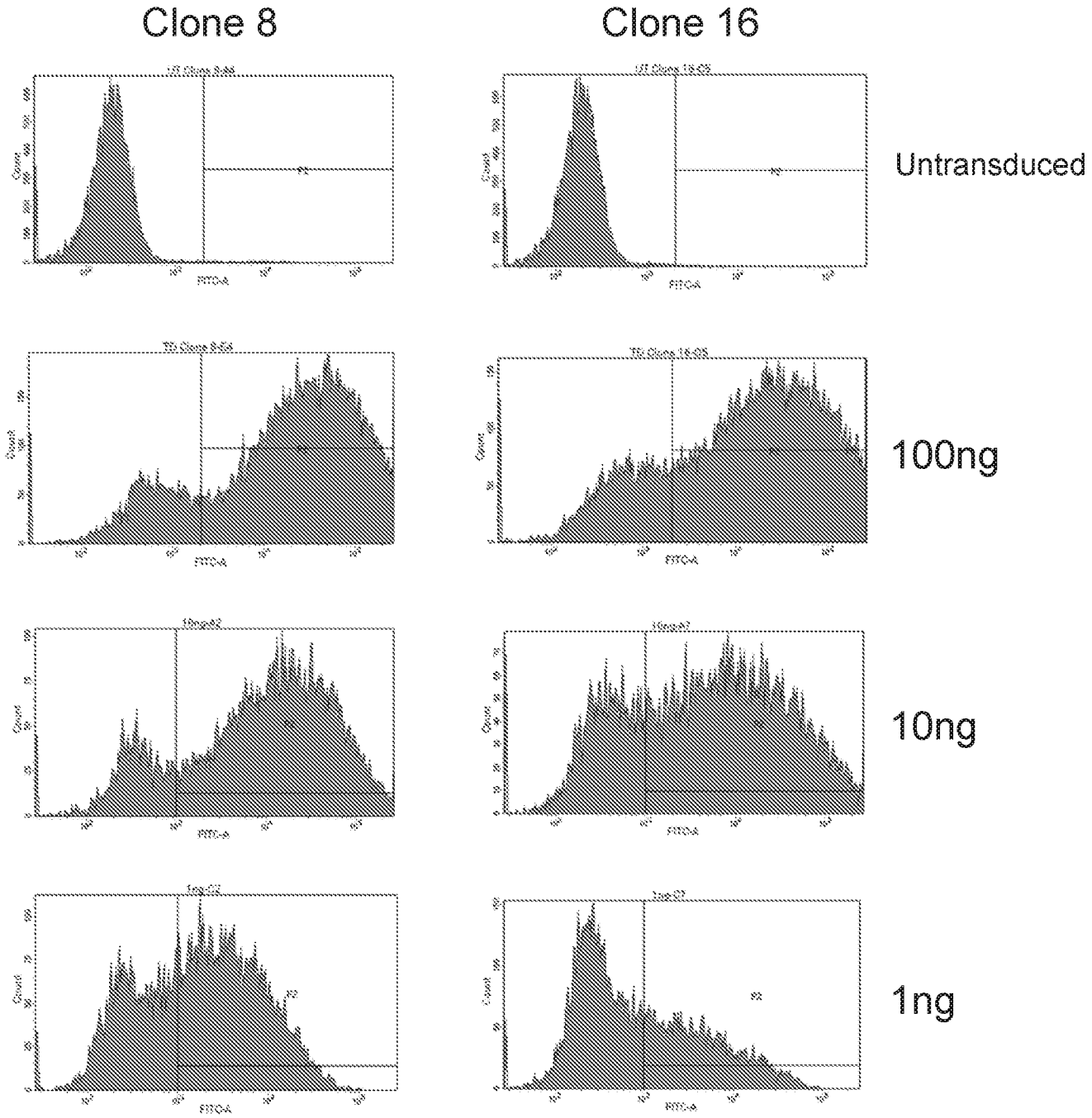
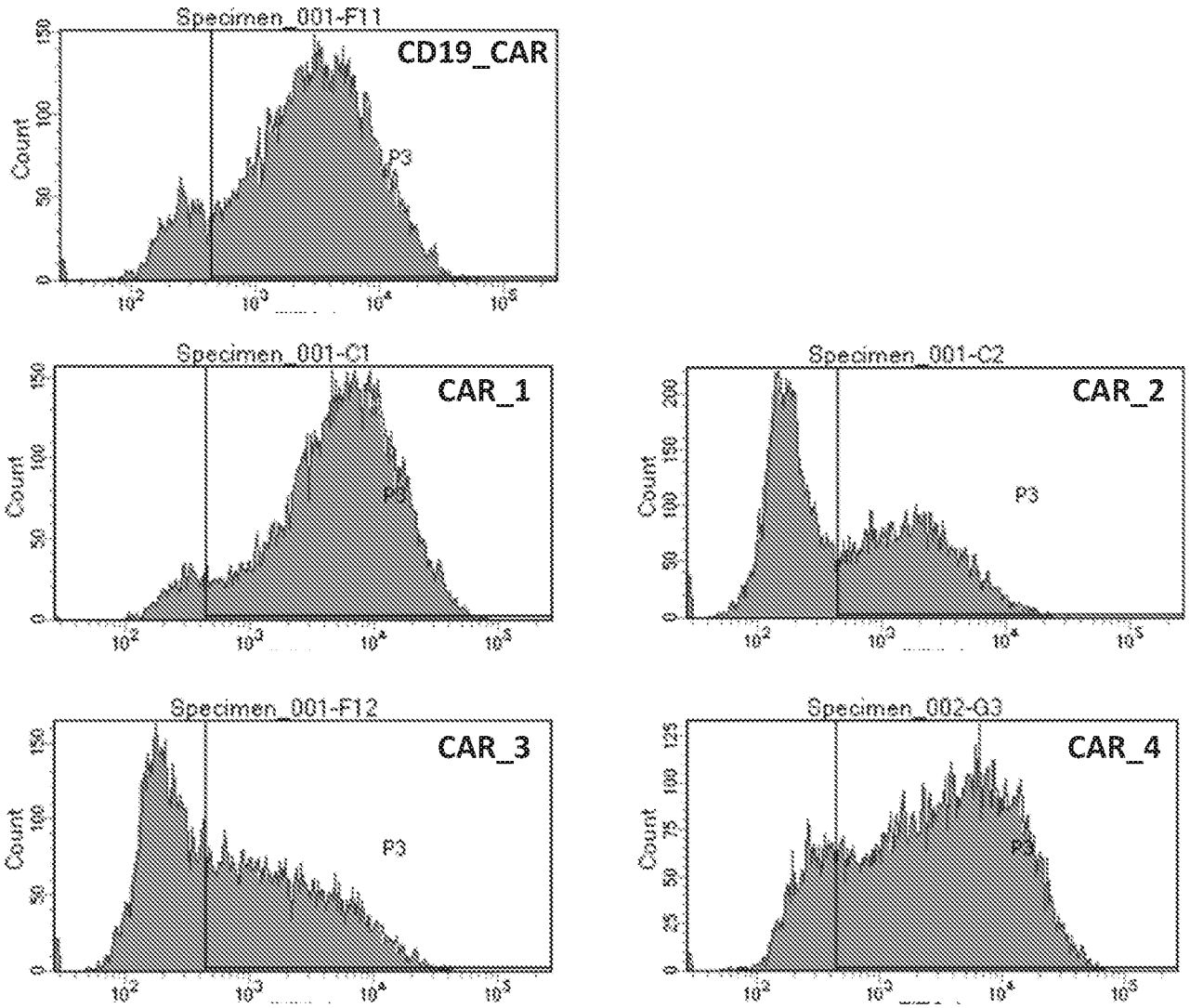


Figure 2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P3
Specimen_001-C1
CAR_1
Specimen_001-C2
CAR_2
Specimen_001-F12
CAR_3
Specimen_002-G3
CAR_4

Figure 3

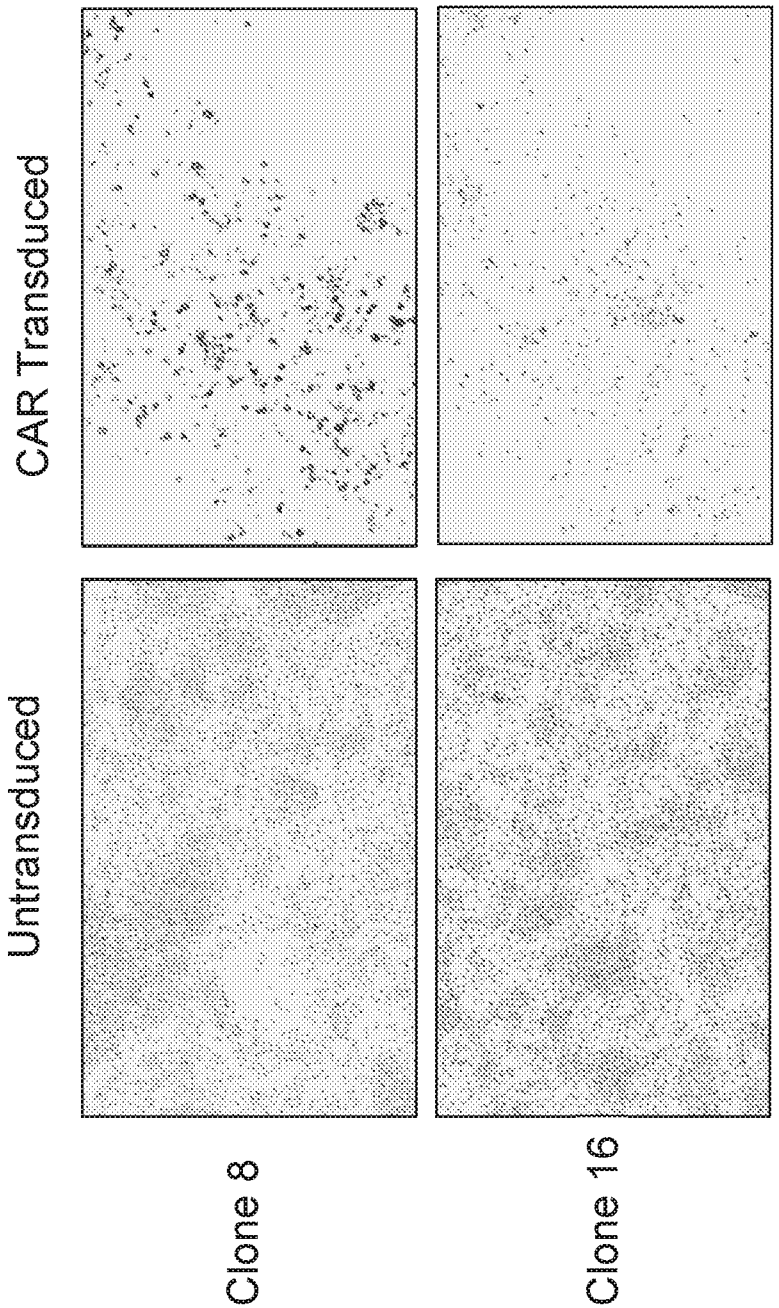
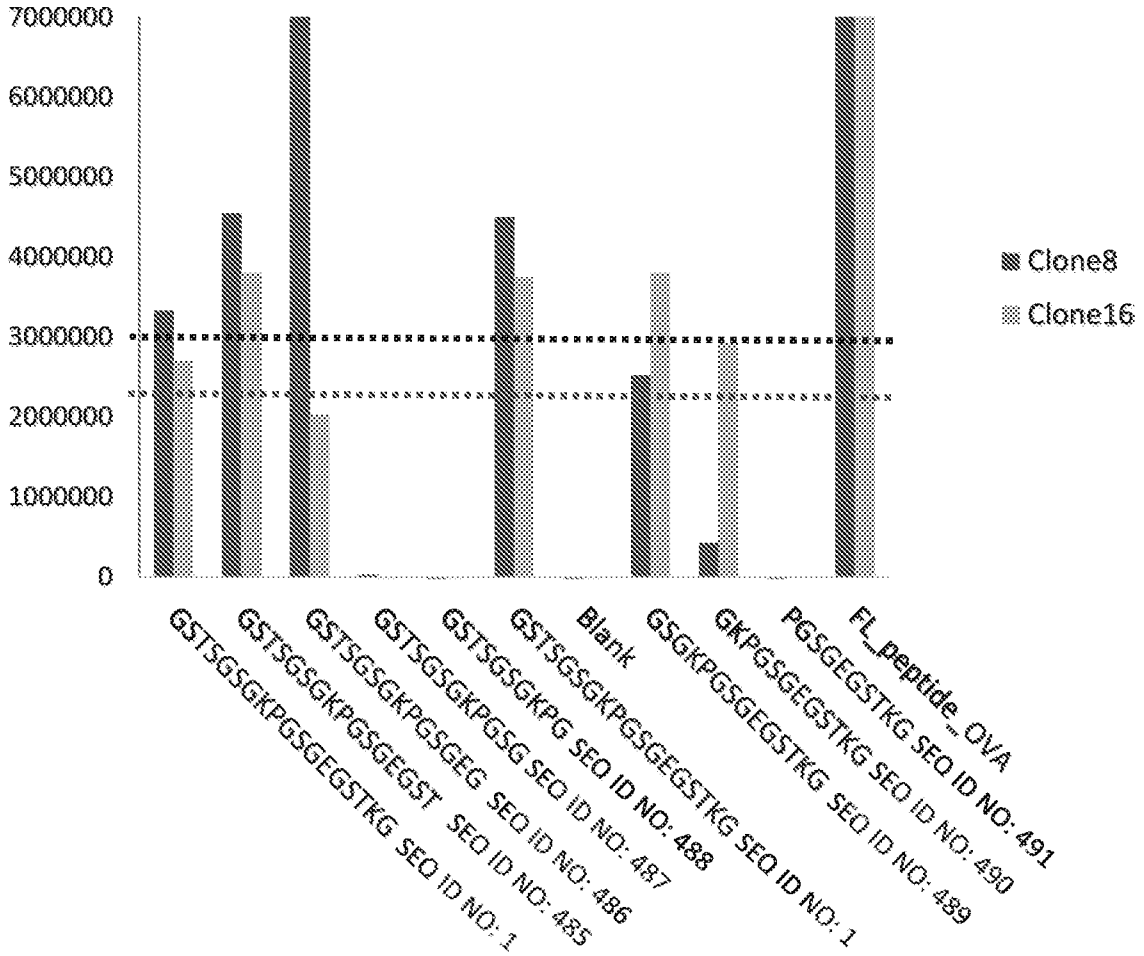


Figure 4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GKPGSGEGSTKG SEQ ID NO: 489
PGSGEGSTKG SEQ ID NO: 490
FL_peptide_OVA
SEQ ID NO: 491

Figure 5

CDR Table (Kabat)

Sequence	CDR1	SEQ ID NO	CDR2	SEQ ID NO	CDR3	SEQ ID NO
8_HC	NLAII	492	DIDGRGDIYCATWAK	8	DGDGSGWGDFNF	9
16_HC	SYHMG	493	IIVSSGSAYYATWAK	20	NQYSGYGFSF	21
8_LC	QASQSISTALA	13	RASTLAS	14	QQGWSTVNVDNV	15
16_LC	QSSHSVYYGDWLA	25	RASNLAS	26	LGGYDDDGETA	27

CDR Table (Chothia)

Sequence	CDR1	SEQ ID NO	CDR2	SEQ ID NO	CDR3	SEQ ID NO
8_HC	GFTISNL	7	DIDGRGDIYCATWAK	8	DGDGSGWGDFNF	9
16_HC	GSDISSY	19	IIVSSGSAYYATWAK	20	NQYSGYGFSF	21
8_LC	QASQSISTALA	13	RASTLAS	14	QQGWSTVNVDNV	15
16_LC	QSSHSVYYGDWLA	25	RASNLAS	26	LGGYDDDGETA	27

CDR Table (IMGT)

Sequence	CDR1	SEQ ID NO	CDR2	SEQ ID NO	CDR3	SEQ ID NO
8_HC	GFTISNLAII	494	DIDGRGDIYCATWAK	8	DGDGSGWGDFNF	9
16_HC	GSDISSYHMG	495	IIVSSGSAYYATWAK	20	NQYSGYGFSF	21
8_LC	QASQSISTALA	13	RASTLAS	14	QQGWSTVNVDNV	15
16_LC	QSSHSVYYGDWLA	25	RASNLAS	26	LGGYDDDGETA	27

Figure 6

Clone 8		SEQ ID NO
VH DNA	ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGTCCAGT GTCAGTCGGTGGAGGAGTCCGGGGGTCGCCTGGTCACGCCTGGGACACCCCTGA CACTCACCTGCACAGCCTCTGGATTCACCATCAGTAACCTTGCAATAATCTGGGTC CGCCAGGCTCCAGGGAAGGGGCTGGAATATATCGGAGACATTGATGGTCGTGGT GACATATACTGTGCGACCTGGGCGAAAGGCCGATTCACCATCTCCAAAACCTCGA CCACACTGGATCTGAGATTCACCAGCCCGACAACCGAGGACACGGCCACCTACTT CTGTGCCGTAGATGGTGATGGTAGTGGTTGGGGTGACTTTAACTTTTGGGGCCCA GGCACCCTGGTCACCGTCTCCTCA	4
VH AA (CDRs underlined)	METGLRWLLLVAVLKGVQCQSVEESGGRLVTPGTPLTLTCTASGFTISNLAIIWVRQA PGKGLEYIGDIDGRGDIYCATWAKGRFTISKTSTTLDLRFTSPTTEDTATYFCAVDGDG SGWGDFNFWGPGTLVTVSS	5
HC AA (CDRs underlined)	METGLRWLLLVAVLKGVQCQSVEESGGRLVTPGTPLTLTCTASGFTISNLAIIWVRQA PGKGLEYIGDIDGRGDIYCATWAKGRFTISKTSTTLDLRFTSPTTEDTATYFCAVDGDG SGWGDFNFWGPGTLVTVSSGQPKAPSVFPLAPCCGDTPSSTVTLGCLVKGYLPEPVT VTWNSGTLTNGVRTFPSVRQSSGLYSLSSVVSVTSSSQPVTCNVAHPATNTKVDKTV APSTCSKPTCPPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVVVDVSQDDPEVQFTW YINNEQVRTARPPLREQQFNSTIRVVSTLPIAHQDWLRGKEFKCKVHNKALPAPIEKTI SKARGQPLEPKVYTMGPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDNYKT TPAVLDSDGSYFLYSKLSVPTSEWQRGDVFTCSVMHEALHNHYTQKSISRSPGK	6
VL DNA	ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCTCCCAG GTGCCAGATGTGCCTATGATATGACCCAGACTCCAGCCTCTGTGGAGGTAGCTGT GGGAGGCACAGTCAGCATCAAGTGCCAGGCCAGTCAGAGCATTAGCACTGCATT AGCCTGGTATCAGCAGAAACCAGGACAGCCTCCCAAGCTCCTGATCTACAGGGC ATCCACTCTGGCATCTGGGGTCTCATCGCGGTTCAAAGGCAGTGGATCTGGGACA CAGTTCACTCTCACCATCAGCGGCGTGGAGTGTGACGATGCTGCCACTTACTACT GTCAACAGGGTTGGAGTACTGTGAATGTTGATAATGTTTTCGGCGGAGGGACCG AGGTGGTGGTCAGA	10
VL AA (CDRs underlined)	MDTRAPTQLLGLLLLWLPGARCAYDMTQTPASVEVAVGGTVSIKCQASQSISTALA WYQQKPGQPPKLLIYRASTLASGVSSRFKGSGSGTQFTLTISGVECDDAATYYCQQG WSTVNVDNVFGGGTEVVVR	11
LC AA (CDRs underlined)	MDTRAPTQLLGLLLLWLPGARCAYDMTQTPASVEVAVGGTVSIKCQASQSISTALA WYQQKPGQPPKLLIYRASTLASGVSSRFKGSGSGTQFTLTISGVECDDAATYYCQQG WSTVNVDNVFGGGTEVVVRDPVAPTVLIFPPAADQVATGTVTIVCVANKYFPDVTV TWEVDGTTQTTGIENSKTPQNSADCTYNLSSTLTLTSTQYNSHKEYTCKVTQGTTSVV QSFNRGDC	12

Figure 6 (Cont.)

Clone 16		SEQ ID NO
VH DNA	ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGTCCAGT GTCAGTCGCTGGAGGAGTCCGGGGGTCGCCTGGTCACGCCTGGGACACCCCTGA CACTCACCTGCACAGTCTCTGGATCCGACATCAGTAGCTACCACATGGGCTGGGT CCGCCAGGCTCCAGGGAAGGGGCTGGAATACATCGGAATCATTGTTAGTAGTGG TAGCGCATACTACGCGACCTGGGCAAAAGGCCGATTCACCATCTCCAGGACCTCG ACCACGGTGGATCTGAAAATCACCAGTCCGACAACCGAGGACTCGGCCACCTATT TCTGTGCCAGAAATCAATATAGTGGTTATGGCTTTAGCTTCTGGGGCCCAGGCAC CCTGGTCACCGTCTCCTCA	16
VH AA (CDRs underlined)	METGLRWLLLVAVLKGVQCQSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVR QAPGKGLEYIGIIVSSGSAYYATWAKGRFTISRTSTTVDLKITSPTTEDSATYFCARNQY SGYGFSFWGPGTLVTVSS	17
HC AA (CDRs underlined)	METGLRWLLLVAVLKGVQCQSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVR QAPGKGLEYIGIIVSSGSAYYATWAKGRFTISRTSTTVDLKITSPTTEDSATYFCARNQY SGYGFSFWGPGTLVTVSSGQPKAPSVFPLAPCCGDTPSSTVTLGCLVKGYLPEPVTVT WNSGTLTNGVRTFPSVRQSSGLYSLSSVVSVTSSSQPVTCNVAHPATNTKVDKTVAP STCSKPTCPPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVVVDVSQDDPEVQFTWYIN NEQVRTARPPLREQQFNSTIRVVSTLPIAHQDWLRGKEFKCKVHNKALPAPIEKTISK ARGQPLEPKVYTMGPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDNYKTTP AVLDSDGSYFLYSKLSVPTSEWQRGDVFTCSVMHEALHNHYTQKSISRSPGK	18
VL DNA	ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCTCCCAG GTGCCACATTTGCCGTCGTGCTGACCCAGACTCCATCCCCAGTGTCTACAGCTGTA GGAGGCACAGTCACCATCAATTGCCAGTCCAGTCACAGTGTTTATTATGGCGACT GGTTAGCCTGGTATCAGCAGAAACCAGGGCAGCCTCCTAAGCTCCTGATCTACAG GGCATCCAATCTGGCATCTGGTGTCCCATCGCGGTTCAAAGGCAGTGGATCTGG GACACAGTTCACTCTCACCATCAGCGGCGTGCAGTGTGACGATGCTGCCACTTAC TACTGTCTAGGCGGTTATGATGATGATGGTGAGACTGCTTTCGGCGGAGGGACC GAGGTGGTGGTCAAA	22
VL AA (CDRs underlined)	MDTRAPTQLLGLLLLWLPGATFAVVLTQTPSPVSTAVGGTVTINCQSSHSVYYGDWL AWYQQKPGQPPKLLIYRASNLASGVPSRFKGSGSGTQFTLTISGVQCDDAATYYCLG GYDDDGETAFGGGTEVVVK	23
LC AA (CDRs underlined)	MDTRAPTQLLGLLLLWLPGATFAVVLTQTPSPVSTAVGGTVTINCQSSHSVYYGDWL AWYQQKPGQPPKLLIYRASNLASGVPSRFKGSGSGTQFTLTISGVQCDDAATYYCLG GYDDDGETAFGGGTEVVVKDPVAPTVLIFPPAADQVATGTVTIVCVANKYFPDVTVT WEVDGTTQTTGIENSKTPQNSADCTYNLSSTLTLTSTQYNSHKEYTCKVTQGTTSVV QSFNRGDC	24

Figure 6 (Cont.)

Antibody Epitopes within Linker Sequence

Linker Sequence	Clone 8 Epitope	Clone 16 Epitope
GSTSGSGKPGSGEGSTKG	GSGKPGSGEG	GKPGSGEG
	SEQ ID NO: 2	SEQ ID NO: 3
	SGKPGSGE	KPGSG
SEQ ID NO: 1	SEQ ID NO: 499	SEQ ID NO: 500

Figure 7

8-4 VH humanized sequences -- IMGT-LigM DB (Abysis) clustered at 90% (18 sequences)

>8_4_HC_humanized_866
VQLQESGGGVVQPGRSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDIYCATWAKGRFTISRDNST
LYLQMNSLRADDTAVYYCARDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 28)
>8_4_HC_humanized_673
QSVVESGGVVVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGPEWVSDIDGRGDIYCATWAKGRFTISRDNSSL
YLQMNSLRTEDTAVYYCAKDGDGSGWGDFNFWGQGTMVTVSS (SEQ ID NO: 29)
>8_4_HC_humanized_631
QSVEESGGRLVTPGATVKISCKVSGFTISNLAIIWVQQAPGKGLEWMGDIDGRGDIYCATWAQGRVTITADSST
AYMELNGLRYADTAVYYCATDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 30)
>8_4_HC_humanized_1002
QSLEESGGGVVQPGKSLRLSCTASGFTISNLAIIWVRQAPGKGLESVADIDGRGDIYCATWATGRFAISRDNSKLY
LHMDNLRAEDTAVYYCARDGDGSGWGDFNFWGQGTTVIVSS (SEQ ID NO: 31)
>8_4_HC_humanized_771
QSLEQSGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISKSKNTL
YLQMNSLRAEDTAVYYCAVDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 32)
>8_4_HC_humanized_849
QSVEESGGDLVKPGGSLRLSCAASGFTISNLAIIWIRQAPGKGLEWLSDIDGRGDIYCATWAKGRFTISRDNASLN
LQMNSLRAEDTAVYYCAVDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 33)
>8_4_HC_humanized_706
VLLLESGGGLAQPGGTLRLSCSASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWARGRFIISRDNSTLY
LQMNSLRAEDTAVYYCAKDGDGSGWGDFNFWGQGILVTVSS (SEQ ID NO: 34)
>8_4_HC_humanized_703
VQLVESGGTLVQPGGSLRLSCSASGFTISNLAIIWVRQAPGKGLEYVSDIDGRGDIYCATWAKGRITISRDNSTLSL
QMSTLRTEDTAVYYCVRDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 35)
>8_4_HC_humanized_278
VQLVQSGGGLVKPGGSLRLSCEASGFTISNLAIIWIRQAPGKGLEWVGDIDGRGDIYCATWAKGRFTISRDDSTL
YLQVNSLKTEDSAVYYCTTDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 36)
>8_4_HC_humanized_800
QSVLESGPGLVKPSETLSLTCTVSGFTISNLAIIWIRQPPGKGLEWIGDIDGRGDIYCATWAKSRLTISTSKNQFSLR
LTSVTAADTAMYYCAVDGDGSGWGDFNFWGQGTLVSVSS (SEQ ID NO: 37)
>8_4_HC_humanized_809
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWLSDIDGRGDIYCATWARGRFAISNARNSL
YLQMNSLRDEDTAVYFCARDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 38)

Figure 8

>8_4_HC_humanized_273
VQLVQSGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQASGKGLEWIGDIDGRGDIYCATWAKGRFTVSRSQNS
VFLQMNSLETEDTAVYYCARDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 39)
>8_4_HC_humanized_716
QSVLESGGGWVQPGRSLRLSCSASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNNS
LYLQMNSLRPEDTALYYCAKDGDGSGWGDFNFWGQGVLVTVSS (SEQ ID NO: 40)
>8_4_HC_humanized_202
VQLQESGEGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEYVSDIDGRGDIYCATWAKGRFTISRDNSTLY
LQMGSLRAEDMAVYYCAVDGDGSGWGDFNFWGQGTMVTVSS (SEQ ID NO: 41)
>8_4_HC_humanized_21
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEFVSDIDGRGDIYCATWAKDRFTISRDNSTVY
LQMDSLRTEDTAMYFCARDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 42)
>8_4_HC_humanized_173
QSVEESGGRLVTPGGSLRLSCTATGFTISNLAIIWFRQAPGKGLEWVGDIDGRGDIYCATWAKGRFTISRDDNSL
YLQMNSLKTEDTAVYYCARDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 43)
>8_4_HC_humanized_23
QSVLESGGDLVQPGGSLRLSCEASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISKSKHTLF
LQMHSLRVEDTAVYYCAKDGDGSGWGDFNFWGQGTTVTVSS (SEQ ID NO: 44)
>8_4_HC_humanized_879
QSVEESGGGLVQPGGSLRLSCTASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDSSTLY
LQMNNLRVEDTALYYCAHDGDGSGWGDFNFWGRGTQVTVSS (SEQ ID NO: 45)

Figure 8 (cont.)

8-4 VL humanized sequences -- IMGT-LigM DB (Abysis) clustered at 90% (39 sequences)

>8_4_LC_humanized_866
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKRLIYRASTLASGVPSRFSGSGSGTEFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 46)
>8_4_LC_humanized_340
DIQMTQSPFSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYFCQQGWSTVNVDNVFGGGTKLEIK (SEQ ID NO: 47)
>8_4_LC_humanized_322
DIQLTQSPSFLSASVGDTVSITCQASQSISTALAWYQQKPGKAPKHLIYRASTLASGVPSRFSGGGSGTDFTLTISSL
QPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 48)
>8_4_LC_humanized_305
DIQLTQSPSSLSASVGDRVTITCQASQSISTALAWFQQKPGKAPKSLIYRASTLASGVPSRFSGSGSGTDFTLTISSL
QPEDSATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 49)
>8_4_LC_humanized_303
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTFTISS
LQPEDIATYYCQQGWSTVNVDNVFGPGTKVDIK (SEQ ID NO: 50)
>8_4_LC_humanized_291
DIQLTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKGPKLLIYRASTLASGVPSRFSGSGSGTDFSLTISSL
QPEDLATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 51)
>8_4_LC_humanized_217
DIVMTQSPDSLAVSLGERATINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASGVPDRFSGSGSGTDFTLTISS
LQAEDVAVYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 52)
>8_4_LC_humanized_197
AYDMTQTPATLSLSPGERATLSCQASQSISTALAWYQQKPGQAPRLLIYRASTLASGIPARFSGSGSGTDFTLTISS
LEPEDFAVYYCQQGWSTVNVDNVFGQGTEVVVR (SEQ ID NO: 53)
>8_4_LC_humanized_169
EIVLTQSPSFLSAFVGDRITITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTEFTLTISGLQ
PEDFASYYCQQGWSTVNVDNVFGGGTKLEIK (SEQ ID NO: 54)
>8_4_LC_humanized_17
DIQLTQSPSSLSAAVGDRVTIACQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLSISSL
QPGDFATYYCQQGWSTVNVDNVFGGGTKVQMK (SEQ ID NO: 55)
>8_4_LC_humanized_13
DIQMTQSPSSLSASVGDSVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTEFTLTING
LQPEDFATYYCQQGWSTVNVDNVFGGGTKLEIK (SEQ ID NO: 56)

Figure 8 (cont.)

>8_4_LC_humanized_791
AYELTQTPLSSPVTLGQPASISCQASQSISTALAWLHQRPGQPPRLLIYRASTLASGVPDRFSGSGAGTAFTLKISR
VEVEDVGIYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 57)
>8_4_LC_humanized_673
AYDMTQTPASVEVSPGERATLSCQASQSISTALAWYQHKPGQAPRLLIYRASTLASGIPARFSGSGSGTEFTLTISS
VQSDDFAVYYCQQGWSTVNVDNVFGPGTKVDIK (SEQ ID NO: 58)
>8_4_LC_humanized_678
AYELTQSPSSLSASVGDRVTITCQASQSISTALAWFQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISSL
LPTDFATYFCQQGWSTVNVDNVFGQGTQVEVK (SEQ ID NO: 59)
>8_4_LC_humanized_631
AYDMTQTPASVEVSVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFGGSGSGTDFTLTIS
SLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 60)
>8_4_LC_humanized_1002
AYELTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVSSRFSGSGSGTDFTLTISSL
QPEDFATYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ ID NO: 61)
>8_4_LC_humanized_775
AYELTQTPLSSPVTLGQPASISCQASQSISTALAWLQQRPGQPPRLLIYRASTLASGVPDRFSGSGARTDFTLNISR
VEAEDAGVYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ ID NO: 62)
>8_4_LC_humanized_771
AYELTQSPATLSLSPGERATLSCQASQSISTALAWYQQKPGQAPRLLIHRASTLASGIPARFSGSGSGTDFTLTISSL
EPEDFAVYYCQQGWSTVNVDNVFGGGTRVEIK (SEQ ID NO: 63)
>8_4_LC_humanized_188
DIQLTQSPSTLSASVGDRITITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPPRFSGSGSGTEFTLTISSLQ
PDDFATYYCQQGWSTVNVDNVFGQGTKVVVR (SEQ ID NO: 64)
>8_4_LC_humanized_717
ELVMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPNLLIYRASTLASGIPSRFSGSGSGTYFTLTING
LQPEDFATYYCQQGWSTVNVDNVFGGGTKVDIK (SEQ ID NO: 65)
>8_4_LC_humanized_1048
SYELTQTPPSVSVSPGQTARITCQASQSISTALAWYQQKPGQAPKVLIYRASTLASGIPERFSGSSSGTTVTLTISGV
QAEDEADYYCQQGWSTVNVDNVFGGGTKLTVL (SEQ ID NO: 66)
>8_4_LC_humanized_849
AYELTQSPLSLSVTPGQPASISCQASQSISTALAWYLQKPGQPPQLLIYRASTLASGVPDRFSGSGSGTDFTLKISR
VEAEDVGVYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 67)
>8_4_LC_humanized_1016
DIELTQSPSSLSASIGDRVSITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISSLQ
PEDFATFYCQQGWSTVNVDNVFGGGTRVEIK (SEQ ID NO: 68)

Figure 8 (cont.)

>8_4_LC_humanized_978
EIVLTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISNL
QPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 69)
>8_4_LC_humanized_706
DIQMTQYPSSLSASVGDRVTIACQASQSISTALAWYQQKPGKPPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISC
LQPEDVATYYCQQGWSTVNVDNVFGQGTRVEFK (SEQ ID NO: 70)
>8_4_LC_humanized_278
ELVLTQSPSSLSASVGDRVTITCQASQSISTALAWCQQKPGKSPTLLIYRASTLASGVPSRFSGSGSGTGFTLTISGL
QPEDFATYYCQQGWSTVNVDNVFGGGTKVEIR (SEQ ID NO: 71)
>8_4_LC_humanized_129
EIVMTQSPSSLSASVGDRVTITCQASQSISTALAWYQHKPGKAPRLLIYRASTLASGVPSRFSGSGSGTDFTLTISSL
QPDDFATYYCQQGWSTVNVDNVFGQGTKVEVK (SEQ ID NO: 72)
>8_4_LC_humanized_1133
AYDMTTQPPSVSVSPGQTASITCQASQSISTALAWYQQKPGQSPVLVIYRASTLASGIPERFSGSNSGNTATLTIS
GTQAMDEADYYCQQGWSTVNVDNVFGTGTEVVVR (SEQ ID NO: 73)
>8_4_LC_humanized_881
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPNLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGGGTKVQIK (SEQ ID NO: 74)
>8_4_LC_humanized_882
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGFGTDFTFTISS
LQPEDSATYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ ID NO: 75)
>8_4_LC_humanized_273
ELVMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGEAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISG
LQSEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 76)
>8_4_LC_humanized_716
ELVMTQSPSSLSASEGDRVTITCQASQSISTALAWYQQKPGRAPKLLIHRASTLASGVPSRFSGSGSGTEFTLTISG
LQSEDFATYYCQQGWSTVNVDNVFGGGTTVDVK (SEQ ID NO: 77)
>8_4_LC_humanized_677
AYDMTQSPSFLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTEFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGQGTRLEIK (SEQ ID NO: 78)
>8_4_LC_humanized_192
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQAEDFTTYYCQQGWSTVNVDNVFGQGTKVEFK (SEQ ID NO: 79)

Figure 8 (cont.)

>8_4_LC_humanized_802
AIRMTQSPSSFSASTGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISCL
QSEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 80)
>8_4_LC_humanized_54
AYGMTQSPDSLAVSLGERASINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASGVPDRFSGGGSGTDFTLTIS
SLQAEDVAVYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 81)
>8_4_LC_humanized_173
AIQMTQSPFSLSASVGDRVTITCQASQSISTALAWFQQKPGKAPKSLIYRASTLASGVSSKFSGSGSGTDFTLTISSL
QPEDFATYYCQQGWSTVNVDNVFGQGTRLVVR (SEQ ID NO: 82)
>8_4_LC_humanized_224
AYDMTQTPASVSLSPGERATLSCQASQSISTALAWYQQKPGQAPRLLIYRASTLASGIPDRFRGSGSATDFTLTIS
RLEPEDFAVYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 83)
>8_4_LC_humanized_657
AYDMTQTPASVEVSVGDRVSITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTIT
SLQPVDFATYYCQQGWSTVNVDNVFGPGTTVDAK (SEQ ID NO: 84)

Figure 8 (cont.)

8-4 VH humanized sequences -- IMGT-LigM DB (Abysis) clustered at 95% (47 sequences)

>cl|CABBABABA|10|117 >8_4_HC_humanized_866 >8_4_HC_humanized_340
>8_4_HC_humanized_336 >8_4_HC_humanized_332 >8_4_HC_humanized_322
VQLVESGGGVVQPGRSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDIYCATWAKGRFTISRDNSTL
YLQMNSLRAEDTAVYYCAVDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 85)
>cl|KABBABABA|13|117 >8_4_HC_humanized_315 >8_4_HC_humanized_314
>8_4_HC_humanized_305 >8_4_HC_humanized_303 >8_4_HC_humanized_296
VQLVQSGGGVVQPGRSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDIYCATWAKGRFTISRDNST
LYLQMNSLRAEDTAVYYCAVDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 86)
>cl|TABBABABA|8|117 >8_4_HC_humanized_217 >8_4_HC_humanized_197
>8_4_HC_humanized_678 >8_4_HC_humanized_978 >8_4_HC_humanized_635
VQLVESGGGLVKPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNASL
YLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 87)
>cl|WABBABABA|7|117 >8_4_HC_humanized_169 >8_4_HC_humanized_122
>8_4_HC_humanized_676 >8_4_HC_humanized_893 >8_4_HC_humanized_57
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNSTL
YLQMNSLRAEDTAVYYCAKDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 88)
>cl|ZABBABABA|1|117 >8_4_HC_humanized_17
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGRGLVWVSDIDGRGDIYCATWAKGRFTISRDNAT
LYLQMNNLRAEDTAVYYCARDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 89)
>cl|CEBBABABA|1|117 >8_4_HC_humanized_791
QSVLESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWARGRFTISRDNSTL
YLQMNSLRAEDTAIYYCAKDGDGSGWGDFNFWGRGTHVTVSS (SEQ ID NO: 90)
>cl|DEBBABABA|1|117 >8_4_HC_humanized_673
QSVVESGGVVVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGPEWVSDIDGRGDIYCATWAKGRFTISRDNSSL
YLQMNSLRTEDTAVYYCAKDGDGSGWGDFNFWGQGTMVTVSS (SEQ ID NO: 91)
>cl|GEBBABABA|1|117 >8_4_HC_humanized_631
QSVEESGGRLVTPGATVKISCKVSGFTISNLAIIWVQQAPGKGLEWMGDIDGRGDIYCATWAQGRVTITADSST
AYMELNGLRYADTAVYYCATDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 92)
>cl|HEBBABABA|1|117 >8_4_HC_humanized_1002
QSLEESGGGVVQPGKSLRLSCTASGFTISNLAIIWVRQAPGKGLESVADIDGRGDIYCATWATGRFAISRDNSKLY
LHMDNLRAEDTAVYYCARDGDGSGWGDFNFWGQGTTVIVSS (SEQ ID NO: 93)
>cl|KEBBABABA|1|117 >8_4_HC_humanized_775
QSLEESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQASGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNSTL
YLQMNSLRAEDTAVYSCAVDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 94)

Figure 8 (cont.)

>cl|LEBBABABA|2|117 >8_4_HC_humanized_771 >8_4_HC_humanized_772
QSLEQSGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISKSKNTL
YLQMNSLRAEDTAVYYCAVDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 95)
>cl|NEBBABABA|1|117 >8_4_HC_humanized_188
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWASDIDGRGDIYCATWAKGRFTISRDSSTL
YLQMNSLRTDDTAVYYCAADGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 96)
>cl|PEBBABABA|9|117 >8_4_HC_humanized_186 >8_4_HC_humanized_292
>8_4_HC_humanized_283 >8_4_HC_humanized_204 >8_4_HC_humanized_201
VQLVESGGGVVQPGRSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDIYCATWAKGRFTISRDNSTL
YLQMNSLRAEDTAVYYCAKDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 97)
>cl|QEBBABABA|1|117 >8_4_HC_humanized_717
QSVLESGGGWVQPGRSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDIYCATWAKGRFTISRDNAS
LYLEMKSLRAEDTAIYYCARDGDGSGWGDFNFWGQGVLVTVSS (SEQ ID NO: 98)
>cl|REBBABABA|2|117 >8_4_HC_humanized_1048 >8_4_HC_humanized_675
QSVEESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNASL
YLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 99)
>cl|SEBBABABA|1|117 >8_4_HC_humanized_849
QSVEESGGDLVKPGGSLRLSCAASGFTISNLAIIWIRQAPGKGLEWLSDIDGRGDIYCATWAKGRFTISRDNASLN
LQMNSLRAEDTAVYYCAVDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 100)
>cl|TEBBABABA|3|117 >8_4_HC_humanized_1016 >8_4_HC_humanized_295
>8_4_HC_humanized_319
VQLVQSGGGLVKPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDIYCATWAKGRFTISRDNSTL
YLQMNSLRAEDTAVYYCAVDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 101)
>cl|XEBBABABA|2|117 >8_4_HC_humanized_868 >8_4_HC_humanized_55
QQLQESGGGLVQPGGSLRLSCSASGFTISNLAIIWVRQAPGKGLEYVSDIDGRGDIYCATWAKGRFTISRDNSTLY
LQMSSLRAEDTAVYYCVKDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 102)
>cl|YEBBABABA|1|117 >8_4_HC_humanized_862
VRLVESGGGVVQPGRSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDIYCATWAKGRFTISRDNSTL
HLQMNSLRAEDTAVYYCAKDGDGSGWGDFNFWGKGTTVTVSS (SEQ ID NO: 103)
>cl|ZEBBABABA|1|117 >8_4_HC_humanized_715
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRSKNTL
YLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGQGTTVTVSS (SEQ ID NO: 104)
>cl|BIBBABABA|1|117 >8_4_HC_humanized_706
VLLLESGGGLAQPGGTLRLSCSASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWARGRFIISRDNSTLY
LQMNSLRAEDTAVYYCAKDGDGSGWGDFNFWGQGILVTVSS (SEQ ID NO: 105)

Figure 8 (cont.)

>cl|CIBBABABA|1|117 >8_4_HC_humanized_703
VQLVESGGTLVQPGGSLRLSCSASGFTISNLAIIWVRQAPGKGLEYVSDIDGRGDIYCATWAKGRITISRDNSTLSL
QMSTLRTEDTAVYYCVRDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 106)
>cl|FIBBABABA|1|117 >8_4_HC_humanized_341
VQLVQSGGSLVQPGRSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDIYCATWAKGRFTTSRDNST
LYLQMNSLRADDTAVYFCAVDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 107)
>cl|KIBBABABA|1|117 >8_4_HC_humanized_301
VQLVESGGDLVQPGESLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNSTL
YLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 108)
>cl|QIBBABABA|1|117 >8_4_HC_humanized_278
VQLVQSGGGLVKPGGSLRLSCEASGFTISNLAIIWIRQAPGKGLEWVGDIDGRGDIYCATWAKGRFTISRDDSTL
YLQVNSLKTEDSAVYYCTTDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 109)
>cl|TIBBABABA|1|117 >8_4_HC_humanized_129
MQLVESGGGLVQPGRSLRLSCVTSGFTISNLAIIWVRQVPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNTSL
YLQMNSLRPEDTAVYYCAKDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 110)
>cl|XIBBABABA|1|117 >8_4_HC_humanized_800
QSVLESGPGLVKPSETLSLTCTVSGFTISNLAIIWIRQPPGKGLEWIGDIDGRGDIYCATWAKSRLTISTSKNQFSLR
LTSVTAADTAMYYCAVDGDGSGWGDFNFWGQGTLVSVSS (SEQ ID NO: 111)
>cl|YIBBABABA|7|117 >8_4_HC_humanized_1133 >8_4_HC_humanized_881
>8_4_HC_humanized_677 >8_4_HC_humanized_192 >8_4_HC_humanized_65
QSVEESGGGVVQPGRSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDIYCATWAKGRFTISRDNSTL
YLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGQGTTVTVSS (SEQ ID NO: 112)
>cl|FOBBABABA|1|117 >8_4_HC_humanized_882
QSVEESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQPPGKGLEWVGDIDGRGDIYCATWAKGRFTISRSKSTV
YLQMNSLKTEDTAVYYCTADGDGSGWGDFNFWGQGMLVTVSS (SEQ ID NO: 113)
>cl|GOBBABABA|1|117 >8_4_HC_humanized_660
QSVEESGGGLIQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLECVSDIDGRGDIYCATWAKGRFTISRDNSTLYL
QMTSLRAEDTAVYYCALDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 114)
>cl|HOBBABABA|2|117 >8_4_HC_humanized_1051 >8_4_HC_humanized_1050
VQLVESGGGLVKPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVGDIDGRGDIYCATWAKGRFTISRSKNTL
YLQMNSLKTEDTAVYYCTVDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 115)
>cl|MOBBABABA|1|117 >8_4_HC_humanized_809
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWLSDIDGRGDIYCATWARGRFAISNARNSL
YLQMNSLRDEDTAVYFCARDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 116)

Figure 8 (cont.)

>cl|VOBBABABA|1|117 >8_4_HC_humanized_273
VQLVQSGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQASGKGLEWIGDIDGRGDIYCATWAKGRFTVSRSQNS
VFLQMNSLETEDTAVYYCARDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 117)
>cl|WOBBABABA|1|117 >8_4_HC_humanized_716
QSVLESGGGWVQPGRSLRLSCSASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNNS
LYLQMNSLRPEDTALYYCAKDGDGSGWGDFNFWGQGVLVTVSS (SEQ ID NO: 118)
>cl|ZOBBABABA|1|117 >8_4_HC_humanized_202
VQLQESGEGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEYVSDIDGRGDIYCATWAKGRFTISRDNSTLY
LQMGSLRAEDMAVYYCAVDGDGSGWGDFNFWGQGTMVTVSS (SEQ ID NO: 119)
>cl|GUBBABABA|1|117 >8_4_HC_humanized_54
VQLVESGGGLVQPGGSLRLSCATSGFTISNLAIIWVRQPPGKGLEWVSDIDGRGDIYCATWAKGRFTISRENATL
YLQMNSLRAEDTAVYYCAVDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 120)
>cl|HUBBABABA|1|117 >8_4_HC_humanized_21
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEFVSDIDGRGDIYCATWAKDRFTISRDNSTVY
LQMDSLRTEDTAMYFCARDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 121)
>cl|KUBBABABA|1|117 >8_4_HC_humanized_788
QSVLESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNSTL
FLQISSLRAEDTAVYYCAKDGDGSGWGDFNFWGPGTLVTVSS (SEQ ID NO: 122)
>cl|MUBBABABA|1|117 >8_4_HC_humanized_762
VKLLESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVADIDGRGDIYCATWAKGRFTISRDNSTL
YLQMNSLGAEDTAVYYCARDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 123)
>cl|PUBBABABA|1|117 >8_4_HC_humanized_173
QSVEESGGRLVTPGGSLRLSCTATGFTISNLAIIWFRQAPGKGLEWVGDIDGRGDIYCATWAKGRFTISRDDNSL
YLQMNSLKTEDTAVYYCARDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 124)
>cl|RUBBABABA|1|117 >8_4_HC_humanized_224
QSVEESGGGLVKPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVGDIDGRGDIYCATWAKGRFTISRSKNTL
YLQMNSLKTEDTAVYYCATDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 125)
>cl|VUBBABABA|1|117 >8_4_HC_humanized_672
QSVVESGGGLIQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNSTL
YLQMNSLRAEDTAVYYCALDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 126)
>cl|XUBBABABA|1|117 >8_4_HC_humanized_267
QSVEQSGGGLVQPGESLRLSCAGSGFTISNLAIIWVRQAPGKGLEWVADIDGRGDIYCATWAKGRFTISRDNAS
LFLQMNSLRVEDTAVYYCARDGDGSGWGDFNFWGQGTLVTVSS (SEQ ID NO: 127)

Figure 8 (cont.)

>cl|YUBBABABA|1|117 >8_4_HC_humanized_23
QSVLESGGDLVQPGGSLRLSCEASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISKSKHTLF
LQMHSLRVEDTAVYYCAKDGDGSGWGDFNFWGQGTTVTVSS (SEQ ID NO: 128)
>cl|ZUBBABABA|1|117 >8_4_HC_humanized_657
QSVEESGGRLVTPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNSSLY
LQMNSLRTEDSALYYCAIDGDGSGWGDFNFWGQGSLVTVSS (SEQ ID NO: 129)
>cl|BACBABABA|1|117 >8_4_HC_humanized_879
QSVEESGGGLVQPGGSLRLSCTASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDSSTLY
LQMNNLRVEDTALYYCAHDGDGSGWGDFNFWGRGTQVTVSS (SEQ ID NO: 130)

Figure 8 (cont.)

8-4 LC humanized sequences -- IMGT-LigM DB (Abysis) clustered at 95% (99 sequences)

>cl|CACBABABA|1|110 >8_4_LC_humanized_866
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKRLIYRASTLASGVPSRFSGSGSGTEFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 131)
>cl|DACBABABA|1|110 >8_4_LC_humanized_340
DIQMTQSPFSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYFCQQGWSTVNVDNVFGGGTKLEIK (SEQ ID NO: 132)
>cl|FACBABABA|1|110 >8_4_LC_humanized_336
DIQLTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISSL
QPEDFATYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ ID NO: 133)
>cl|GACBABABA|1|110 >8_4_LC_humanized_332
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLVYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 134)
>cl|HACBABABA|1|110 >8_4_LC_humanized_322
DIQLTQSPSFLSASVGDTVSITCQASQSISTALAWYQQKPGKAPKHLIYRASTLASGVPSRFSGGGSGTDFTLTISSL
QPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 135)
>cl|KACBABABA|1|110 >8_4_LC_humanized_315
DIQLTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTGFTLTISSL
QPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 136)
>cl|LACBABABA|1|110 >8_4_LC_humanized_314
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPNLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 137)
>cl|MACBABABA|1|110 >8_4_LC_humanized_305
DIQLTQSPSSLSASVGDRVTITCQASQSISTALAWFQQKPGKAPKSLIYRASTLASGVPSRFSGSGSGTDFTLTISSL
QPEDSATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 138)
>cl|NACBABABA|1|110 >8_4_LC_humanized_303
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTFTISS
LQPEDIATYYCQQGWSTVNVDNVFGPGTKVDIK (SEQ ID NO: 139)
>cl|PACBABABA|1|110 >8_4_LC_humanized_296
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSTFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 140)
>cl|QACBABABA|1|110 >8_4_LC_humanized_294
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 141)

Figure 8 (cont.)

>cl|RACBABABA|1|110 >8_4_LC_humanized_291
DIQLTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKGPKLLIYRASTLASGVPSRFSGSGSGTDFSLTISSL
QPEDLATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 142)
>cl|SACBABABA|1|110 >8_4_LC_humanized_284
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKSLIYRASTLASGVPSKFSGSGSGTEFTLTISSL
QPDDFATYYCQQGWSTVNVDNVFGQGTRLEIK (SEQ ID NO: 143)
>cl|TACBABABA|1|110 >8_4_LC_humanized_217
DIVMTQSPDSLAVSLGERATINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASGVPDRFSGSGSGTDFTLTISS
LQAEDVAVYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 144)
>cl|VACBABABA|1|110 >8_4_LC_humanized_197
AYDMTQTPATLSLSPGERATLSCQASQSISTALAWYQQKPGQAPRLLIYRASTLASGIPARFSGSGSGTDFTLTISS
LEPEDFAVYYCQQGWSTVNVDNVFGQGTEVVVR (SEQ ID NO: 145)
>cl|WACBABABA|1|110 >8_4_LC_humanized_169
EIVLTQSPSFLSAFVGDRITITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTEFTLTISGLQ
PEDFASYYCQQGWSTVNVDNVFGGGTKLEIK (SEQ ID NO: 146)
>cl|XACBABABA|1|110 >8_4_LC_humanized_122
DVVMTQSPASLSASVGDRVTIICQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSRTDFTFTISS
LQPEDIATYYCQQGWSTVNVDNVFGPGTKVDIK (SEQ ID NO: 147)
>cl|YACBABABA|1|110 >8_4_LC_humanized_44
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKRLIYRASTLASGVPSRFSGSGSGTEFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 148)
>cl|ZACBABABA|1|110 >8_4_LC_humanized_17
DIQLTQSPSSLSAAVGDRVTIACQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLSISSL
QPGDFATYYCQQGWSTVNVDNVFGGGTKVQMK (SEQ ID NO: 149)
>cl|BECBABABA|1|110 >8_4_LC_humanized_13
DIQMTQSPSSLSASVGDSVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTEFTLTING
LQPEDFATYYCQQGWSTVNVDNVFGGGTKLEIK (SEQ ID NO: 150)
>cl|CECBABABA|1|110 >8_4_LC_humanized_791
AYELTQTPLSSPVTLGQPASISCQASQSISTALAWLHQRPGQPPRLLIYRASTLASGVPDRFSGSGAGTAFTLKISR
VEVEDVGIYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 151)
>cl|DECBABABA|1|110 >8_4_LC_humanized_673
AYDMTQTPASVEVSPGERATLSCQASQSISTALAWYQHKPGQAPRLLIYRASTLASGIPARFSGSGSGTEFTLTISS
VQSDDFAVYYCQQGWSTVNVDNVFGPGTKVDIK (SEQ ID NO: 152)

Figure 8 (cont.)

>cl|FECBABABA|1|110 >8_4_LC_humanized_678
AYELTQSPSSLSASVGDRVTITCQASQSISTALAWFQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISSL
LPTDFATYFCQQGWSTVNVDNVFGQGTQVEVK (SEQ ID NO: 153)
>cl|GECBABABA|1|110 >8_4_LC_humanized_631
AYDMTQTPASVEVSVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFGGSGSGTDFTLTIS
SLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 154)
>cl|HECBABABA|1|110 >8_4_LC_humanized_1002
AYELTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVSSRFSGSGSGTDFTLTISSL
QPEDFATYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ ID NO: 155)
>cl|KECBABABA|1|110 >8_4_LC_humanized_775
AYELTQTPLSSPVTLGQPASISCQASQSISTALAWLQQRPGQPPRLLIYRASTLASGVPDRFSGSGARTDFTLNISR
VEAEDAGVYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ ID NO: 156)
>cl|LECBABABA|2|110 >8_4_LC_humanized_771 >8_4_LC_humanized_772
AYELTQSPATLSLSPGERATLSCQASQSISTALAWYQQKPGQAPRLLIHRASTLASGIPARFSGSGSGTDFTLTISSL
EPEDFAVYYCQQGWSTVNVDNVFGGGTRVEIK (SEQ ID NO: 157)
>cl|MECBABABA|1|110 >8_4_LC_humanized_676
AYDMTQSPATLSLSPGERATLSCQASQSISTALAWYQQKPGQAPRLLIYRASTLASGIPARFSGSGSGTDFTLTISS
LEPEDFAVYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 158)
>cl|NECBABABA|1|110 >8_4_LC_humanized_188
DIQLTQSPSTLSASVGDRITITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPPRFSGSGSGTEFTLTISSLQ
PDDFATYYCQQGWSTVNVDNVFGQGTKVVVR (SEQ ID NO: 159)
>cl|PECBABABA|1|110 >8_4_LC_humanized_186
DIQLTQSPSTLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTEFTLTISSL
QPDDFATYYCQQGWSTVNVDNVFGQGTKVVVR (SEQ ID NO: 160)
>cl|QECBABABA|1|110 >8_4_LC_humanized_717
ELVMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPNLLIYRASTLASGIPSRFSGSGSGTYFTLTING
LQPEDFATYYCQQGWSTVNVDNVFGGGTKVDIK (SEQ ID NO: 161)
>cl|RECBABABA|1|110 >8_4_LC_humanized_1048
SYELTQTPPSVSVSPGQTARITCQASQSISTALAWYQQKPGQAPKVLIYRASTLASGIPERFSGSSSGTTVTLTISGV
QAEDEADYYCQQGWSTVNVDNVFGGGTKLTVL (SEQ ID NO: 162)
>cl|SECBABABA|1|110 >8_4_LC_humanized_849
AYELTQSPLSLSVTPGQPASISCQASQSISTALAWYLQKPGQPPQLLIYRASTLASGVPDRFSGSGSGTDFTLKISR
VEAEDVGVYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 163)

Figure 8 (cont.)

>cl|TECBABABA|1|110 >8_4_LC_humanized_1016
DIELTQSPSSLSASIGDRVSITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISSLQ
PEDFATFYCQQGWSTVNVDNVFGGGTRVEIK (SEQ ID NO: 164)
>cl|VECBABABA|1|110 >8_4_LC_humanized_978
EIVLTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISNL
QPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 165)
>cl|WECBABABA|1|110 >8_4_LC_humanized_893
DIEMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKRLIQRASTLASGVPSRFSGSGSGTEFTLTISS
LQPEDFATYHCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 166)
>cl|XECBABABA|1|110 >8_4_LC_humanized_868
DIVMTQSPDSLAVSLGERATINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASGVPDRFSGSGSGTDFTLTISS
LQAEDVAVYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ ID NO: 167)
>cl|YECBABABA|1|110 >8_4_LC_humanized_862
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 168)
>cl|ZECBABABA|1|110 >8_4_LC_humanized_715
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKFLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 169)
>cl|BICBABABA|1|110 >8_4_LC_humanized_706
DIQMTQYPSSLSASVGDRVTIACQASQSISTALAWYQQKPGKPPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISC
LQPEDVATYYCQQGWSTVNVDNVFGQGTRVEFK (SEQ ID NO: 170)
>cl|CICBABABA|1|110 >8_4_LC_humanized_703
DIVMTQSPDSLAVSLGERATINCQASQSISTALAWYQQKAGQPPKLLIYRASTLASGVPDRFSGSGSGTDFTLTIS
SLQAEDVAVYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 171)
>cl|DICBABABA|1|110 >8_4_LC_humanized_635
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKVPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDVATYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ ID NO: 172)
>cl|FICBABABA|1|110 >8_4_LC_humanized_341
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGGGTKLEIK (SEQ ID NO: 173)
>cl|GICBABABA|1|110 >8_4_LC_humanized_328
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGRGTKVEIK (SEQ ID NO: 174)

Figure 8 (cont.)

>cl|HICBABABA|1|110 >8_4_LC_humanized_324
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGNAPKSLIYRASTLASGVPSKFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 175)
>cl|KICBABABA|1|110 >8_4_LC_humanized_301
DIQMTQSPDSLAVSLGERATINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASGVPDRFSGSGSGTDFTLTIS
SLQAEDVAVYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ ID NO: 176)
>cl|LICBABABA|1|110 >8_4_LC_humanized_295
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGQGTRLEIK (SEQ ID NO: 177)
>cl|MICBABABA|1|110 >8_4_LC_humanized_292
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPNLLIYRASTLASGVPSRFSGSVSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 178)
>cl|NICBABABA|1|110 >8_4_LC_humanized_283
DIQLTQSPSSVSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISSL
QPEDFATYYCQQGWSTVNVDNVFGQGTRLEIK (SEQ ID NO: 179)
>cl|PICBABABA|1|110 >8_4_LC_humanized_282
DIQMTQSPSSVSASVGDRVTITCQASQSISTALAWYQQKLGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 180)
>cl|QICBABABA|1|110 >8_4_LC_humanized_278
ELVLTQSPSSLSASVGDRVTITCQASQSISTALAWCQQKPGKSPTLLIYRASTLASGVPSRFSGSGSGTGFTLTISGL
QPEDFATYYCQQGWSTVNVDNVFGGGTKVEIR (SEQ ID NO: 181)
>cl|RICBABABA|1|110 >8_4_LC_humanized_204
DIQLTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISSL
QPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 182)
>cl|SICBABABA|1|110 >8_4_LC_humanized_201
DIRVTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTFTISSL
QPEDIATYYCQQGWSTVNVDNVFGGGTKVDIK (SEQ ID NO: 183)
>cl|TICBABABA|1|110 >8_4_LC_humanized_129
EIVMTQSPSSLSASVGDRVTITCQASQSISTALAWYQHKPGKAPRLLIYRASTLASGVPSRFSGSGSGTDFTLTISSL
QPDDFATYYCQQGWSTVNVDNVFGQGTKVEVK (SEQ ID NO: 184)
>cl|VICBABABA|1|110 >8_4_LC_humanized_108
DVVMTQSPSSVSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTIT
SLQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 185)

Figure 8 (cont.)

>cl|WICBABABA|1|110 >8_4_LC_humanized_57
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKRLIYRASTLASGVPSRFSGSGSGTEFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGQGTRLEIK (SEQ ID NO: 186)
>cl|XICBABABA|1|110 >8_4_LC_humanized_800
AYELTQTPPSLSVTPGQPASISCQASQSISTALAWYLQKPGQPPQLLIYRASTLASGVPDRFSGSGSGTDFTLKISR
VEAEDVGVYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 187)
>cl|YICBABABA|1|110 >8_4_LC_humanized_1133
AYDMTTQPPSVSVSPGQTASITCQASQSISTALAWYQQKPGQSPVLVIYRASTLASGIPERFSGSNSGNTATLTIS
GTQAMDEADYYCQQGWSTVNVDNVFGTGTEVVVR (SEQ ID NO: 188)
>cl|ZICBABABA|1|110 >8_4_LC_humanized_621
AYELTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISSL
QPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 189)
>cl|COCBABABA|1|110 >8_4_LC_humanized_881
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPNLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGGGTKVQIK (SEQ ID NO: 190)
>cl|DOCBABABA|1|110 >8_4_LC_humanized_55
AYDMTQTPASVEVSPGERATLSCQASQSISTALAWYQQKPGQAPRLLIYRASTLASGIPARFSGSGSGTEFTLTISS
LQSEDFAVYYCQQGWSTVNVDNVFGQGTEVVVR (SEQ ID NO: 191)
>cl|FOCBABABA|1|110 >8_4_LC_humanized_882
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGFGTDFTFTISS
LQPEDSATYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ ID NO: 192)
>cl|GOCBABABA|1|110 >8_4_LC_humanized_660
AYVMTQSPATLSLSPGERATLSCQASQSISTALAWYQQRPGQAPRLLIYRASTLASGIPARFSGSGSGTDFTLTISS
LEPEDFAVYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 193)
>cl|HOCBABABA|1|110 >8_4_LC_humanized_1051
SYELTQTPPSVSVSPGQTARITCQASQSISTALAWYQQKPGQAPVLVIYRASTLASGIPERFSGSSSGTTVTLTISGV
QAEDEADYYCQQGWSTVNVDNVFGTGTKVTVL (SEQ ID NO: 194)
>cl|KOCBABABA|1|110 >8_4_LC_humanized_1050
SYELTQTPPSVSVSPGQTARITCQASQSISTALAWYQQKPGQAPVLVIYRASTLASGIPERFSGSSSGTTVTLTISGV
QAEDEADYYCQQGWSTVNVDNVFGTGTKVTVL (SEQ ID NO: 195)
>cl|LOCBABABA|1|110 >8_4_LC_humanized_860
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 196)

Figure 8 (cont.)

>cl|MOCBABABA|1|110 >8_4_LC_humanized_809
DIQMTQSPSSVSASVRDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGPGTKVDIK (SEQ ID NO: 197)
>cl|NOCBABABA|1|110 >8_4_LC_humanized_346
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 198)
>cl|POCBABABA|1|110 >8_4_LC_humanized_345
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTFTISS
LQPDDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 199)
>cl|QOCBABABA|1|110 >8_4_LC_humanized_334
DIQMTQSPSFVSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 200)
>cl|ROCBABABA|1|110 >8_4_LC_humanized_319
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 201)
>cl|SOCBABABA|1|110 >8_4_LC_humanized_308
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 202)
>cl|TOCBABABA|1|110 >8_4_LC_humanized_281
DIQLTQSPSSVSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISSL
QPEDFATYYCQQGWSTVNVDNVFGGGTKVDIK (SEQ ID NO: 203)
>cl|VOCBABABA|1|110 >8_4_LC_humanized_273
ELVMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGEAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISG
LQSEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 204)
>cl|WOCBABABA|1|110 >8_4_LC_humanized_716
ELVMTQSPSSLSASEGDRVTITCQASQSISTALAWYQQKPGRAPKLLIHRASTLASGVPSRFSGSGSGTEFTLTISG
LQSEDFATYYCQQGWSTVNVDNVFGGGTTVDVK (SEQ ID NO: 205)
>cl|XOCBABABA|1|110 >8_4_LC_humanized_677
AYDMTQSPSFLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTEFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGQGTRLEIK (SEQ ID NO: 206)
>cl|YOCBABABA|1|110 >8_4_LC_humanized_192
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQAEDFTTYYCQQGWSTVNVDNVFGQGTKVEFK (SEQ ID NO: 207)

Figure 8 (cont.)

>cl|ZOCBABABA|1|110 >8_4_LC_humanized_202
DIRMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKVPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISSL
QPEDVATYYCQQGWSTVNVDNVFGPGTKVVVR (SEQ ID NO: 208)
>cl|BUCBABABA|1|110 >8_4_LC_humanized_802
AIRMTQSPSSFSASTGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISCL
QSEDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 209)
>cl|CUCBABABA|1|110 >8_4_LC_humanized_347
DIQMTQSPSSLSASVGDRVSITCQASQSISTALAWYQQKPGKAPKRLIYRASTLASGVPSRFSGSGSGTEFTLTISS
LQPDDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 210)
>cl|DUCBABABA|1|110 >8_4_LC_humanized_339
DIQLTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTEFTLTISSL
QPDDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 211)
>cl|FUCBABABA|1|110 >8_4_LC_humanized_168
DIVMTQSPSTLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTEFTLTISG
LQPEDFATYYCQQGWSTVNVDNVFGGGTKLEIK (SEQ ID NO: 212)
>cl|GUCBABABA|1|110 >8_4_LC_humanized_54
AYGMTQSPDSLAVSLGERASINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASGVPDRFSGGGSGTDFTLTIS
SLQAEDVAVYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 213)
>cl|HUCBABABA|1|110 >8_4_LC_humanized_21
DIQMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKVLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGPGTKVEVR (SEQ ID NO: 214)
>cl|KUCBABABA|1|110 >8_4_LC_humanized_788
AYELTQTPLSSPVTLGQPASISCQASQSISTALAWLQQRPGQPPRLLIYRASTLASGVPDRFSGSGAGTDFTLKISR
VEAEDVGIYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 215)
>cl|LUCBABABA|1|110 >8_4_LC_humanized_675
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTEFTLTITS
LQPEDFATYYCQQGWSTVNVDNVFGPGTKLEIK (SEQ ID NO: 216)
>cl|MUCBABABA|1|110 >8_4_LC_humanized_762
AYELTQSPDSLAVSLGERATINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASGVPDRFSGSGSGTDFTLTISS
LQAEDVAVYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 217)

Figure 8 (cont.)

>cl|NUCBABABA|1|110 >8_4_LC_humanized_818
AYDMTQTPSSVSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 218)
>cl|PUCBABABA|1|110 >8_4_LC_humanized_173
AIQMTQSPFSLSASVGDRVTITCQASQSISTALAWFQQKPGKAPKSLIYRASTLASGVSSKFSGSGSGTDFTLTISSL
QPEDFATYYCQQGWSTVNVDNVFGQGTRLVVR (SEQ ID NO: 219)
>cl|QUCBABABA|1|110 >8_4_LC_humanized_65
DIQMTQSPSTLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTEFTLTISSL
QPDDFATYYCQQGWSTVNVDNVFGQGTKVEIK (SEQ ID NO: 220)
>cl|RUCBABABA|1|110 >8_4_LC_humanized_224
AYDMTQTPASVSLSPGERATLSCQASQSISTALAWYQQKPGQAPRLLIYRASTLASGIPDRFRGSGSATDFTLTIS
RLEPEDFAVYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 221)
>cl|SUCBABABA|1|110 >8_4_LC_humanized_230
AYDMTQTPASVSASVGDRVTITCQASQSISTALAWYQQKPGKAPKVLIYRASTLASGVPSRFSGSGSGTDFTLTIS
TLQPEDFATYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ ID NO: 222)
>cl|TUCBABABA|1|110 >8_4_LC_humanized_880
AYDMTQSPSSLSASVGDRVNITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGPGTKVDIK (SEQ ID NO: 223)
>cl|VUCBABABA|1|110 >8_4_LC_humanized_672
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGQGTKLEIK (SEQ ID NO: 224)
>cl|WUCBABABA|1|110 >8_4_LC_humanized_299
DIQMTQSPSSVSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTEFTLTISS
LQPDDFATYYCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 225)
>cl|XUCBABABA|1|110 >8_4_LC_humanized_267
AYDMTQSPSTLAASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTEFTLTISS
LQPDDFATYYCQQGWSTVNVDNVFGQGTKVEVK (SEQ ID NO: 226)
>cl|YUCBABABA|1|110 >8_4_LC_humanized_23
AYELTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISSL
QPEDFATYYCQQGWSTVNVDNVFGPGTKVDIK (SEQ ID NO: 227)
>cl|ZUCBABABA|1|110 >8_4_LC_humanized_657
AYDMTQTPASVEVSVGDRVSITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTIT
SLQPVDFATYYCQQGWSTVNVDNVFGPGTTVDAK (SEQ ID NO: 228)
>cl|BADBABABA|1|110 >8_4_LC_humanized_879
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYFCQQGWSTVNVDNVFGGGTKVEIK (SEQ ID NO: 229)

Figure 8 (cont.)

8-4 VH humanized sequences -- germline database clustered at 90% (2 sequences)

>cl|CABBABABA|15|117 >8_4_HC_humanized_356 >8_4_HC_humanized_340
>8_4_HC_humanized_335 >8_4_HC_humanized_303 >8_4_HC_humanized_287
VQLVESGGGVVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNSSL
YLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGPGTLVTVSS (SEQ ID NO: 230)
>cl|LABBABABA|85|117 >8_4_HC_humanized_2049 >8_4_HC_humanized_2033
>8_4_HC_humanized_1360 >8_4_HC_humanized_1344 >8_4_HC_humanized_777
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNSTL
YLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGPGTLVTVSS (SEQ ID NO: 231)

8-4 VL humanized sequences -- germline database clustered at 90% (5 sequences)

>cl|CACBABABA|76|110 >8_4_LC_humanized_356 >8_4_LC_humanized_340
>8_4_LC_humanized_335 >8_4_LC_humanized_303 >8_4_LC_humanized_287
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 232)
>cl|LACBABABA|2|110 >8_4_LC_humanized_2049 >8_4_LC_humanized_2033
AYDMTQSPDSLAVSLGERATINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASGVPDRFSGSGSGTDFTLTIS
SLQAEDVAVYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 233)
>cl|NACBABABA|2|110 >8_4_LC_humanized_1360 >8_4_LC_humanized_1344
AYDMTQTPLSLSVTPGQPASISCQASQSISTALAWYLQKPGQPPQLLIYRASTLASGVPDRFSGSGSGTDFTLKIS
RVEAEDVGVYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 234)
>cl|CECBABABA|5|110 >8_4_LC_humanized_2207 >8_4_LC_humanized_2206
>8_4_LC_humanized_2197 >8_4_LC_humanized_2208 >8_4_LC_humanized_2192
AYDMTQSPAFLSVTPGEKVTITCQASQSISTALAWYQQKPDQAPKLLIKRASTLASGVPSRFSGSGSGTDFTFTISS
LEAEDAATYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 235)
>cl|DICBABABA|15|110 >8_4_LC_humanized_2263 >8_4_LC_humanized_2262
>8_4_LC_humanized_2258 >8_4_LC_humanized_2257 >8_4_LC_humanized_2256
AYDMTQSPASLAVSPGQRATITCQASQSISTALAWYQQKPGQPPKLLIYRASTLASGVPARFSGSGSGTDFTLTI
NPVEANDTANYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 236)

Figure 8 (cont.)

8-4 VH humanized sequences -- germline database clustered at 95% (7 sequences)

>cl|CABBABABA|2|117 >8_4_HC_humanized_356 >8_4_HC_humanized_303
VQLVESRGVLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNSTL
HLQMNSLRAEDTAVYYCKKDGDGSGWGDFNFWGPGTLVTVSS (SEQ ID NO: 237)
>cl|DABBABABA|17|117 >8_4_HC_humanized_340 >8_4_HC_humanized_335
>8_4_HC_humanized_287 >8_4_HC_humanized_282 >8_4_HC_humanized_2207
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNASL
YLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGPGTLVTVSS (SEQ ID NO: 238)
>cl|LABBABABA|37|117 >8_4_HC_humanized_2049 >8_4_HC_humanized_2033
>8_4_HC_humanized_1360 >8_4_HC_humanized_1344 >8_4_HC_humanized_777
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVGDIDGRGDIYCATWAKGRFTISRSKNTL
YLQMNSLKTEDTAVYYCTRDGDGSGWGDFNFWGPGTLVTVSS (SEQ ID NO: 239)
>cl|DEBBABABA|22|117 >8_4_HC_humanized_2206 >8_4_HC_humanized_988
>8_4_HC_humanized_987 >8_4_HC_humanized_935 >8_4_HC_humanized_934
VQLVESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNSTL
YLQMNSLRAEDTAVYYCARDGDGSGWGDFNFWGPGTLVTVSS (SEQ ID NO: 240)
>cl|FEBBABABA|16|117 >8_4_HC_humanized_2197 >8_4_HC_humanized_978
>8_4_HC_humanized_925 >8_4_HC_humanized_660 >8_4_HC_humanized_395
VQLLESGGGLVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNSTL
YLQMNSLRAEDTAVYYCAKDGDGSGWGDFNFWGPGTLVTVSS (SEQ ID NO: 241)
>cl|HIBBABABA|3|117 >8_4_HC_humanized_2257 >8_4_HC_humanized_349
>8_4_HC_humanized_296
VQLVESGGGLVQPGRSLRLSCTASGFTISNLAIIWFRQAPGKGLEWVGDIDGRGDIYCATWAKGRFTISRSKSIAY
LQMNSLKTEDTAVYYCTRDGDGSGWGDFNFWGPGTLVTVSS (SEQ ID NO: 242)
>cl|LIBBABABA|3|117 >8_4_HC_humanized_2254 >8_4_HC_humanized_346
>8_4_HC_humanized_293
VQLVESGGVVVQPGGSLRLSCAASGFTISNLAIIWVRQAPGKGLEWVSDIDGRGDIYCATWAKGRFTISRDNSSL
YLQMNSLRTEDTALYYCAKDGDGSGWGDFNFWGPGTLVTVSS (SEQ ID NO: 243)

Figure 8 (cont.)

8-4 VL humanized sequences -- germline database clustered at 95% (12 sequences)

>cl|CACBABABA|1|110 >8_4_LC_humanized_356
AYDMTQSPSSVSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 244)
>cl|LACBABABA|2|110 >8_4_LC_humanized_2049 >8_4_LC_humanized_2033
AYDMTQSPDSLAVSLGERATINCQASQSISTALAWYQQKPGQPPKLLIYRASTLASGVPDRFSGSGSGTDFTLTIS
SLQAEDVAVYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 245)
>cl|NACBABABA|2|110 >8_4_LC_humanized_1360 >8_4_LC_humanized_1344
AYDMTQTPLSLSVTPGQPASISCQASQSISTALAWYLQKPGQPPQLLIYRASTLASGVPDRFSGSGSGTDFTLKIS
RVEAEDVGVYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 246)
>cl|QACBABABA|1|110 >8_4_LC_humanized_777
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTFTISS
LQPEDIATYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 247)
>cl|VACBABABA|1|110 >8_4_LC_humanized_565
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKRLIYRASTLASGVPSRFSGSGSGTEFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 248)
>cl|XACBABABA|2|110 >8_4_LC_humanized_247 >8_4_LC_humanized_231
AYDMTQSPSFLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTEFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 249)
>cl|ZACBABABA|2|110 >8_4_LC_humanized_141 >8_4_LC_humanized_125
AYDMTQSPSSFSASTGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISC
LQSEDFATYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 250)
>cl|CECBABABA|1|110 >8_4_LC_humanized_2207
AYDMTQSPAFLSVTPGEKVTITCQASQSISTALAWYQQKPDQAPKLLIKRASTLASGVPSRFSGSGSGTDFTFTISS
LEAEDAATYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 251)
>cl|GECBABABA|1|110 >8_4_LC_humanized_988
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDFATYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 252)
>cl|PECBABABA|1|110 >8_4_LC_humanized_670
AYDMTQSPSSLSASVGDRVTITCQASQSISTALAWYQQKPGKVPKLLIYRASTLASGVPSRFSGSGSGTDFTLTISS
LQPEDVATYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 253)
>cl|ZECBABABA|1|110 >8_4_LC_humanized_34
AYDMTQSPSTLSASVGDRVTITCQASQSISTALAWYQQKPGKAPKLLIYRASTLASGVPSRFSGSGSGTEFTLTISS
LQPDDFATYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 254)
>cl|DICBABABA|15|110 >8_4_LC_humanized_2263 >8_4_LC_humanized_2262
>8_4_LC_humanized_2258 >8_4_LC_humanized_2257 >8_4_LC_humanized_2256
AYDMTQSPASLAVSPGQRATITCQASQSISTALAWYQQKPGQPPKLLIYRASTLASGVPARFSGSGSGTDFTLTI
NPVEANDTANYYCQQGWSTVNVDNVFGGGTEVVVR (SEQ ID NO: 255)

Figure 8 (cont.)

16-6 VH humanized sequences -- IMGT-LigM DB (Abysis) clustered at 90% (41 sequences)

>cl|CABBABABA|1|115 >16_6_HC_humanized_586
VQLQESGGGVVQPGTSLRLSCVVSGSDISSYHMGWVRQAPGKGLEWLAIIVSSGSAYYATWAKGRFTVSRSKST
LFLKMNSLRADDTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 256)
>cl|DABBABABA|2|115 >16_6_HC_humanized_411 >16_6_HC_humanized_213
LQLQESGPRLVKPSETLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYYATWAKSRLTISTSKNQFSL
RLSSVTAADSAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 257)
>cl|FABBABABA|1|115 >16_6_HC_humanized_372
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEAVAIIVSSGSAYYATWAKGRFTISRDSSTL
FLQLNSLRVEDSGIYYCAKNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 258)
>cl|GABBABABA|7|115 >16_6_HC_humanized_1996 >16_6_HC_humanized_230
>16_6_HC_humanized_2056 >16_6_HC_humanized_672 >16_6_HC_humanized_657
QSLEESGGRLVTPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNSTL
YLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 259)
>cl|HABBABABA|2|115 >16_6_HC_humanized_1907 >16_6_HC_humanized_716
QSLLESGGGWVQPGRSLRLSCSASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRDNN
SLYLQMNSLRPEDTALYYCAKNQYSGYGFSFWGQGVLVTVSS (SEQ ID NO: 260)
>cl|LABBABABA|3|115 >16_6_HC_humanized_1945 >16_6_HC_humanized_1451
>16_6_HC_humanized_65
QSLEESGGGLVKPGESLRLSCAASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRDDST
VYLEMNSLKTEDTAVYYCATNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 261)
>cl|NABBABABA|1|115 >16_6_HC_humanized_1004
QSLLESGPRLVKPSETLSLTCSVSGSDISSYHMGWVRQPPGQGLEWIGIIVSSGSAYYATWARSRVSISTSQNQVS
LKLTSVTAADTAVYYCARNQYSGYGFSFWGQGILVTVSS (SEQ ID NO: 262)
>cl|PABBABABA|13|115 >16_6_HC_humanized_1971 >16_6_HC_humanized_305
>16_6_HC_humanized_1877 >16_6_HC_humanized_860 >16_6_HC_humanized_283
VQLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKGRFTISRDNS
TLYLQMNSLRAEDTAVYYCAKNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 263)

Figure 8 (cont.)

>cl|QABBABABA|22|115 >16_6_HC_humanized_802 >16_6_HC_humanized_587
>16_6_HC_humanized_1012 >16_6_HC_humanized_988 >16_6_HC_humanized_129
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNST
LYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 264)
>cl|RABBABABA|1|115 >16_6_HC_humanized_609
VQLVESGGGLVQPGGSLRLSCTTSGSDISSYHMGWVRQVPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNST
SYLQMTSLTPEDTAVYYCAKNQYSGYGFSFWGQGTVVSVSS (SEQ ID NO: 265)
>cl|YABBABABA|4|115 >16_6_HC_humanized_910 >16_6_HC_humanized_218
>16_6_HC_humanized_912 >16_6_HC_humanized_917
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYYATWAKSRVTISTSKNQLS
LKLTSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 266)
>cl|GEBBABABA|1|115 >16_6_HC_humanized_136
VQLQQSGPGLVKTSETLPLTCTVSGSDISSYHMGWIRQPPGKGLEYIGIIVSSGSAYYATWAKNRVTISTSKNQFS
LKLSSVTAADTALYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 267)
>cl|KEBBABABA|1|115 >16_6_HC_humanized_109
VQLVESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGKGLEYIGIIVSSGSAYYATWAKSRLTMSVDTSNY
QLKLSSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 268)
>cl|LEBBABABA|1|115 >16_6_HC_humanized_103
VQLQQSGPGLVKPSGTLSLTCDVSGSDISSYHMGWVRQPPGKGLEWIGIIVSSGSAYYATWAKSRVTISKSKNQF
SLRLTSVTAADTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 269)
>cl|NEBBABABA|6|115 >16_6_HC_humanized_902 >16_6_HC_humanized_1982
>16_6_HC_humanized_734 >16_6_HC_humanized_920 >16_6_HC_humanized_149
VQLVESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYYATWAKSRVTISTSKNQFS
LKLSSVTAADTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 270)
>cl|PEBBABABA|1|115 >16_6_HC_humanized_851
VQLVQSGGGVVQPGGSLRVSCAASGSDISSYHMGWVRQAPGKGLEWMAIIVSSGSAYYATWAKGRFTISRDN
STVSLQMSSLRAEDTAVYYCAKNQYSGYGFSFWGRGTLVTVSS (SEQ ID NO: 271)
>cl|SEBBABABA|1|115 >16_6_HC_humanized_926
VQLVESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQHSGKTLEWIGIIVSSGSAYYATWAESRVTISADTSKISL
KLSSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 272)

Figure 8 (cont.)

>cl|VEBBABABA|1|115 >16_6_HC_humanized_904
VQLVESGPGLVKPSQTLSLTCNVSGSDISSYHMGWIRQSPGKGLEWIGIIVSSGSAYYATWARSRVTISADTSKVS
LELSPMTAADTAVYYCARNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 273)

>cl|WEBBABABA|1|115 >16_6_HC_humanized_903
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGTGLEWIGIIVSSGSAYYATWAKSRVTISGDTSKFS
LMLRSVTAADTAVYYCARNQYSGYGFSFWGQGTMVTVSS (SEQ ID NO: 274)
>cl|YEBBABABA|1|115 >16_6_HC_humanized_946
VQLVESGGGLIKPGGSLRLSCEVPGSDISSYHMGWVRQGPGRGLEWVGIIVSSGSAYYATWARGRFTISRSKSTV
YLEMNALKTEDTGIYYCVTNQYSGYGFSFWGQGTMVTVSS (SEQ ID NO: 275)
>cl|ZEBBABABA|1|115 >16_6_HC_humanized_882
QSLEESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQPPGKGLEWVGIIVSSGSAYYATWAKGRFTISRSKST
VYLQMNSLKTEDTAVYYCTANQYSGYGFSFWGQGMLVTVSS (SEQ ID NO: 276)
>cl|CIBBABABA|1|115 >16_6_HC_humanized_2041
QSLVQSGTEVRKPGASVKVSCKASGSDISSYHMGWVRQAPGQGLEWMGIIVSSGSAYYATWAQGRVTMSDT
STTVYMELSSLTSEDTAIYYCARNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 277)
>cl|KIBBABABA|1|115 >16_6_HC_humanized_1944
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQPPGKGLEWIGIIVSSGSAYYATWAKNRVTISTSKNQF
SLRLNSVTAADTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 278)
>cl|LIBBABABA|4|115 >16_6_HC_humanized_1895 >16_6_HC_humanized_1992
>16_6_HC_humanized_1995 >16_6_HC_humanized_1949
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLVWVSIIVSSGSAYYATWAKGRFTISRDNATL
YLQMNSLRAEDTAVYYCARNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 279)
>cl|SIBBABABA|2|115 >16_6_HC_humanized_993 >16_6_HC_humanized_994
VQLVESGGGLIQPGRPLRLSCSGSGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRDDSV
VHLQMNSLRSEDTAVYYCTRNQYSGYGFSFWGQGTMVTVSS (SEQ ID NO: 280)
>cl|TIBBABABA|2|115 >16_6_HC_humanized_956 >16_6_HC_humanized_965
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQHPGKGLEWIGIIVSSGSAYYATWAESRLTISADTSNIQ
LRLSSVTAADTAVYFCARNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 281)
>cl|WIBBABABA|1|115 >16_6_HC_humanized_278
VQLVQSGGGLVKPGGSLRLSCEASGSDISSYHMGWIRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRDDST
LYLQVNSLKTEDSAVYYCTTNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 282)

Figure 8 (cont.)

>cl|GOBBABABA|1|115 >16_6_HC_humanized_1894
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNASL
YLQMNSLRAEDTAVYYCARNQYSGYGFSFFSDYWLVTVSS (SEQ ID NO: 283)
>cl|MOBBABABA|3|115 >16_6_HC_humanized_1917 >16_6_HC_humanized_677
>16_6_HC_humanized_267
QSLEESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKRRFTISRDNST
LYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 284)
>cl|POBBABABA|1|115 >16_6_HC_humanized_2038
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKGRFTISRDNASL
YLQMNSLRAEDTAVYYCARNQYSGYGFSFPTSGYYYMDVS (SEQ ID NO: 285)
>cl|QOBBABABA|1|115 >16_6_HC_humanized_23
QSLLESGGDLVQPGGSLRLSCEASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDKSTL
FLQMHSLRVEDTAVYYCAKNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 286)
>cl|VOBBABABA|1|115 >16_6_HC_humanized_1013
VQLVQSGGGVVQPGRSLRLSCEVSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKGRFTISRSNN
TLYLQMNSLTAEDTALYFCARNQYSGYGFSFWGKGTTVTVSS (SEQ ID NO: 287)
>cl|YOBBABABA|1|115 >16_6_HC_humanized_113
LQLQESGPGLVKPSQTLSLTCSVSGSDISSYHMGWIRQHPGKGLEWIGIIVSSGSAYYATWAKSRITISTSKNQFSL
KLTSVTAADTALYYCARNQYSGYGFSFWGRGTLVTVSS (SEQ ID NO: 288)
>cl|HUBBABABA|1|115 >16_6_HC_humanized_12
VQLVQSGGGVVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAQGRVTISRDN
STVHLQITSLKSEDTAVYYCAKNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 289)
>cl|LUBBABABA|1|115 >16_6_HC_humanized_273
VQLVQSGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQASGKGLEWIGIIVSSGSAYYATWAKGRFTVSRSQN
SVFLQMNSLETEDTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 290)
>cl|NUBBABABA|1|115 >16_6_HC_humanized_879
QSLEESGGGLVQPGGSLRLSCTASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDSSTL
YLQMNNLRVEDTALYYCAHNQYSGYGFSFWGRGTQVTVSS (SEQ ID NO: 291)
>cl|TUBBABABA|1|115 >16_6_HC_humanized_1934
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNASL
YLQMNSLRAEDTAVYYCARNQYSGYGFSFGIFDYWVTVSS (SEQ ID NO: 292)

Figure 8 (cont.)

>cl|VUBBABABA|1|115 >16_6_HC_humanized_200
VQLQESGPGLVKPSETLSLTCSVSGSDISSYHMGWIRQPAGKGLEWIGIIVSSGSAYYATWARSRVTMSMSKNH
FSLKLRSVTAADTAVYFCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 293)
>cl|WUBBABABA|1|115 >16_6_HC_humanized_1977
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKGRFTISRSKNTL
YLQMNSLRAEDTAVYYCARNQYSGYGFSFTCPYFDYWVSS (SEQ ID NO: 294)
>cl|XUBBABABA|1|115 >16_6_HC_humanized_2027
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAEGRFTISRDNSTL
YLQMYSLRTEDTAVYYCARNQYSGYGFSFYYYGMGVWVSS (SEQ ID NO: 295)
>cl|YUBBABABA|1|115 >16_6_HC_humanized_1958
VHLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAEGRFTISRDNS
KLYLQMNSLRAEDSATYYCARNQYSGYGFSFFGPPYYYYYMS (SEQ ID NO: 296)
>cl|BACBABABA|1|115 >16_6_HC_humanized_1905
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNSTL
YLQMNSLRAEDTALYYCARNQYSGYGFSFVRGGYFYHMDS (SEQ ID NO: 297)

Figure 8 (cont.)

16-6 VL humanized sequences -- IMGT-LigM DB (Abysis) clustered at 90% (21 sequences)

>cl|CACBABABA|1|110 >16_6_LC_humanized_586
IVLTQTPSSLSASVGDRITITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSRSGTDFTFTIS
SLRPEDIATYYCLGGYDDDGETAFGGGTKVEIK (SEQ ID NO: 298)
>cl|DACBABABA|27|110 >16_6_LC_humanized_411 >16_6_LC_humanized_1004
>16_6_LC_humanized_587 >16_6_LC_humanized_305 >16_6_LC_humanized_988
IVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTIS
SLQPEDFATYYCLGGYDDDGETAFGGGTKVEIK (SEQ ID NO: 299)
>cl|FACBABABA|15|110 >16_6_LC_humanized_372 >16_6_LC_humanized_1877
>16_6_LC_humanized_1012 >16_6_LC_humanized_860 >16_6_LC_humanized_283
IQLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTIS
SLQPDDFATYYCLGGYDDDGETAFGQGTKVEIK (SEQ ID NO: 300)
>cl|GACBABABA|1|110 >16_6_LC_humanized_1996
VVLTQTPSPVSTAVGGTVTLSCQSSHSVYYGDWLAWYQQKPGQAPRLLIYRASNLASGIPDRFSGSGSGTDFTLT
ISRLEPEDFAVYYCLGGYDDDGETAKGPGTEVVVK (SEQ ID NO: 301)
>cl|HACBABABA|2|110 >16_6_LC_humanized_1907 >16_6_LC_humanized_716
LVMTQSPSSLSASEGDRVTITCQSSHSVYYGDWLAWYQQKPGRAPKLLIHRASNLASGVPSRFSGSGSGTEFTLT
ISGLQSEDFATYYCLGGYDDDGETAFGGGTTVDVK (SEQ ID NO: 302)
>cl|LACBABABA|2|110 >16_6_LC_humanized_1945 >16_6_LC_humanized_1451
VELTQPPSPVSAAPGQKVTISCQSSHSVYYGDWLAWYQQLPGTAPKLLIYRASNLASGIPDRFSGSKSGTSATLGI
TGLQTGDEADYYCLGGYDDDGETAFGGGTRLTVL (SEQ ID NO: 303)
>cl|PACBABABA|10|110 >16_6_LC_humanized_1971 >16_6_LC_humanized_2041
>16_6_LC_humanized_2038 >16_6_LC_humanized_2008 >16_6_LC_humanized_1992
VVLTQTPSPVSTAVGGTVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLT
ISSLQPEDFATYYCLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 304)
>cl|QACBABABA|5|110 >16_6_LC_humanized_802 >16_6_LC_humanized_609
>16_6_LC_humanized_851 >16_6_LC_humanized_908 >16_6_LC_humanized_108
VVMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLT
ISSLQPEDFATYYCLGGYDDDGETAFGGGTKVEIK (SEQ ID NO: 305)
>cl|CECBABABA|7|110 >16_6_LC_humanized_253 >16_6_LC_humanized_103
>16_6_LC_humanized_882 >16_6_LC_humanized_1982 >16_6_LC_humanized_734
IVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTIS
SLQPEDSATYYCLGGYDDDGETAFGQGTKVEIK (SEQ ID NO: 306)

Figure 8 (cont.)

>cl|KECBABABA|2|110 >16_6_LC_humanized_109 >16_6_LC_humanized_334
IQLTQSPSFVSASVGDRITITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSRSGTDFTLTIS
SLQPEDFATYYCLGGYDDDGETAFGQGTKVEIK (SEQ ID NO: 307)
>cl|RECBABABA|2|110 >16_6_LC_humanized_17 >16_6_LC_humanized_21
IQLTQSPSSLSAAVGDRVTIACQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLSI
SSLQPEDFATYYCLGGYDDDGETAFGGGTKVQMK (SEQ ID NO: 308)
>cl|DICBABABA|1|110 >16_6_LC_humanized_202
IRMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKVPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDVATYYCLGGYDDDGETAFGPGTKVVVK (SEQ ID NO: 309)
>cl|FICBABABA|14|110 >16_6_LC_humanized_192 >16_6_LC_humanized_956
>16_6_LC_humanized_230 >16_6_LC_humanized_880 >16_6_LC_humanized_2056
VVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDFATYYCLGGYDDDGETAFGQGTKVEIK (SEQ ID NO: 310)
>cl|NICBABABA|2|110 >16_6_LC_humanized_1938 >16_6_LC_humanized_762
VELTQSPDSLAVSLGERATINCQSSHSVYYGDWLAWYQQKPGQPPKLLIYRASNLASGVPDRFSGSGSGTDFTLT
ISSLQAEDVAVYYCLGGYDDDGETAFGGGTKVEIK (SEQ ID NO: 311)
>cl|WICBABABA|1|110 >16_6_LC_humanized_278
LVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWCQQKPGKSPTLLIYRASNLASGVPSRFSGSGSGTGFTLTI
SGLQPEDFATYYCLGGYDDDGETAFGGGTKVEIR (SEQ ID NO: 312)
>cl|YICBABABA|1|110 >16_6_LC_humanized_169
IVLTQSPSFLSAFVGDRITITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTIS
GLQPEDFASYYCLGGYDDDGETAFGGGTKLEIK (SEQ ID NO: 313)
>cl|GOCBABABA|1|110 >16_6_LC_humanized_1894
VVLTQTPSPVSTAVGDRVTITCQSSHSVYYGDWLAWYRQKPGKVPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDVATYYGLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 314)
>cl|LOCBABABA|1|110 >16_6_LC_humanized_657
VVLTQTPSPVSTSVGDRVSITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
TSLQPVDFATYYCLGGYDDDGETAFGPGTTVDAK (SEQ ID NO: 315)
>cl|YOCBABABA|1|110 >16_6_LC_humanized_113
IVLTQSPSSVSASVGDRVTITCQSSHSVYYGDWLAWYQLKPGKAPKLLINRASNLASGVPSRFSGSGSGTDFTLTI
SGLQPEDFATYYCLGGYDDDGETAFGPGTTVDIK (SEQ ID NO: 316)
>cl|MUCBABABA|3|110 >16_6_LC_humanized_2032 >16_6_LC_humanized_200
>16_6_LC_humanized_1905
VVLTQTPSPVSTAVGGTGTINCQSSHSVYYGDWLAWYQQKPGQPPKLLIYRASNLASGVPDRFSGSGSGTDFTL
TISSLQAEDVAVYYCLGGYDDDGETAFGGGTKVVVK (SEQ ID NO: 317)
>cl|RUCBABABA|1|110 >16_6_LC_humanized_1995
VVLTQTPSPVSTAVGGTVTINCQSSHSVYYGDWLAWYQQKPGQPXKLLIYRASNLASGVPDRFSGSGSGTDFTL
TISSLQAEDVAVYYCLGGYDDDGETAFGQGTEVVVK (SEQ ID NO: 318)

Figure 8 (cont.)

16-6 VH humanized sequences -- IMGT-LigM DB (Abysis) clustered at 95% (81 sequences)

>cl|CABBABABA|1|115 >16_6_HC_humanized_586
VQLQESGGGVVQPGTSLRLSCVVSGSDISSYHMGWVRQAPGKGLEWLAIIVSSGSAYYATWAKGRFTVSRSKST
LFLKMNSLRADDTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 319)
>cl|DABBABABA|1|115 >16_6_HC_humanized_411
LQLQESGPRLVKPSETLSLTCTVSGSDISSYHMGWIRQSPGKGLEWIGIIVSSGSAYYATWAKSRLTMSTSKNQFS
LRLSSVTAADSAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 320)
>cl|FABBABABA|1|115 >16_6_HC_humanized_372
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEAVAIIVSSGSAYYATWAKGRFTISRDSSTL
FLQLNSLRVEDSGIYYCAKNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 321)
>cl|GABBABABA|1|115 >16_6_HC_humanized_1996
QSLEESGGRLVTPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRDNST
LYLQMNSLRVEDTARYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 322)
>cl|HABBABABA|2|115 >16_6_HC_humanized_1907 >16_6_HC_humanized_716
QSLLESGGGWVQPGRSLRLSCSASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRDNN
SLYLQMNSLRPEDTALYYCAKNQYSGYGFSFWGQGVLVTVSS (SEQ ID NO: 323)
>cl|LABBABABA|2|115 >16_6_HC_humanized_1945 >16_6_HC_humanized_1451
QSLEESGGGLVKPGESLRLSCAASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRDDST
VYLEMNSLKTEDTAVYYCATNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 324)
>cl|NABBABABA|1|115 >16_6_HC_humanized_1004
QSLLESGPRLVKPSETLSLTCSVSGSDISSYHMGWVRQPPGQGLEWIGIIVSSGSAYYATWARSRVSISTSQNQVS
LKLTSVTAADTAVYYCARNQYSGYGFSFWGQGILVTVSS (SEQ ID NO: 325)
>cl|PABBABABA|1|115 >16_6_HC_humanized_1971
VQLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWLAIIVSSGSAYYATWAKGRFTISRDNSS
LYLQLSSLRNEDTAVYYCAKNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 326)
>cl|QABBABABA|2|115 >16_6_HC_humanized_802 >16_6_HC_humanized_988
VQLVESGGGLIQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNAS
LYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 327)
>cl|RABBABABA|1|115 >16_6_HC_humanized_609
VQLVESGGGLVQPGGSLRLSCTTSGSDISSYHMGWVRQVPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNST
SYLQMTSLTPEDTAVYYCAKNQYSGYGFSFWGQGTVVSVSS (SEQ ID NO: 328)
>cl|SABBABABA|1|115 >16_6_HC_humanized_587
VQLVESGGGLVKPGGSLRLSCVVSGSDISSYHMGWVRQAPGKGLEWLSIIVSSGSAYYATWAKGRFTISRDNAS
LFLQMNSLRADDTALYFCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 329)

Figure 8 (cont.)

>cl|TABBABABA|6|115 >16_6_HC_humanized_305 >16_6_HC_humanized_283
>16_6_HC_humanized_334 >16_6_HC_humanized_281 >16_6_HC_humanized_339
VQLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKGRFTISRDNS
TLYLQMNSLRAEDTAVYYCAKNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 330)
>cl|VABBABABA|4|115 >16_6_HC_humanized_1877 >16_6_HC_humanized_860
>16_6_HC_humanized_204 >16_6_HC_humanized_818
VQLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKGRFTISRDNS
TLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 331)
>cl|WABBABABA|1|115 >16_6_HC_humanized_1012
VQLQEWGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKGRFTISRDN
STLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 332)
>cl|YABBABABA|1|115 >16_6_HC_humanized_910
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYYATWAQSRVLISTSKSQLS
LKLTSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 333)
>cl|CEBBABABA|1|115 >16_6_HC_humanized_253
VQLVESGGGLVQPGRSLRLSCATSGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRDNAS
LYLQMSSLRAEDTALYYCAKNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 334)
>cl|DEBBABABA|1|115 >16_6_HC_humanized_218
VQLQESGPGLVKPSETLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYYATWAKSRVTISTSKNQFS
LKLSSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 335)
>cl|FEBBABABA|1|115 >16_6_HC_humanized_213
LQLQESGPGLVKPSETLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYYATWAKSRVTISTSKNQFSL
KLSSVTAADTAVYYCASNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 336)
>cl|GEBBABABA|1|115 >16_6_HC_humanized_136
VQLQQSGPGLVKTSETLPLTCTVSGSDISSYHMGWIRQPPGKGLEYIGIIVSSGSAYYATWAKNRVTISTSKNQFS
LKLSSVTAADTALYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 337)
>cl|HEBBABABA|1|115 >16_6_HC_humanized_129
MQLVESGGGLVQPGRSLRLSCVTSGSDISSYHMGWVRQVPGKGLEWVGIIVSSGSAYYATWAKGRFTISRDNT
SLYLQMNSLRPEDTAVYYCAKNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 338)
>cl|KEBBABABA|1|115 >16_6_HC_humanized_109
VQLVESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGKGLEYIGIIVSSGSAYYATWAKSRLTMSVDTSNY
QLKLSSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 339)

Figure 8 (cont.)

>cl|LEBBABABA|1|115 >16_6_HC_humanized_103
VQLQQSGPGLVKPSGTLSLTCDVSGSDISSYHMGWVRQPPGKGLEWIGIIVSSGSAYYATWAKSRVTISKSKNQF
SLRLTSVTAADTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 340)
>cl|MEBBABABA|1|115 >16_6_HC_humanized_954
VQLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKGRFTISRDNS
TLYLQMNSLRAEDTAVYYCAKNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 341)
>cl|NEBBABABA|1|115 >16_6_HC_humanized_902
VQLVESGPGLVKPSQTLSLTCTVSGSDISSYHMGWLRQPPGRGLEWIGIIVSSGSAYYATWAKSRVTLSTSKNQF
SLKLNSVTAADTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 342)
>cl|PEBBABABA|1|115 >16_6_HC_humanized_851
VQLVQSGGGVVQPGGSLRVSCAASGSDISSYHMGWVRQAPGKGLEWMAIIVSSGSAYYATWAKGRFTISRDN
STVSLQMSSLRAEDTAVYYCAKNQYSGYGFSFWGRGTLVTVSS (SEQ ID NO: 343)
>cl|REBBABABA|1|115 >16_6_HC_humanized_17
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGRGLVWVSIIVSSGSAYYATWAKGRFTISRDNA
TLYLQMNNLRAEDTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 344)
>cl|SEBBABABA|1|115 >16_6_HC_humanized_926
VQLVESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQHSGKTLEWIGIIVSSGSAYYATWAESRVTISADTSKISL
KLSSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 345)
>cl|TEBBABABA|1|115 >16_6_HC_humanized_908
VQLVESGGGLVEPGGSLRLSCAASGSDISSYHMGWIRQAPGKGLEWLSIIVSSGSAYYATWAKGRFTISRDNASL
YLQMNSLRAEDTAVYYCVRNQYSGYGFSFWGQGTMVTVSS (SEQ ID NO: 346)
>cl|VEBBABABA|1|115 >16_6_HC_humanized_904
VQLVESGPGLVKPSQTLSLTCNVSGSDISSYHMGWIRQSPGKGLEWIGIIVSSGSAYYATWARSRVTISADTSKVS
LELSPMTAADTAVYYCARNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 347)
>cl|WEBBABABA|1|115 >16_6_HC_humanized_903
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGTGLEWIGIIVSSGSAYYATWAKSRVTISGDTSKFS
LMLRSVTAADTAVYYCARNQYSGYGFSFWGQGTMVTVSS (SEQ ID NO: 348)
>cl|XEBBABABA|1|115 >16_6_HC_humanized_108
VQLVESGGGLVKPGGSLRLSCAASGSDISSYHMGWIRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNASL
FLQMNSLRAEDTAVYYCAKNQYSGYGFSFWGQGTLITVSS (SEQ ID NO: 349)
>cl|YEBBABABA|1|115 >16_6_HC_humanized_946
VQLVESGGGLIKPGGSLRLSCEVPGSDISSYHMGWVRQGPGRGLEWVGIIVSSGSAYYATWARGRFTISRSKSTV
YLEMNALKTEDTGIYYCVTNQYSGYGFSFWGQGTMVTVSS (SEQ ID NO: 350)

Figure 8 (cont.)

>cl|ZEBBABABA|1|115 >16_6_HC_humanized_882
QSLEESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQPPGKGLEWVGIIVSSGSAYYATWAKGRFTISRSKST
VYLQMNSLKTEDTAVYYCTANQYSGYGFSFWGQGMLVTVSS (SEQ ID NO: 351)
>cl|BIBBABABA|1|115 >16_6_HC_humanized_186
VQLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLESVAIIVSSGSAYYATWAKGRFTISRDNST
LYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 352)
>cl|CIBBABABA|1|115 >16_6_HC_humanized_2041
QSLVQSGTEVRKPGASVKVSCKASGSDISSYHMGWVRQAPGQGLEWMGIIVSSGSAYYATWAQGRVTMSDT
STTVYMELSSLTSEDTAIYYCARNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 353)
>cl|DIBBABABA|1|115 >16_6_HC_humanized_202
VQLQESGEGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEYVSIIVSSGSAYYATWAKGRFTISRDNSTL
YLQMGSLRAEDMAVYYCARNQYSGYGFSFWGQGTMVTVSS (SEQ ID NO: 354)
>cl|FIBBABABA|2|115 >16_6_HC_humanized_192 >16_6_HC_humanized_880
QHLEESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKGRFTISRDNS
TLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 355)
>cl|GIBBABABA|2|115 >16_6_HC_humanized_1982 >16_6_HC_humanized_734
QSLLESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYYATWAKSRVTMSTSKNHF
SLRLSSVTAADTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 356)
>cl|KIBBABABA|1|115 >16_6_HC_humanized_1944
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQPPGKGLEWIGIIVSSGSAYYATWAKNRVTISTSKNQF
SLRLNSVTAADTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 357)
>cl|LIBBABABA|1|115 >16_6_HC_humanized_1895
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLVWVSIIVSSGSAYYATWAKGRFTISRDNATL
YLQMNSLRAEDTAVYYCARNQYSGYGFSFWGKGTTVTVSS (SEQ ID NO: 358)
>cl|MIBBABABA|1|115 >16_6_HC_humanized_65
QSLEESGGGLVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRDNAS
LYLQMNSLRAEDTALYYCAKNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 359)
>cl|NIBBABABA|2|115 >16_6_HC_humanized_1938 >16_6_HC_humanized_762
VKLLESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKGRFTISRDNST
LYLQMNSLGAEDTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 360)
>cl|QIBBABABA|2|115 >16_6_HC_humanized_2031 >16_6_HC_humanized_621
VQLVESGGGLVKPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNST
LYLQMNNLRAEDTAVYYCARNQYSGYGFSFWGQGTLVTVLS (SEQ ID NO: 361)

Figure 8 (cont.)

>cl|SIBBABABA|1|115 >16_6_HC_humanized_993
VQLVESGGGLIQPGRPLRLSCSGSGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRDDSV
VHLQMNSLKSEDTAVYYCTRNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 362)
>cl|TIBBABABA|1|115 >16_6_HC_humanized_956
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWFRQHPGKGLEWIGIIVSSGSAYYATWAESRLTISEDTSNIQ
LRLTSVTAADTAVYFCARNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 363)
>cl|VIBBABABA|1|115 >16_6_HC_humanized_920
VQLVESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQFPGKGLEWIGIIVSSGSAYYATWAKSRFTISTSKNQFSL
KVDSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 364)
>cl|WIBBABABA|1|115 >16_6_HC_humanized_278
VQLVQSGGGLVKPGGSLRLSCEASGSDISSYHMGWIRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRDDST
LYLQVNSLKTEDSAVYYCTTNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 365)
>cl|YIBBABABA|2|115 >16_6_HC_humanized_169 >16_6_HC_humanized_168
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNST
LYLQMDSLRAEDTAIYYCAKNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 366)
>cl|ZIBBABABA|1|115 >16_6_HC_humanized_994
VQLVESGGGLIQPGRSLRLSCSGSGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRDDSV
VYLQMNSLRSEDTAVYYCTRNQYSGYGFSFWGQGTMVTVSS (SEQ ID NO: 367)
>cl|BOBBABABA|2|115 >16_6_HC_humanized_975 >16_6_HC_humanized_978
VQLVESGGGVVRPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRDNA
SLYLEMNSLRAEDTALYFCARNQYSGYGFSFWGQGTMVTVSS (SEQ ID NO: 368)
>cl|DOBBABABA|1|115 >16_6_HC_humanized_230
QSLEESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNST
LYLQMNSLRAEDTAVYYCAKNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 369)
>cl|GOBBABABA|1|115 >16_6_HC_humanized_1894
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNASL
YLQMNSLRAEDTAVYYCARNQYSGYGFSFFSDYWLVTVSS (SEQ ID NO: 370)
>cl|HOBBABABA|2|115 >16_6_HC_humanized_2056 >16_6_HC_humanized_672
QSLVESGGGLIQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNSTL
YLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 371)
>cl|LOBBABABA|1|115 >16_6_HC_humanized_657
QSLEESGGRLVTPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNSSL
YLQMNSLRTEDSALYYCALNQYSGYGFSFWGQGSLVTVSS (SEQ ID NO: 372)

Figure 8 (cont.)

>cl|MOBBABABA|2|115 >16_6_HC_humanized_1917 >16_6_HC_humanized_677
QSLEESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKRRFTISRDNST
LYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 373)
>cl|POBBABABA|1|115 >16_6_HC_humanized_2038
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKGRFTISRDNASL
YLQMNSLRAEDTAVYYCARNQYSGYGFSFPTSGYYYMDVS (SEQ ID NO: 374)
>cl|QOBBABABA|1|115 >16_6_HC_humanized_23
QSLLESGGDLVQPGGSLRLSCEASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDKSTL
FLQMHSLRVEDTAVYYCAKNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 375)
>cl|ROBBABABA|1|115 >16_6_HC_humanized_21
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEFVSIIVSSGSAYYATWAKDRFTISRDNSTV
YLQMDSLRTEDTAMYFCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 376)
>cl|SOBBABABA|1|115 >16_6_HC_humanized_469
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKGRFTISRDNTS
LFLHMSSLRGEDTAIYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 377)
>cl|TOBBABABA|1|115 >16_6_HC_humanized_2008
QSLEESGGRLVTPGTSLRLSCAVSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNSTV
YLQMNSLRAEDTAVFYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 378)
>cl|VOBBABABA|1|115 >16_6_HC_humanized_1013
VQLVQSGGGVVQPGRSLRLSCEVSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKGRFTISRSNN
TLYLQMNSLTAEDTALYFCARNQYSGYGFSFWGKGTTVTVSS (SEQ ID NO: 379)
>cl|XOBBABABA|1|115 >16_6_HC_humanized_149
VQLVQSGPGLVKPSRTLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYYATWAQNRLTISTSKNQFS
LKLASVTAADTAVYFCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 380)
>cl|YOBBABABA|1|115 >16_6_HC_humanized_113
LQLQESGPGLVKPSQTLSLTCSVSGSDISSYHMGWIRQHPGKGLEWIGIIVSSGSAYYATWAKSRITISTSKNQFSL
KLTSVTAADTALYYCARNQYSGYGFSFWGRGTLVTVSS (SEQ ID NO: 381)
>cl|BUBBABABA|1|115 >16_6_HC_humanized_965
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQHPGKGLEWIGIIVSSGSAYYATWAKSRVTISADTSKIS
LKLSSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 382)
>cl|CUBBABABA|1|115 >16_6_HC_humanized_912
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYYATWAKSRVLISTSKNQVS
LKLSSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 383)

Figure 8 (cont.)

>cl|HUBBABABA|1|115 >16_6_HC_humanized_12
VQLVQSGGGVVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAQGRVTISRDN
STVHLQITSLKSEDTAVYYCAKNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 384)
>cl|KUBBABABA|1|115 >16_6_HC_humanized_924
VQLVESGPGLVKPSQTLSLTCTVSGSDISSYHMGWFRQPPGKGLEWIGIIVSSGSAYYATWAKSRVTISTSKNQV
SLKLSPVTGADTAVYFCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 385)
>cl|LUBBABABA|1|115 >16_6_HC_humanized_273
VQLVQSGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQASGKGLEWIGIIVSSGSAYYATWAKGRFTVSRSQN
SVFLQMNSLETEDTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 386)
>cl|MUBBABABA|1|115 >16_6_HC_humanized_2032
QSLEESGGRLVTPGGSLRLSCAGSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAEGRFTISRDNATL
YLQMNSLRVEDTAVYYCATNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 387)
>cl|NUBBABABA|1|115 >16_6_HC_humanized_879
QSLEESGGGLVQPGGSLRLSCTASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDSSTL
YLQMNNLRVEDTALYYCAHNQYSGYGFSFWGRGTQVTVSS (SEQ ID NO: 388)
>cl|PUBBABABA|1|115 >16_6_HC_humanized_267
QSLEQSGGGLVQPGESLRLSCAGSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKGRFTISRDNAS
LFLQMNSLRVEDTAVYYCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 389)
>cl|QUBBABABA|1|115 >16_6_HC_humanized_1992
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLVWVSIIVSSGSAYYATWAKGRFTISRDNATL
YLQMNSLRVEDTAVYYCARNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 390)
>cl|RUBBABABA|1|115 >16_6_HC_humanized_1995
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNSTL
YLQMNSLRAEDTAVYYCAKNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 391)
>cl|SUBBABABA|1|115 >16_6_HC_humanized_917
VQLQESGPGLVKPSQTLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYYATWARSRITISETSKNLSL
KLTSVTAADTAVYYCARNQYSGYGFSFWGQGTTVTVSS (SEQ ID NO: 392)
>cl|TUBBABABA|1|115 >16_6_HC_humanized_1934
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNASL
YLQMNSLRAEDTAVYYCARNQYSGYGFSFGIFDYWVTVSS (SEQ ID NO: 393)
>cl|VUBBABABA|1|115 >16_6_HC_humanized_200
VQLQESGPGLVKPSETLSLTCSVSGSDISSYHMGWIRQPAGKGLEWIGIIVSSGSAYYATWARSRVTMSMSKNH
FSLKLRSVTAADTAVYFCARNQYSGYGFSFWGQGTLVTVSS (SEQ ID NO: 394)

Figure 8 (cont.)

>cl|WUBBABABA|1|115 >16_6_HC_humanized_1977
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKGRFTISRSKNTL
YLQMNSLRAEDTAVYYCARNQYSGYGFSFTCPYFDYWVSS (SEQ ID NO: 395)
>cl|XUBBABABA|1|115 >16_6_HC_humanized_2027
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAEGRFTISRDNSTL
YLQMYSLRTEDTAVYYCARNQYSGYGFSFYYYGMGVWVSS (SEQ ID NO: 396)
>cl|YUBBABABA|1|115 >16_6_HC_humanized_1958
VHLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAEGRFTISRDNS
KLYLQMNSLRAEDSATYYCARNQYSGYGFSFFGPPYYYYYMS (SEQ ID NO: 397)
>cl|ZUBBABABA|1|115 >16_6_HC_humanized_1949
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEYVSIIVSSGSAYYATWAKGRFTISRDNSTLY
LQMSSLRAEDTAVYYCVKNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 398)
>cl|BACBABABA|1|115 >16_6_HC_humanized_1905
QSLEESGGRLVTPGTPLTLTCTVSGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNSTL
YLQMNSLRAEDTALYYCARNQYSGYGFSFVRGGYFYHMDS (SEQ ID NO: 399)

Figure 8 (cont.)

16-6 VL humanized sequences -- IMGT-LigM DB (Abysis) clustered at 95% (64 sequences)

>cl|CACBABABA|1|110 >16_6_LC_humanized_586
IVLTQTPSSLSASVGDRITITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSRSGTDFTFTIS
SLRPEDIATYYCLGGYDDDGETAFGGGTKVEIK (SEQ ID NO: 400)
>cl|DACBABABA|1|110 >16_6_LC_humanized_411
IVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPNLLIYRASNLASGVPSRFSGSGSATDFTLTI
SSLQPEDFATYYCLGGYDDDGETAFGGGTRVEIK (SEQ ID NO: 401)
>cl|FACBABABA|1|110 >16_6_LC_humanized_372
IQLTQSPSTLSASVGDRVTITCQSSHSVYYGDWLAWYQQKAGKAPTLLIYRASNLASGVPSRFSGSGSGTEFTLTIS
SLQPDDFATYYCLGGYDDDGETAFGQGTKVDIK (SEQ ID NO: 402)
>cl|GACBABABA|1|110 >16_6_LC_humanized_1996
VVLTQTPSPVSTAVGGTVTLSCQSSHSVYYGDWLAWYQQKPGQAPRLLIYRASNLASGIPDRFSGSGSGTDFTLT
ISRLEPEDFAVYYCLGGYDDDGETAKGPGTEVVVK (SEQ ID NO: 403)
>cl|HACBABABA|2|110 >16_6_LC_humanized_1907 >16_6_LC_humanized_716
LVMTQSPSSLSASEGDRVTITCQSSHSVYYGDWLAWYQQKPGRAPKLLIHRASNLASGVPSRFSGSGSGTEFTLT
ISGLQSEDFATYYCLGGYDDDGETAFGGGTTVDVK (SEQ ID NO: 404)
>cl|LACBABABA|2|110 >16_6_LC_humanized_1945 >16_6_LC_humanized_1451
VELTQPPSPVSAAPGQKVTISCQSSHSVYYGDWLAWYQQLPGTAPKLLIYRASNLASGIPDRFSGSKSGTSATLGI
TGLQTGDEADYYCLGGYDDDGETAFGGGTRLTVL (SEQ ID NO: 405)
>cl|NACBABABA|2|110 >16_6_LC_humanized_1004 >16_6_LC_humanized_283
IQLTQSPSSVSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFALTI
SSLQPEDFATYYCLGGYDDDGETAFGQGTRLEIK (SEQ ID NO: 406)
>cl|PACBABABA|1|110 >16_6_LC_humanized_1971
VVLTQTPSPVSTAVGGTVTITCQSSHSVYYGDWLAWYQQKSGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDFATYYCLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 407)
>cl|QACBABABA|1|110 >16_6_LC_humanized_802
IRMTQSPSSFSASTGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SCLQSEDFATYYCLGGYDDDGETAFGGGTKVEIK (SEQ ID NO: 408)
>cl|RACBABABA|1|110 >16_6_LC_humanized_609
IRLTQSPSFLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTIS
TLQPEDFATYYCLGGYDDDGETAFGQGTKLEIK (SEQ ID NO: 409)

Figure 8 (cont.)

>cl|SACBABABA|1|110 >16_6_LC_humanized_587
VVMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWFQQKPGKAPNLLIYRASNLASGVPSRFSGSGSGTEFTLT
ISSLQPEDFATYYCLGGYDDDGETAFGQGTKVEIK (SEQ ID NO: 410)
>cl|TACBABABA|1|110 >16_6_LC_humanized_305
IQLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWFQQKPGKAPKSLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDSATYYCLGGYDDDGETAFGGGTKVEIK (SEQ ID NO: 411)
>cl|VACBABABA|12|110 >16_6_LC_humanized_1877 >16_6_LC_humanized_860
>16_6_LC_humanized_213 >16_6_LC_humanized_902 >16_6_LC_humanized_334
IQLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDFATYYCLGGYDDDGETAFGGGTKVEIK (SEQ ID NO: 412)
>cl|WACBABABA|2|110 >16_6_LC_humanized_1012 >16_6_LC_humanized_65
IQLTQSPSTLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTIS
SLQPDDFATYYCLGGYDDDGETAFGQGTKLEIK (SEQ ID NO: 413)
>cl|XACBABABA|6|110 >16_6_LC_humanized_988 >16_6_LC_humanized_910
>16_6_LC_humanized_956 >16_6_LC_humanized_2056 >16_6_LC_humanized_672
IVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTIS
SLQPEDFATYYCLGGYDDDGETAFGQGTRLEIK (SEQ ID NO: 414)
>cl|CECBABABA|1|110 >16_6_LC_humanized_253
IVLTQSPSAMSASVGDRVTITCQSSHSVYYGDWLAWFQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTI
SSLQPEDSATYYCLGGYDDDGETAFGQGTKVDIK (SEQ ID NO: 415)
>cl|DECBABABA|1|110 >16_6_LC_humanized_218
IVMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKVPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDVATYYCLGGYDDDGETAFGPGTKVEIK (SEQ ID NO: 416)
>cl|GECBABABA|1|110 >16_6_LC_humanized_136
VVMTQSPSTLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKVLIYRASNLASGVPSRFSGSGSGTEFTL
TISSLQPDDFASYYCLGGYDDDGETAFGPGTKVDIK (SEQ ID NO: 417)
>cl|HECBABABA|1|110 >16_6_LC_humanized_129
IVMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQHKPGKAPRLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPDDFATYYCLGGYDDDGETAFGQGTKVEVK (SEQ ID NO: 418)
>cl|KECBABABA|1|110 >16_6_LC_humanized_109
IQLTQSPSSVSASVGDTITITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSRSGTDFTLTIS
SLQPEDFATYYCLGGYDDDGETAFGQGTKVEIK (SEQ ID NO: 419)

Figure 8 (cont.)

>cl|LECBABABA|1|110 >16_6_LC_humanized_103
IVLTQSPSTLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGQAPKLLIYRASNLASGVPSRFSGSGSGTEFTLSI
NSLQPDDSATYFCLGGYDDDGETAFGQGTKVEIK (SEQ ID NO: 420)
>cl|MECBABABA|1|110 >16_6_LC_humanized_954
IVLTQSPSTLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTIS
SLQPDDFATYYCLGGYDDDGETAFGQGTKAEIK (SEQ ID NO: 421)
>cl|PECBABABA|3|110 >16_6_LC_humanized_851 >16_6_LC_humanized_908
>16_6_LC_humanized_912
VVMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLT
ISSLQPEDFATYYCLGGYDDDGETAFGGGTKVEIK (SEQ ID NO: 422)
>cl|RECBABABA|1|110 >16_6_LC_humanized_17
IQLTQSPSSLSAAVGDRVTIACQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLSI
SSLQPGDFATYYCLGGYDDDGETAFGGGTKVQMK (SEQ ID NO: 423)
>cl|XECBABABA|2|110 >16_6_LC_humanized_108 >16_6_LC_humanized_946
IVLTQSPSSVSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDFATYYCLGGYDDDGETAFGGGTKVEIK (SEQ ID NO: 424)
>cl|ZECBABABA|1|110 >16_6_LC_humanized_882
VVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGFGTDFTFTI
SSLQPEDSATYYCLGGYDDDGETAFGQGTKLEIK (SEQ ID NO: 425)
>cl|BICBABABA|1|110 >16_6_LC_humanized_186
IQLTQSPSTLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTIS
SLQPDDFATYYCLGGYDDDGETAFGQGTKVVVK (SEQ ID NO: 426)
>cl|CICBABABA|1|110 >16_6_LC_humanized_2041
VVLTQTPSPVSTAVGGTVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLT
ISCLQSEDFATYYCLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 427)
>cl|DICBABABA|1|110 >16_6_LC_humanized_202
IRMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKVPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDVATYYCLGGYDDDGETAFGPGTKVVVK (SEQ ID NO: 428)
>cl|FICBABABA|1|110 >16_6_LC_humanized_192
VVMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLT
ISSLQAEDFTTYYCLGGYDDDGETAFGQGTKVEFK (SEQ ID NO: 429)
>cl|GICBABABA|2|110 >16_6_LC_humanized_1982 >16_6_LC_humanized_734
VELTQSPSSVSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFSLTI
SSLQPEDSATYYCLGGYDDDGETAFGQGTKVEIK (SEQ ID NO: 430)

Figure 8 (cont.)

>cl|KICBABABA|2|110 >16_6_LC_humanized_1944 >16_6_LC_humanized_1895
IELTQSPSTLSASVGDRVIISCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFSLTIN
SLQPDDFATYYCLGGYDDDGETAFGPGTKVDIK (SEQ ID NO: 431)
>cl|NICBABABA|2|110 >16_6_LC_humanized_1938 >16_6_LC_humanized_762
VELTQSPDSLAVSLGERATINCQSSHSVYYGDWLAWYQQKPGQPPKLLIYRASNLASGVPDRFSGSGSGTDFTLT
ISSLQAEDVAVYYCLGGYDDDGETAFGGGTKVEIK (SEQ ID NO: 432)
>cl|QICBABABA|2|110 >16_6_LC_humanized_2031 >16_6_LC_humanized_621
VELTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDFATYYCLGGYDDDGETAFGQGTKVEIK (SEQ ID NO: 433)
>cl|SICBABABA|4|110 >16_6_LC_humanized_993 >16_6_LC_humanized_880
>16_6_LC_humanized_23 >16_6_LC_humanized_917
VVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDFATYYCLGGYDDDGETAFGPGTKVDIK (SEQ ID NO: 434)
>cl|VICBABABA|1|110 >16_6_LC_humanized_920
IVMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDIATYYCLGGYDDDGETAFGQGTKVEIK (SEQ ID NO: 435)
>cl|WICBABABA|1|110 >16_6_LC_humanized_278
LVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWCQQKPGKSPTLLIYRASNLASGVPSRFSGSGSGTGFTLTI
SGLQPEDFATYYCLGGYDDDGETAFGGGTKVEIR (SEQ ID NO: 436)
>cl|YICBABABA|1|110 >16_6_LC_humanized_169
IVLTQSPSFLSAFVGDRITITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTIS
GLQPEDFASYYCLGGYDDDGETAFGGGTKLEIK (SEQ ID NO: 437)
>cl|ZICBABABA|1|110 >16_6_LC_humanized_994
IVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKVPKLLIYRASNLASGVPSRFSGSGSGTDFTLTIS
SLQPEDVATYYCLGGYDDDGETAFGQGTKVEIK (SEQ ID NO: 438)
>cl|BOCBABABA|1|110 >16_6_LC_humanized_975
IVLTQSPSTQSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTI
SSLQPDDFATYYCLGGYDDDGETAFGQGTKLEIK (SEQ ID NO: 439)
>cl|DOCBABABA|1|110 >16_6_LC_humanized_230
VVLTQTPSPVSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKVLIYRASNLASGVPSRFSGSGSGTDFTLT
ISTLQPEDFATYYCLGGYDDDGETAFGQGTKLEIK (SEQ ID NO: 440)
>cl|GOCBABABA|1|110 >16_6_LC_humanized_1894
VVLTQTPSPVSTAVGDRVTITCQSSHSVYYGDWLAWYRQKPGKVPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDVATYYGLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 441)

Figure 8 (cont.)

>cl|LOCBABABA|1|110 >16_6_LC_humanized_657
VVLTQTPSPVSTSVGDRVSITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
TSLQPVDFATYYCLGGYDDDGETAFGPGTTVDAK (SEQ ID NO: 442)
>cl|MOCBABABA|2|110 >16_6_LC_humanized_1917 >16_6_LC_humanized_677
VVLTQSPSFLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTI
SSLQ
PEDFATYYCLGGYDDDGETAFGQGTRLEIK (SEQ ID NO: 443)
>cl|POCBABABA|1|110 >16_6_LC_humanized_2038
VVLTQTPSPVSTAVGGRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTI
SSLQDKPFATYYCLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 444)
>cl|ROCBABABA|1|110 >16_6_LC_humanized_21
IQMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKVLIYRASNLASGVPSRFSGSGSGTDFTLT
ISSLQPEDFATYYCLGGYDDDGETAFGPGTKVEVK (SEQ ID NO: 445)
>cl|SOCBABABA|1|110 >16_6_LC_humanized_469
IVLTQSPSLLSASIGDRVTIPCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTISS
LQPEDFATYYCLGGYDDDGETAFGGGTKVDIK (SEQ ID NO: 446)
>cl|TOCBABABA|1|110 >16_6_LC_humanized_2008
VVLTQTPSPVSTAVGGRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLT
IGSLQPEDFAAYFCLGGYDDDGETAFGGGTKVEIK (SEQ ID NO: 447)
>cl|WOCBABABA|1|110 >16_6_LC_humanized_168
IVMTQSPSTLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTI
SGLQPEDFATYYCLGGYDDDGETAFGGGTKLEIK (SEQ ID NO: 448)
>cl|XOCBABABA|1|110 >16_6_LC_humanized_149
IVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKRLIYRASNLASGVPSRFSGSGSGTEFTLTIS
GLQPEDIATYYCLGGYDDDGETAFGQGTKVEIK (SEQ ID NO: 449)
>cl|YOCBABABA|1|110 >16_6_LC_humanized_113
IVLTQSPSSVSASVGDRVTITCQSSHSVYYGDWLAWYQLKPGKAPKLLINRASNLASGVPSRFSGSGSGTDFTLTI
SGLQPEDFATYYCLGGYDDDGETAFGPGTTVDIK (SEQ ID NO: 450)
>cl|ZOCBABABA|4|110 >16_6_LC_humanized_978 >16_6_LC_humanized_965
>16_6_LC_humanized_924 >16_6_LC_humanized_879
IVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTIS
SLQPEDFATYYCLGGYDDDGETAFGGGTKVEIK (SEQ ID NO: 451)

Figure 8 (cont.)

>cl|GUCBABABA|1|110 >16_6_LC_humanized_818
VVLTQTPSSVSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDFATYYCLGGYDDDGETAFGQGTKVEIK (SEQ ID NO: 452)
>cl|HUCBABABA|1|110 >16_6_LC_humanized_12
VVMTQSPSTVSASVGDRVTLTCQSSHSVYYGDWLAWYQQKPGQPPKLLIYRASNLASGVPDRFSGSGSGTDFT
LTISSLQADDFATYYCLGGYDDDGETAFGQGTKVEIK (SEQ ID NO: 453)
>cl|LUCBABABA|1|110 >16_6_LC_humanized_273
LVMTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGEAPKLLIYRASNLASGVPSRFSGSGSGTDFTLT
ISGLQSEDFATYYCLGGYDDDGETAFGQGTKVEIK (SEQ ID NO: 454)
>cl|MUCBABABA|1|110 >16_6_LC_humanized_2032
VVLTQTPSPVSTAVGGTGPINCQSSHSVYYGDWLAWYQQKPGQPPKLLIYRASNLASGVPDRFSGSGSGTDFTL
TISSLQAEDVAVYYCLGGYDDDGETAFGGGTKLEIK (SEQ ID NO: 455)
>cl|PUCBABABA|1|110 >16_6_LC_humanized_267
VVLTQSPSTLAASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTI
SSLQPDDFATYYCLGGYDDDGETAFGQGTKVEVK (SEQ ID NO: 456)
>cl|QUCBABABA|1|110 >16_6_LC_humanized_1992
VVLTQTPSPVSTAVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLT
ISSLQPEDFATYYCLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 457)
>cl|RUCBABABA|1|110 >16_6_LC_humanized_1995
VVLTQTPSPVSTAVGGTVTINCQSSHSVYYGDWLAWYQQKPGQPXKLLIYRASNLASGVPDRFSGSGSGTDFTL
TISSLQAEDVAVYYCLGGYDDDGETAFGQGTEVVVK (SEQ ID NO: 458)
>cl|TUCBABABA|2|110 >16_6_LC_humanized_1934 >16_6_LC_humanized_1977
VVLTQTPSPVSTAVGGTVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTFT
ISSLQPEDIATYYCLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 459)
>cl|VUCBABABA|1|110 >16_6_LC_humanized_200
VVLTQTPSPVSTAVGERATINCQSSHSVYYGDWLAWYQQKPGQPPKLLIYRASNLASGVPDRFSGTGSGTDFTL
TISSLQAEDVAVYYCLGGYDDDGETAFGGGTKVVVK (SEQ ID NO: 460)
>cl|XUCBABABA|1|110 >16_6_LC_humanized_2027
VVLTQTPSPVSTAVGGTVTITCQSSHSVYYGDWLAWYQQKPGKAPKRLIYRASNLASGVPSRFSGSGSGTEFTLT
ISSLQPEDFATYYXLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 461)
>cl|YUCBABABA|2|110 >16_6_LC_humanized_1958 >16_6_LC_humanized_1949
VVLTQTPSPVSTAVGGTVTIPCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTI
SSLQPDDFATYYCLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 462)
>cl|BADBABABA|1|110 >16_6_LC_humanized_1905
VVLTQTPSPVSTAVGGTVTINCQSSHSVYYGDWLAWYQQKPGQPPKLLIYRASNLASGVPDRFSGSGSGTDFTL
TISSLQAEDVAVYYCLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 463)

Figure 8 (cont.)

16-6 VH humanized sequences -- germline database clustered at 90% (3 sequences)

>cl|CABBABABA|43|115 >16_6_HC_humanized_775 >16_6_HC_humanized_722 >16_6_HC_humanized_563 >16_6_HC_humanized_139 >16_6_HC_humanized_988
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNST
LYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 464)
>cl|DABBABABA|39|115 >16_6_HC_humanized_724 >16_6_HC_humanized_565 >16_6_HC_humanized_141 >16_6_HC_humanized_990 >16_6_HC_humanized_985
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRSKNT
LYLQMNSLKTEDTAVYYCTRNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 465)
>cl|REBBABABA|18|115 >16_6_HC_humanized_365 >16_6_HC_humanized_364 >16_6_HC_humanized_363 >16_6_HC_humanized_360 >16_6_HC_humanized_359
VQLQESGPGLVKPSETLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYYATWAKSRVTISTSKNQFS
LKLSSVTAADTAVYYCARNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 466)

16-6 VL humanized sequences -- germline database clustered at 90% (1 sequences)

>cl|CACBABABA|100|110 >16_6_LC_humanized_775 >16_6_LC_humanized_724 >16_6_LC_humanized_722 >16_6_LC_humanized_565 >16_6_LC_humanized_563
VVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDFATYYCLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 467)

Figure 8 (cont.)

16-6 VH humanized sequences -- germline database clustered at 95% (10 sequences)

>cl|CABBABABA|13|115 >16_6_HC_humanized_775 >16_6_HC_humanized_722
>16_6_HC_humanized_563 >16_6_HC_humanized_139 >16_6_HC_humanized_987
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEYVSIIVSSGSAYYATWAKGRFTISRDNSTL
YLQMGSLRAEDMAVYYCARNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 468)
>cl|DABBABABA|12|115 >16_6_HC_humanized_724 >16_6_HC_humanized_565
>16_6_HC_humanized_141 >16_6_HC_humanized_989 >16_6_HC_humanized_936
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRSKNS
LYLQMNSLKTEDTAVYYCARNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 469)
>cl|MABBABABA|9|115 >16_6_HC_humanized_990 >16_6_HC_humanized_937
>16_6_HC_humanized_672 >16_6_HC_humanized_407 >16_6_HC_humanized_248
VQLVESGGGLVQPGGSLKLSCAASGSDISSYHMGWVRQASGKGLEWVGIIVSSGSAYYATWAKGRFTISRSKNT
AYLQMNSLKTEDTAVYYCTRNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 470)
>cl|NABBABABA|27|115 >16_6_HC_humanized_988 >16_6_HC_humanized_935
>16_6_HC_humanized_670 >16_6_HC_humanized_405 >16_6_HC_humanized_246
VQLVESGGGLVQPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVSIIVSSGSAYYATWAKGRFTISRDNST
LYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 471)
>cl|PABBABABA|9|115 >16_6_HC_humanized_985 >16_6_HC_humanized_932
>16_6_HC_humanized_667 >16_6_HC_humanized_402 >16_6_HC_humanized_243
VQLVESGGGLVQPGRSLRLSCTASGSDISSYHMGWFRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRSKSIA
YLQMNSLKTEDTAVYYCTRNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 472)
>cl|QABBABABA|9|115 >16_6_HC_humanized_973 >16_6_HC_humanized_920
>16_6_HC_humanized_655 >16_6_HC_humanized_390 >16_6_HC_humanized_231
VQLVESGGGLVKPGGSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVGIIVSSGSAYYATWAKGRFTISRSKNT
LYLQMNSLKTEDTAVYYCTTNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 473)
>cl|REBBABABA|12|115 >16_6_HC_humanized_365 >16_6_HC_humanized_364
>16_6_HC_humanized_363 >16_6_HC_humanized_360 >16_6_HC_humanized_312
VQLQESGPGLVKPSETLSLTCTVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYYATWAKSRVTISTSKNQFS
LKLSSVTAADTAVYYCARNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 474)
>cl|WEBBABABA|3|115 >16_6_HC_humanized_359 >16_6_HC_humanized_306
>16_6_HC_humanized_41
LQLQESGSGLVKPSQTLSLTCAVSGSDISSYHMGWIRQPPGKGLEWIGIIVSSGSAYYATWAKSRVTISRSKNQFS
LKLSSVTAADTAVYYCARNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 475)

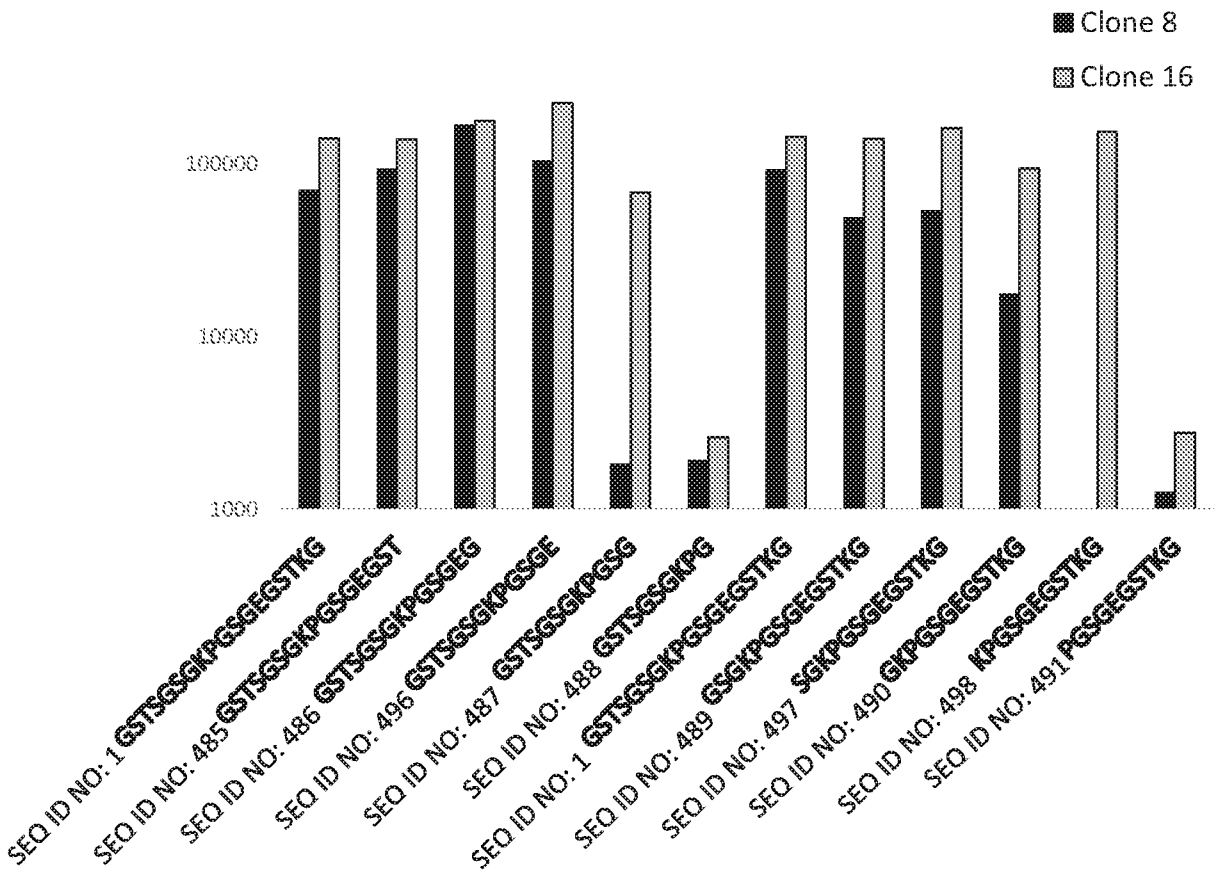
Figure 8 (cont.)

>cl|XEBBABABA|3|115 >16_6_HC_humanized_357 >16_6_HC_humanized_304
>16_6_HC_humanized_39
VQLQESGPGLVKPPGTLSLTCAVSGSDISSYHMGWVRQPPGKGLEWIGIIVSSGSAYYATWAKSRVTISKSKNQF
SLKLSSVTAADTAVYCCARNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 476)
>cl|CIBBABABA|3|115 >16_6_HC_humanized_343 >16_6_HC_humanized_290
>16_6_HC_humanized_25
VQLVESGGGVVQPGRSLRLSCAASGSDISSYHMGWVRQAPGKGLEWVAIIVSSGSAYYATWAKGRFTISRDNS
TLYLQMNSLRAEDTAVYYCARNQYSGYGFSFWGPGTLVTVSS (SEQ ID NO: 477)

16-6 VL humanized sequences -- germline database clustered at 95% (7 sequences)

>cl|CACBABABA|3|110 >16_6_LC_humanized_775 >16_6_LC_humanized_724
>16_6_LC_humanized_722
VVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTFTI
SSLQPEDIATYYCLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 478)
>cl|GACBABABA|2|110 >16_6_LC_humanized_565 >16_6_LC_humanized_563
VVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKRLIYRASNLASGVPSRFSGSGSGTEFTLTI
SSLQPEDFATYYCLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 479)
>cl|KACBABABA|2|110 >16_6_LC_humanized_141 >16_6_LC_humanized_139
VVLTQSPSSFSASTGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SCLQSEDFATYYCLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 480)
>cl|MACBABABA|62|110 >16_6_LC_humanized_990 >16_6_LC_humanized_988
>16_6_LC_humanized_985 >16_6_LC_humanized_973 >16_6_LC_humanized_937
VVLTQSPSSVSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDFATYYCLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 481)
>cl|WACBABABA|6|110 >16_6_LC_humanized_672 >16_6_LC_humanized_670
>16_6_LC_humanized_667 >16_6_LC_humanized_655 >16_6_LC_humanized_671
VVLTQSPSSLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKVPKLLIYRASNLASGVPSRFSGSGSGTDFTLTI
SSLQPEDVATYYCLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 482)
>cl|GECBABABA|6|110 >16_6_LC_humanized_248 >16_6_LC_humanized_246
>16_6_LC_humanized_243 >16_6_LC_humanized_231 >16_6_LC_humanized_247
VVLTQSPSFLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTI
SSLQPEDFATYYCLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 483)
>cl|YICBABABA|19|110 >16_6_LC_humanized_47 >16_6_LC_humanized_46
>16_6_LC_humanized_45 >16_6_LC_humanized_42 >16_6_LC_humanized_41
VVLTQSPSTLSASVGDRVTITCQSSHSVYYGDWLAWYQQKPGKAPKLLIYRASNLASGVPSRFSGSGSGTEFTLTI
SSLQPDDFATYYCLGGYDDDGETAFGGGTEVVVK (SEQ ID NO: 484)

Figure 8 (cont.)



Clone 8
GSTSGSGKPGSGEGSTKG

Clone 16
GSTSGSGKPGSGEGSTKG

Figure 9

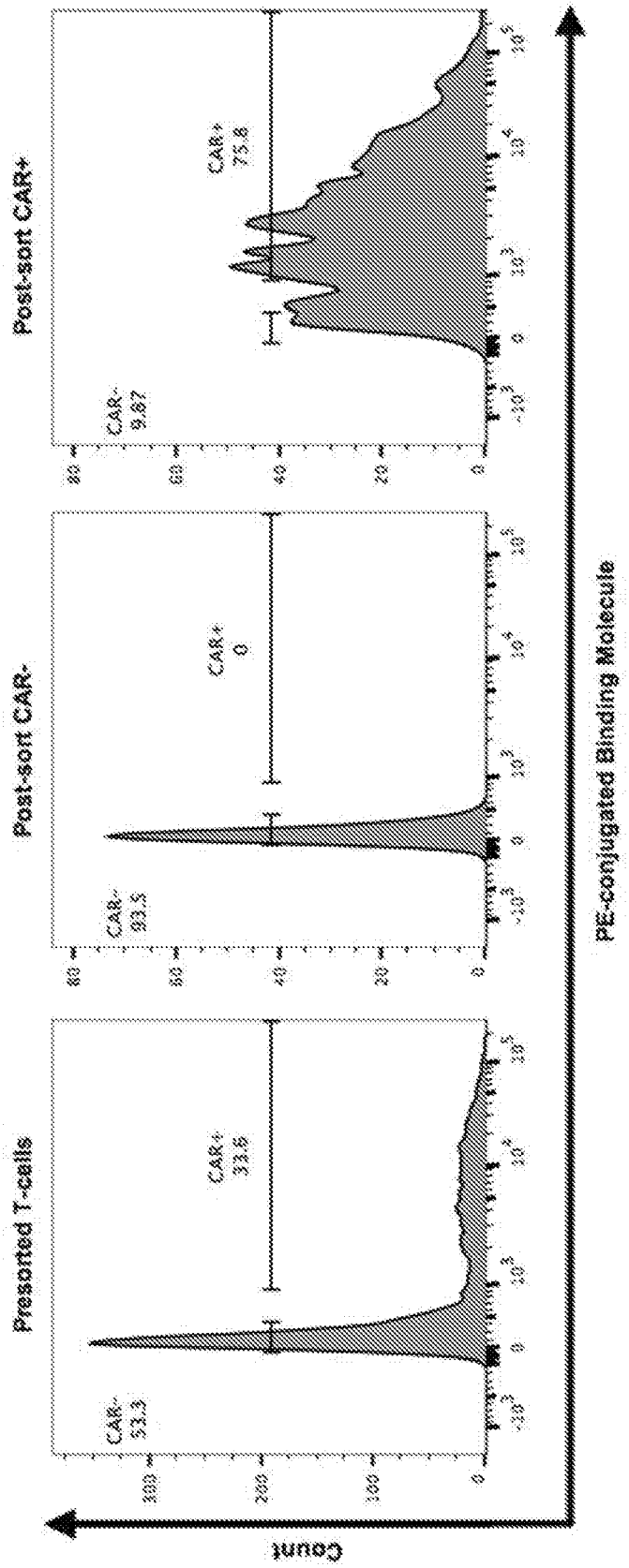

Presorted T-cells
CAR-
53.3
CAR+
33.6
Post-sort CAR-
CAR-
93.5
CAR+
0
Post-sort CAR+
CAR-
9.67
CAR+
75.8
Count
PE-conjugated Binding Molecule

Figure 10

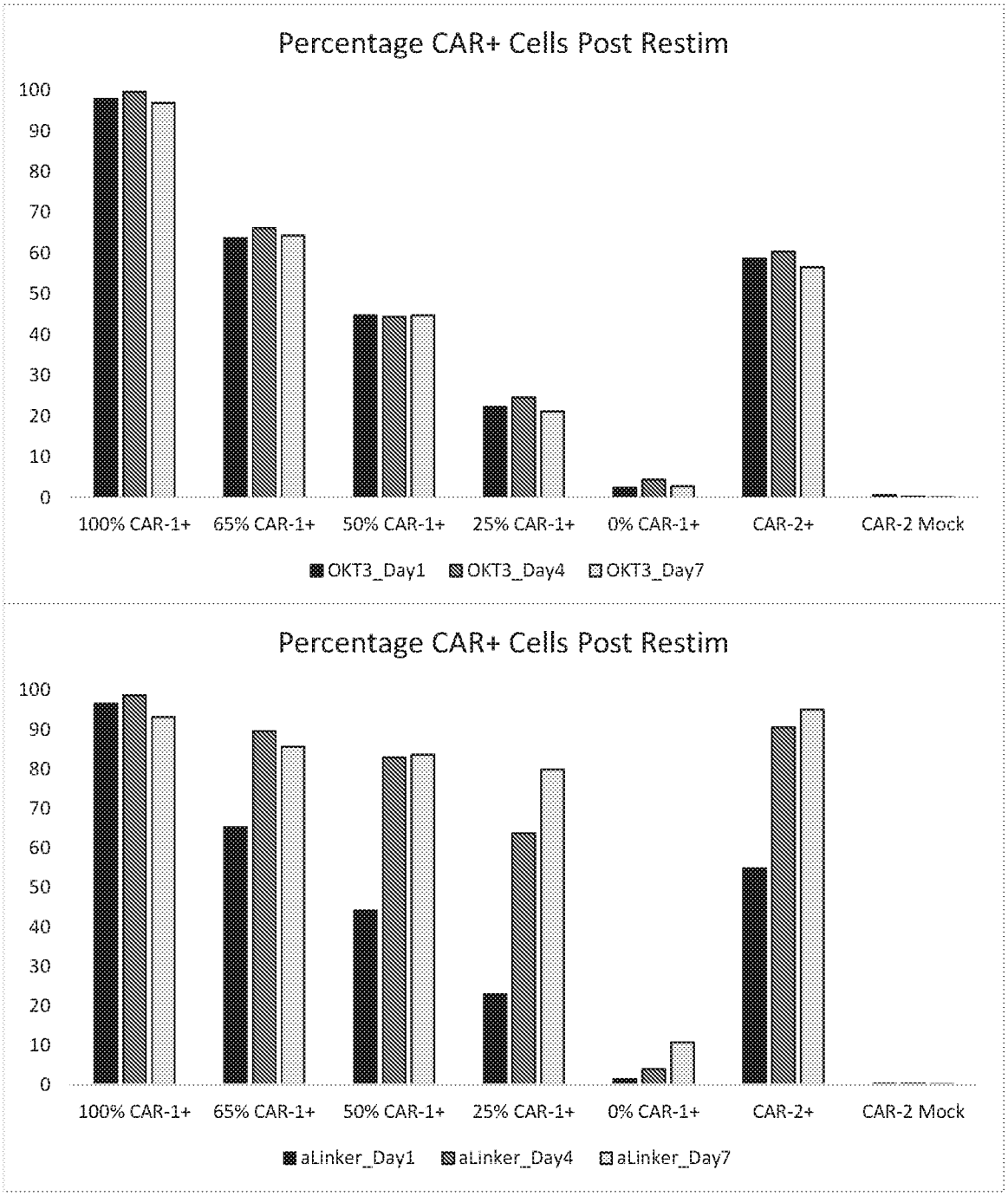
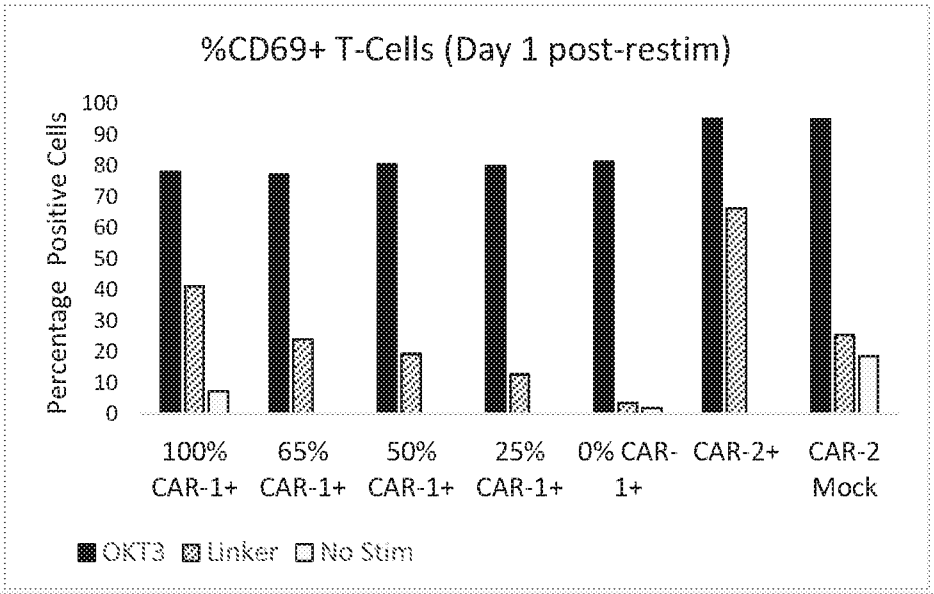

Percentage CAR+ Cells Post Restim
100
90
80
70
60
50
40
30
20
10
0
100% CAR-1+
65% CAR-1+
50% CAR-1+
25% CAR-1+
0% CAR-1+
CAR-2+
CAR-2 Mock
OKT3_Day1
OKT3_Day4
OKT3_Day7
Percentage CAR+ Cells Post Restim
100
90
80
70
60
50
40
30
20
10
0
100% CAR-1+
65% CAR-1+
50% CAR-1+
25% CAR-1+
0% CAR-1+
CAR-2+
CAR-2 Mock
aLinker_Day1
aLinker_Day4
aLinker_Day7

Figure 11


%CD69+ T-Cells (Day 1 post-restim)
Percentage Positive Cells
100
90
80
70
60
50
40
30
20
10
0
100% CAR-1+
65% CAR-1+
50% CAR-1+
25% CAR-1+
0% CAR-1+
CAR-2+
CAR-2 Mock
OKT3
Linker
No Stim

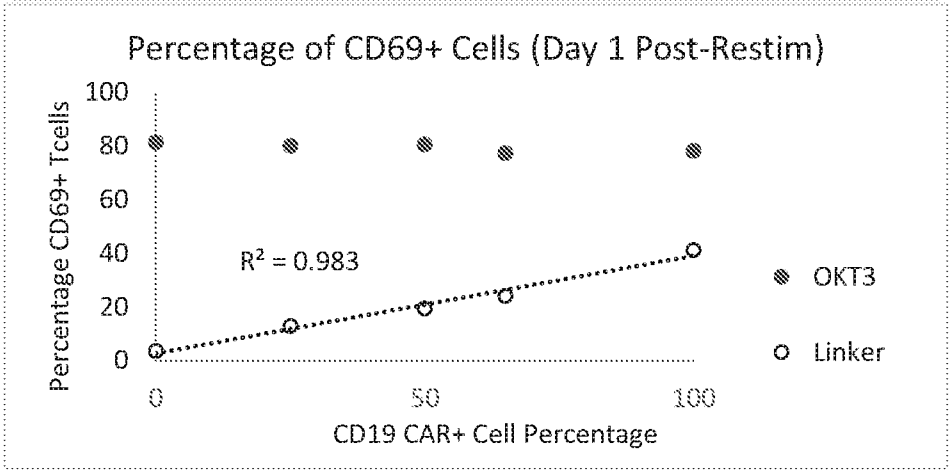
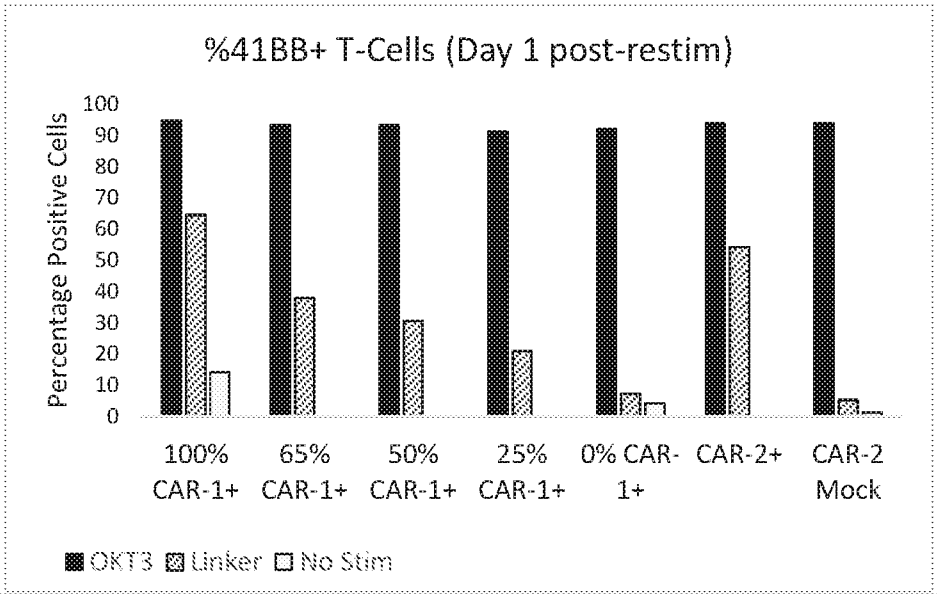

Percentage of CD69+ Cells (Day 1 Post-Restim)
Percentage CD69+ Tcells
100
80
60
40
20
0
R² = 0.983
0
50
100
CD19 CAR+ Cell Percentage
OKT3
Linker

Figure 12A


%41BB+ T-Cells (Day 1 post-restim)
Percentage Positive Cells
100
90
80
70
60
50
40
30
20
10
0
100% CAR-1+
65% CAR-1+
50% CAR-1+
25% CAR-1+
0% CAR-1+
CAR-2+
CAR-2 Mock
OKT3
Linker
No Stim

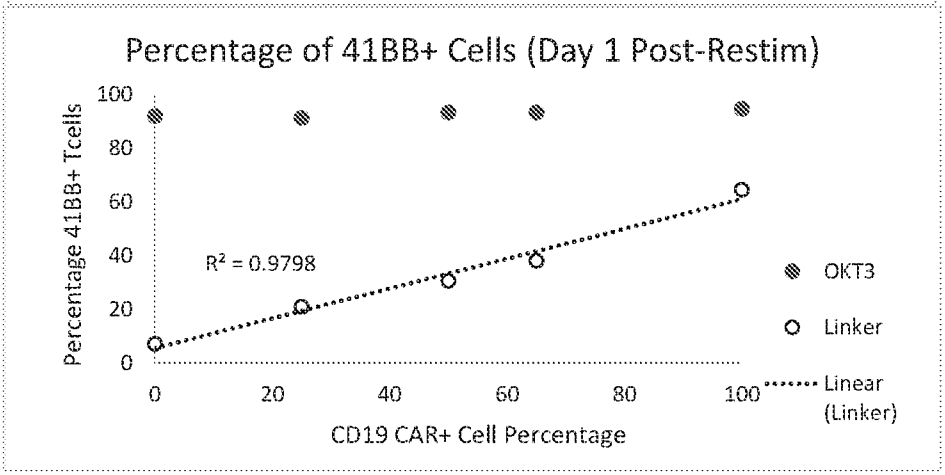

Percentage of 41BB+ Cells (Day 1 Post-Restim)
Percentage 41BB+ Tcells
100
80
60
40
20
0
R² = 0.9798
0
20
40
60
80
100
CD19 CAR+ Cell Percentage
OKT3
Linker
Linear (Linker)

Figure 12B

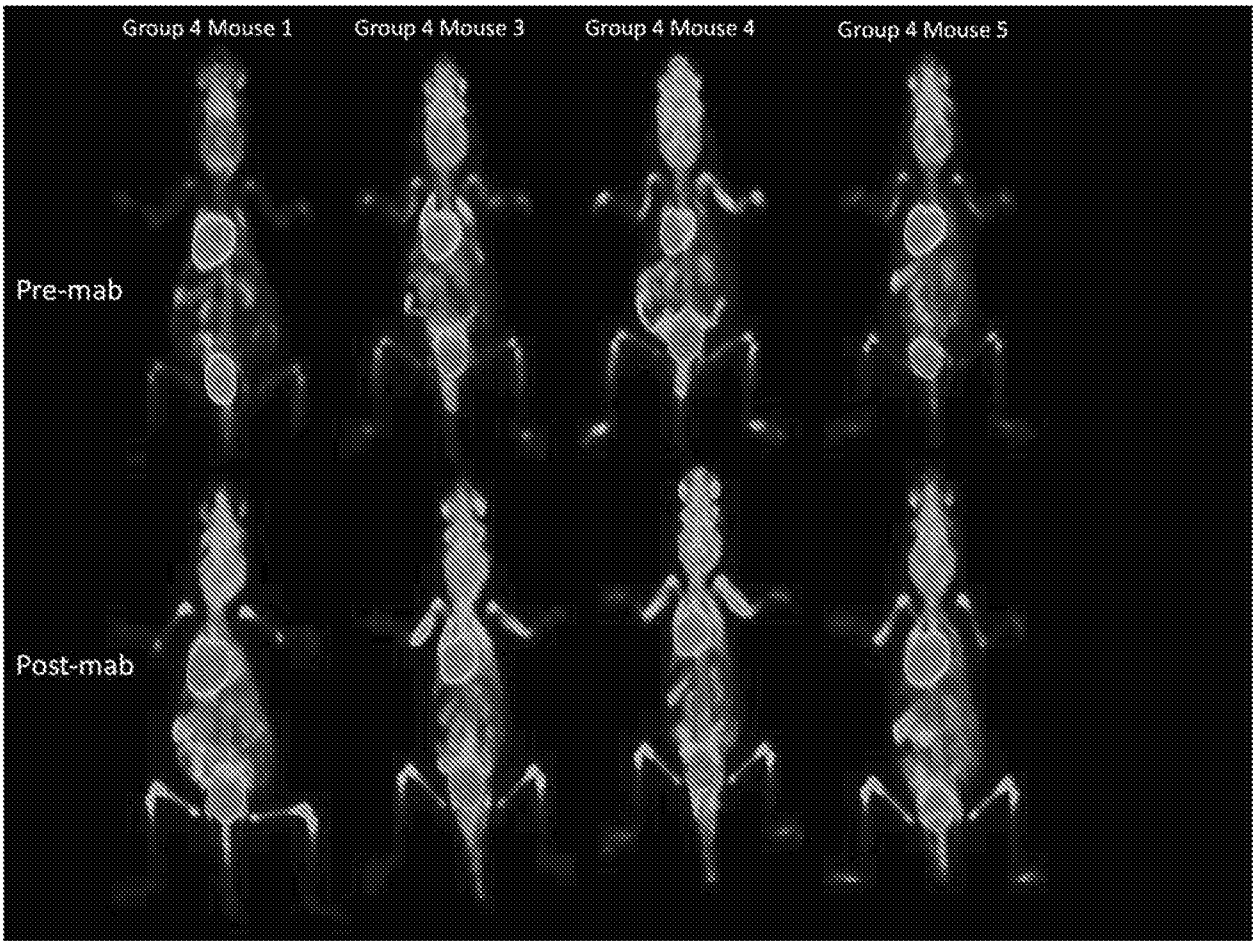

Group 4 Mouse 1
Group 4 Mouse 3
Group 4 Mouse 4
Group 4 Mouse 5
Pre-mab
Post-mab

Figure 13

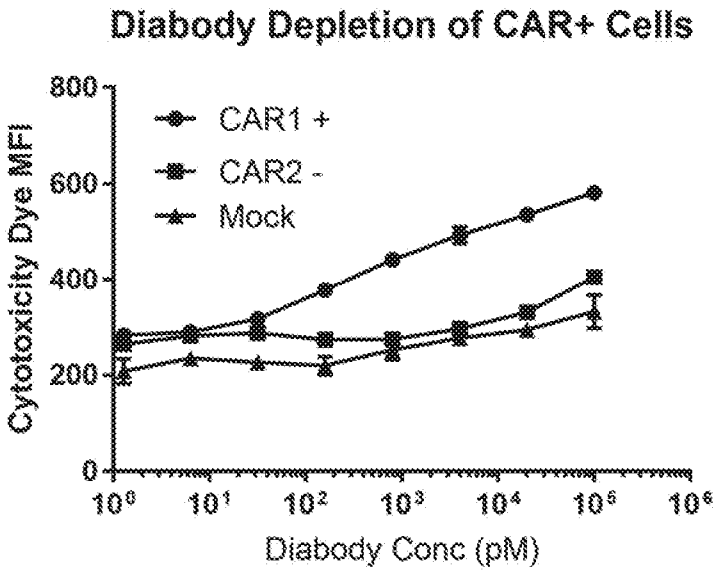


Figure 14A

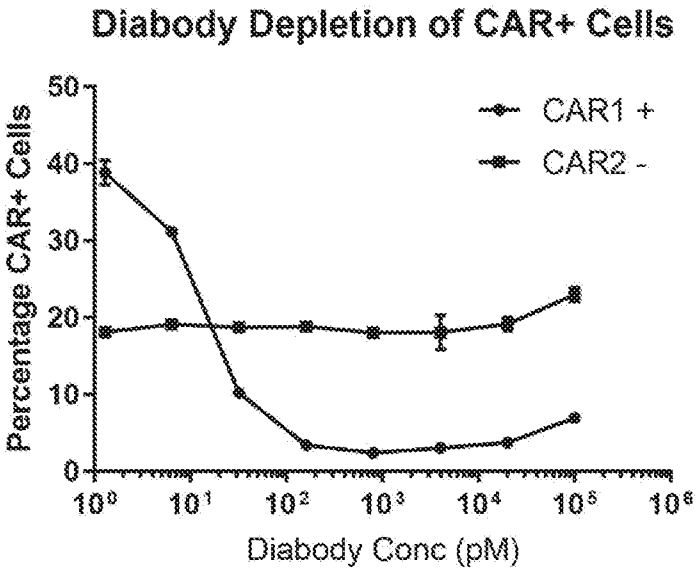


Figure 14B