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

(57) Abstract: Isolated antigen binding molecules that specifically bind to an anti-CD19 scFv comprising SEQ ID NO: 1 are provided. The antigen binding molecules can be used in the methods provided herein.

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ANTIGEN BINDING MOLECULES AND METHODS OF USE THEREOF

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Patent Application Serial Number 62/401,007 filed September 28, 2016, the entire disclosure of which is hereby incorporated by reference.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing, which has been submitted electronically in ASCII format, and is hereby incorporated by reference in its entirety. Said ASCII copy, created on September 26, 2017, is named K-103602_SL.txt and is 74,224 bytes in size.

FIELD OF THE INVENTION

[0003] This disclosure relates to antigen binding molecules, such as antibodies, which specifically bind to the anti-CD19 scFv FMC63, as well as 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, and fragments such as Fabs, $F(ab')_2$, scFvs, etc, are used in immunotherapy and solid phase-based applications such as biosensors, affinity chromatography, and immunoassays. These antibodies and other antigen binding molecules gain their utility by virtue of their ability to specifically bind their targets.

[0005] Anti-idiotypic antibodies are a subset of antibodies, and are antibodies raised against immunizing antibodies. These anti-idiotypic antibodies

demonstrated specific binding against the idiotopes (unique antigenic determinants on the surface of the antibodies) of the immunizing antibodies. Anti-idiotypic antibodies can be generally classified into three distinct groups: (1) antibodies are those that recognize idiotopes distinct from the antigen-binding site (ABS) on immunizing antibodies; (2) antibodies that recognize epitopes within the ABS and mimic the structure, and forming the so-called "internal image," of the nominal antigen; and (3) antibodies that recognize epitopes within the ABS without the structural resemblance of the nominal antigen (*see*, *e.g.*, Pan *et al.*, (1995) *FASEB J* 9:43-49).

[0006] FMC63 is an IgG2a mouse monoclonal antibody that recognizes CD19, which is expressed on the surface of B cells (Zola *et al.*, (1991) *Immunol Cell Biol* 69:411-22). Single chain variable fragments (scFv) formed from FMC63 comprise the targeting component of some chimeric antigen receptors (CARs) (Kochenderfer *et al.*, (2009) *J Immunother* 32(7):689-702), and the scFv of FMC63 has previously been used to generate anti-FMC63 antibodies (Jena *et al.*, (2013) *PLoS ONE* 8(3):e57838).

[0007] Disclosed herein are rabbit antigen binding molecules, including antibodies, that specifically bind to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), as well as molecules comprising these sequences and cells presenting such molecules. Humanized forms of the disclosed rabbit antigen binding molecules also form as aspect of the disclosure. Applications and uses of these antigen binding molecules are also disclosed.

SUMMARY OF THE INVENTION

[0008] In one aspect, an isolated antigen binding molecule that specifically binds a molecule comprising SEQ ID NO: 1 is provided. In some embodiments, the antigen binding molecule specifically binds a molecule comprising one or more peptides (e.g., complementarity determining regions (CDRs)) selected from the group consisting of SEQ ID NOs:74-82. In some 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 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 IgG3 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.

[0009] In some embodiments, the antigen binding molecule comprises a heavy chain (HC) and in further embodiments the HC comprises a heavy chain variable region (VH) sequence selected from the group consisting of SEQ ID NOs: 3, 15, 21, 33, 39 and 51. In still other embodiments, the variable region (VH) of the antigen binding molecule 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: 5, 23, 41 and 53. In some embodiments, the antigen binding molecule comprises a heavy chain CDR2 selected from the group consisting of SEQ ID NOs: 6, 24, 42 and 54. In some embodiments the antigen binding molecule comprises a heavy chain CDR3 selected from the group consisting of SEQ ID NOs: 7, 25, 43 and 55. In additional embodiments, the antigen binding molecule comprises a heavy chain comprising a heavy chain CDR1, a heavy chain CDR2, and a heavy chain CDR3, each CDR comprising an amino acid sequence shown in FIGURES 5-21. In still further embodiments, an antigen binding molecule 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 provided herein.

[0010] In some embodiments, the antigen binding molecule comprises a light chain (LC) and in further embodiments the LC comprises a light chain variable region (VL) sequence selected from the group consisting of SEQ ID NOs: 8, 18, 27, 36, 45 and 57. In additional embodiments, the variable region (VL) and 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: 11, 29, 47 and 59. In some embodiments, the antigen binding molecule comprises a light chain CDR2 selected from the group consisting of SEQ ID NOs: 12, 30, 48 and 60. In some embodiments, the antigen binding molecule comprises a light chain CDR3 selected from the group consisting of SEQ ID NOs: 13, 31, 49 and 61. In some embodiments, 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 one of FIGURES 5-21. In still further embodiments, an antigen binding molecule 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 VL of an antigen binding molecule provided herein.

[0011] In some embodiments, an antigen binding molecule comprises (a) a VH comprising the amino acid sequence of SEQ ID NO: 3; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 9. In some embodiments, an antigen binding molecule comprises: (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 5; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 6; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 7; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 11; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 12; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 13.

[0012] In some embodiments, an antigen binding molecule comprises (a) a VH comprising the amino acid sequence of SEQ ID NO: 15; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 18. In some embodiments, an antigen binding molecule comprises (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 5; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 6; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 7; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 11; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 12; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 13.

[0013] In some embodiments, an antigen binding molecule comprises (a) a VH comprising the amino acid sequence of SEQ ID NO: 21; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 27. In some embodiments, an antigen binding molecule comprises (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 23; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 24; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 25; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 29; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 30; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 31.

[0014] In some embodiments, an antigen binding molecule comprises (a) a VH comprising the amino acid sequence of SEQ ID NO: 33; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 36. In some embodiments, an antigen binding molecule comprises (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 23;

(b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 24; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 25; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 29; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 30; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 31.

[0015] In some embodiments, an antigen binding molecule comprises (a) a VH comprising the amino acid sequence of SEQ ID NO: 39; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 45. In some embodiments, an antigen binding molecule comprises (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 41; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 42; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 43; (d) VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 47; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 48; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 49.

[0016] In a specific embodiment, an antigen binding molecule comprises (a) a VH comprising the amino acid sequence of SEQ ID NO: 51; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 57. In some embodiments, an antigen binding molecule comprises (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 53; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 54; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 55; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 59; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 60; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 61.

[0017] In various embodiments, an antigen binding molecule provided herein further comprises a detectable label, and 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 various embodiments, a fluorescent label is 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-phycoeryhring (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

[0018] In another aspect, a composition comprising an antigen binding molecule disclosed herein is provided. Also provided is a polynucleotide encoding the heavy chain of an antigen binding molecule disclosed herein, and a polynucleotide encoding the light chain of an antigen binding molecule disclosed herein. A vector comprising the polynucleotides is also disclosed. Further, a cell comprising one or more such vectors is disclosed. In various embodiments, 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. A method of making an antigen binding molecule disclosed herein comprising incubating a cell disclosed herein under suitable conditions is provided.

[0019] 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 SEQ ID NO: 1, is provided. In some embodiments the method comprises (a) providing 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 SEQ ID NO: 1; (b) providing an aliquot of the sample comprising a population of cells presenting a therapeutic molecule comprising SEQ ID NO: 1; (c) providing an antigen binding molecule that specifically binds the SEQ ID NO: 1, the antigen binding molecule further comprising 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 SEQ ID NO: 1 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.

[0020] In some embodiments of the method, (a) the molecule comprising SEQ ID NO: 1 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 another embodiment, the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof. In an additional embodiment, 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. In further embodiments, the fluorescent label is 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-phycoeryhring (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry. In additional embodiments, the immune cell is a T cell and in still further embodiments the T cell is disposed *in vitro* or the T cell is disposed *in vivo*. In other embodiments, the T cell is in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media. In some embodiments, the T cell is an autologous T cell, and in other embodiments the T cell is an allogenic T cell. In an embodiment, the dose is $1.0x10^6$ cells per kilogram of the subject. Additionally, in various embodiments of the disclosed method the antigen binding molecule comprises an antigen binding molecule disclosed herein, and humanized forms thereof.

[0021] 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 CDR sequences according to any one of SEQ ID Nos: 74-82, is provided. In some embodiments, the method comprises (a) providing 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 CDR sequences according to any one of SEQ ID Nos: 74-82; (b) providing an aliquot of the sample comprising a population of cells presenting a therapeutic molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82; (c) providing an antigen binding molecule that specifically binds a molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82, the antigen binding molecule further comprising 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 CDR sequences according to any one of SEQ ID Nos: 74-82 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.

[0022] In some embodiments of the method, (a) the molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82 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 some embodiments, the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof. In some 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. In further embodiments, the fluorescent label is 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-phycoeryhring (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry. In additional embodiments, the immune cell is a T cell and in still further embodiments the T cell is disposed *in vitro* or the T cell is disposed *in vivo*. In other embodiments, the T cell is in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media. In some embodiments, the T cell is an autologous T cell, and in other embodiments the T cell is an allogenic T cell. In an embodiment, the dose is $1.0x10^6$ cells per kilogram of the subject. Additionally, in various embodiments of the disclosed method the antigen binding molecule comprises an antigen binding molecule disclosed herein, and humanized forms thereof.

[0023] In another aspect, a method of determining a number of cells presenting a molecule comprising SEQ ID NO: 1 in a sample is provided. In an embodiment, the method comprises (a) providing a sample comprising cells known or suspected to be presenting a molecule comprising SEQ ID NO: 1; (b) contacting the sample of (a) with an antigen binding molecule that specifically binds the molecule comprising SEQ ID NO: 1, the antigen binding molecule further comprising 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.

[0024] In some embodiments of the disclosed method, (a) the molecule comprising SEQ ID NO: 1 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 some embodiments, the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors,

BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof. In some 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. In some embodiments, the fluorescent label is 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-phycoeryhring (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry. In additional embodiments, the immune cell is a T cell and in still further embodiments the T cell is disposed *in vitro* or the T cell is disposed *in vivo*. In other embodiments, the T cell is in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media. In some embodiments, the T cell is an autologous T cell, and in other embodiments the T cell is an allogenic T cell. Additionally, in various embodiments of the disclosed method, the antigen

binding molecule comprises an antigen binding molecule disclosed herein, and humanized forms thereof.

[0025] In another aspect, a method of determining a number of cells presenting a molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82 in a sample is provided. In some embodiments, the method comprises (a) providing a sample comprising cells known or suspected to be presenting a molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82; (b) contacting the sample of (a) with an antigen binding molecule that specifically binds the molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82 is provided, the antigen binding molecule further comprising 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.

[0026] In some embodiments of the disclosed method, (a) the molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82 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 some embodiments, the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that

specifically binds with CD83, and combinations thereof. In some 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. In some embodiments, the fluorescent label is 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-phycoeryhring (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry. In additional embodiments, the immune cell is a T cell and in still further embodiments the T cell is disposed *in vitro* or the T cell is disposed *in vivo*. In other embodiments, the T cell is in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media. In some embodiments, the T cell is an autologous T cell, and in other embodiments the T cell is an allogenic T cell. Additionally, in various embodiments of the disclosed method the antigen binding molecule comprises an antigen binding molecule disclosed herein, and humanized forms thereof.

[0027] In another aspect, a method of isolating a molecule comprising SEQ ID NO: 1, is provided. In an embodiment, the method comprises (a) providing a sample known or suspected to comprise a molecule comprising SEQ ID NO: 1; (b) providing an antigen binding molecule that specifically binds a molecule comprising SEQ ID NO: 1, 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 the molecule comprising SEQ ID NO: 1 and the antigen binding molecule; (d) separating any molecules not part of a binding complex from formed binding complexes; and (e) separating a formed

binding complex into: (a) a molecule comprising SEQ ID NO: 1, and (b) an antigen binding molecule.

[0028] In embodiments of the disclosed method, the molecule comprising SEQ ID NO: 1 is a CAR. In embodiments, the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof. In some 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. some 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. In some embodiments, the fluorescent label is 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-phycoeryhring (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry. Additionally, in various embodiments of the disclosed method the antigen binding molecule comprises an antigen binding molecule disclosed herein, and humanized forms thereof.

[0029] In another aspect, a method of isolating a molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82, is provided. In an embodiment, the method comprises (a) providing a sample known or suspected to comprise a molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82; (b) providing an antigen binding molecule that specifically binds a molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82, 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 the molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82 and the antigen binding molecule; (d) separating any molecules not part of a binding complex from formed binding complexes; and (e) separating a formed binding complex into: (a) a molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82, and (b) an antigen binding molecule.

[0030] In some embodiments of the disclosed method, the molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82 is a CAR. In embodiments, the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT,

HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof. In some 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 some 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. In some embodiments, the fluorescent label is 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-phycoeryhring (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry. Additionally, in various embodiments of the disclosed method the antigen binding molecule comprises an antigen binding molecule disclosed herein, and humanized forms thereof.

[0031] In another aspect, a method of determining the presence or absence of a molecule comprising SEQ ID NO: 1 in a sample. In some embodiments, the method comprises (a) providing a sample known or suspected to comprise a molecule comprising SEQ ID NO: 1; (b) providing an antigen binding molecule comprising a detectable label that specifically binds a molecule comprising SEQ ID NO: 1; (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.

[0032] In some embodiments, the molecule comprising SEQ ID NO: 1 is a CAR, and in further embodiments, the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof. In additional 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 further 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. In still further embodiments, the fluorescent label is 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-phycoeryhring (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry. Additionally, in various embodiments of the disclosed method the antigen binding molecule comprises an antigen binding molecule disclosed herein, and humanized forms thereof.

[0033] In another aspect, a method of determining the presence or absence of a molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82 in a sample. In some embodiments, the method comprises (a) providing a sample known or suspected to comprise a molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82; (b) providing an antigen binding molecule comprising a detectable label that specifically binds a molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82; (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.

[0034] In some embodiments, the molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82 is a CAR, and in further embodiments, the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3),

LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof. In additional 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 further 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. In still further embodiments, the fluorescent label is 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-phycoeryhring (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP),

mKate (TagFP635), TurboFP635, mPlum, and mRaspberry. Additionally, in various embodiments of the disclosed method the antigen binding molecule comprises an antigen binding molecule disclosed herein, and humanized forms thereof.

[0035] In yet another aspect, a method of increasing the concentration of cells presenting a molecule comprising SEQ ID NO: 1 is provided. In some embodiments, the method comprises (a) providing a sample comprising a cell known or suspected to present a molecule comprising SEQ ID NO: 1; (b) providing an antigen binding molecule that specifically binds a molecule comprising SEQ ID NO: 1, 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 the molecule comprising SEQ ID NO: 1 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.

[0036] In an embodiment, (a) the molecule comprising SEQ ID NO: 1 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 other embodiments, the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof. In additional embodiments, the

immune cell is a T cell and in still further embodiments the T cell is disposed *in vitro* or the T cell is disposed *in vivo*. In other embodiments, the T cell is in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media. In some embodiments, the T cell is an autologous T cell, and in other embodiments the T cell is an allogenic T cell. Additionally, in various embodiments of the disclosed method the antigen binding molecule comprises an antigen binding molecule disclosed herein, and humanized forms thereof. In further 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. In embodiments, the fluorescent label is 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-phycoeryhring (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

[0037] In yet another aspect, a method of increasing the concentration of cells presenting a molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82 is provided. In an embodiment, the method comprises (a) providing a sample comprising a cell known or suspected to present a molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82; (b) providing an antigen binding molecule that specifically binds a molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82, 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 the molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82 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.

[0038] In an embodiment, (a) the molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82 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 other embodiments, the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof. In additional embodiments, the immune cell is a T cell and in still further embodiments the T cell is disposed *in vitro* or the T cell is disposed *in vivo*. In other embodiments, the T cell is in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media. In some embodiments, the T cell is an autologous T cell, and in other embodiments the T cell is an allogenic T cell. Additionally, in various embodiments of the disclosed method the antigen binding molecule comprises an antigen binding molecule disclosed herein, and humanized forms thereof. In further 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. In embodiments, the fluorescent label is 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-phycoeryhring (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

[0039] In another aspect, a method of depleting a population of immune cells presenting a molecule comprising SEQ ID NO: 1 is provided. In some embodiments, the method comprises (a) providing a population of immune cells to be depleted, wherein the immune cells are known or suspected to be presenting a molecule comprising SEQ ID NO: 1; and (b) contacting the immune cells with an antigen binding molecule that specifically binds to (a) the molecule comprising SEQ ID NO: 1, and (b) an activating molecule expressed on the surface of the an immune cell not presenting the molecule comprising SEQ ID NO:1, under conditions that permit the formation of a ternary binding complex comprising the molecule comprising SEQ ID NO: 1, the activating molecule and the antigen binding molecule. In further embodiments, (a) the molecule comprising SEQ ID NO: 1 is a CAR; and (b) 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 still further embodiments, the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic

Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof. In additional embodiments, the immune cell is a T cell and in still further embodiments the T cell is disposed *in vitro* or the T cell is disposed *in vivo*. In other embodiments, the T cell is in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media. In some embodiments, the T cell is an autologous T cell, and in other embodiments the T cell is an allogenic T cell. Additionally, in various embodiments of the disclosed method the antigen binding molecule comprises an antigen binding molecule disclosed herein, and humanized forms thereof.

[0040] In another aspect, a method of depleting a population of immune cells presenting a molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82 is provided. In some embodiments, the method comprises (a) providing a population of immune cells to be depleted, wherein the immune cells are known or suspected to be presenting a molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82; and (b) contacting the immune cells with an antigen binding molecule that specifically binds to (a) the molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82, and (b) an activating molecule expressed on the surface of the an immune cell not presenting the molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82, under conditions that permit the formation of a ternary binding complex comprising the molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82, the activating molecule and the antigen binding molecule.

[0041] In further embodiments, (a) the molecule comprising CDR sequences according to any one of SEQ ID Nos: 74-82 is a CAR; and (b) 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 still further embodiments,

the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof. In additional embodiments, the immune cell is a T cell and in still further embodiments the T cell is disposed *in vitro* or the T cell is disposed *in vivo*. In other embodiments, the T cell is in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media. In some embodiments, the T cell is an autologous T cell, and in other embodiments the T cell is an allogenic T cell. Additionally, in various embodiments of the disclosed method the antigen binding molecule comprises an antigen binding molecule disclosed herein, and humanized forms thereof.

BRIEF DESCRIPTION OF THE FIGURES

[0042] Figure 1 is a series of plots showing the results of flow cytometry experiments performed using untransduced cells (Figure 1A) and cells transduced with a construct encoding a CAR comprising the anti-CD19 scFv FMC63 (Figure 1B) and then contacted with anti-scFv antibodies corresponding to three different parental clones (Clone 14, Clone 15 and Clone 17); the plots demonstrate specific binding of the antibodies to the expressed CAR.

[0043] Figure 2 is a series of plots showing the results of flow cytometry experiments performed using cells transduced with a construct encoding a CAR comprising the anti-CD19

scFv FMC63 and then contacted with anti-scFv antibodies corresponding to five different clones (Clone 14-1, Clone 14-7, Clone 15, Clone 17-1 and Clone 17-4); the plots demonstrate specific binding of the antibodies to the expressed CAR.

[0044] Figure 3 is a series of images depicting the results of immunohistochemistry (IHC) studies performed using cells presenting a CAR comprising the anti-CD19 scFv FMC63; the left figure demonstrates the specific binding of antibody Clone 7 to the CAR, while the right figure demonstrates the specific binding of antibody Clone 13 to the CAR.

[0045] Figure 4 is a series of photographs depicting the results of immunohistochemistry (IHC) studies performed using cells presenting a CAR comprising the anti-CD19 scFv FMC63; Figure 4A demonstrates the specific binding of antibody Clones 7 and 13 to the CAR, while Figure 4B demonstrates the results for both antibodies using a PBMC control.

[0046] Figure 5 is a series of sequences showing the coding and amino acid sequences for the VH region of Clone 7, the full length heavy chain amino acid sequence, and the heavy chain CDR1, CDR 2 and CDR 3 amino acid sequences for this clone.

[0047] Figure 6 is a series of sequences showing the coding and amino acid sequences for the VL region of Clone 7, the full length light chain amino acid sequence, and the light chain CDR1, CDR 2 and CDR 3 amino acid sequences for this clone.

[0048] Figure 7 is a series of sequences showing the coding and amino acid sequences for the VH region of Clone 13, the full length heavy chain amino acid sequence and the heavy chain CDR1, CDR 2 and CDR 3 amino acid sequences for this clone.

[0049] Figure 8 is a series of sequences showing the coding and amino acid sequences for the VL region of Clone 13, the full length light chain amino acid sequence and the light chain CDR1, CDR 2 and CDR 3 amino acid sequences for this clone.

[0050] Figure 9 is a series of sequences showing the coding and amino acid sequences for the VH region of Clone 14-1, the full length heavy chain amino acid sequence and the heavy chain CDR1, CDR 2 and CDR 3 amino acid sequences for this clone.

[0051] Figure 10 is a series of sequences showing the coding and amino acid sequences for the VL region of Clone 14-1, the full length light chain amino acid sequence and the light chain CDR1, CDR 2 and CDR 3 amino acid sequences for this clone.

[0052] Figure 11 is a series of sequences showing the coding and amino acid sequences for the VH region of Clone 14-7, the full length heavy chain amino acid sequence and the heavy chain CDR1, CDR 2 and CDR 3 amino acid sequences for this clone.

[0053] Figure 12 is a series of sequences showing the coding and amino acid sequences for the VL region of Clone 14-7, the full length light chain amino acid sequence and the light chain CDR1, CDR 2 and CDR 3 amino acid sequences for this clone.

[0054] Figure 13 is a series of sequences showing the coding and amino acid sequences for the VH region of Clone 15, the full length heavy chain amino acid sequence and the heavy chain CDR1, CDR 2 and CDR 3 amino acid sequences for this clone.

[0055] Figure 14 is a series of sequences showing the coding and amino acid sequences for the VL region of Clone 15, the full length light chain amino acid sequence and the light chain CDR1, CDR 2 and CDR 3 amino acid sequences for this clone.

[0056] Figure 15 is a series of sequences showing the coding and amino acid sequences for the VH region of Clone 17, the full length heavy chain amino acid sequence and the heavy chain CDR1, CDR 2 and CDR 3 amino acid sequences for this clone.

[0057] Figure 16 is a series of sequences showing the coding and amino acid sequences for the VL region of Clone 17, the full length light chain amino acid sequence and the light chain CDR1, CDR 2 and CDR 3 amino acid sequences for this clone.

[0058] Figure 17 is an alignment showing the variable heavy chain sequences of the six distinct antibodies identified (Figure 17A), and a clading diagram (Figure 17B) showing the relationship of the sequences to one another.

[0059] Figure 18 is an alignment showing the variable light chain sequences of the six distinct antibodies identified (Figure 18A), and a clading diagram (Figure 18B) showing the relationship of the sequences to one another.

[0060] Figure 19 is a table showing the CDR1, CDR2 and CDR3 sequences of the heavy and light chains of the six distinct antibodies identified, assigned based on the Kabat numbering scheme.

[0061] Figure 20 is a table showing the CDR1, CDR2 and CDR3 sequences of the heavy and light chains of the six distinct antibodies identified, assigned based on the Chothia numbering scheme.

[0062] Figure 21 is a table showing the CDR1, CDR2 and CDR3 sequences of the heavy and light chains of the six distinct antibodies identified, assigned based on the IMGT numbering scheme.

[0063] Figure 22 shows flow cytometry plots used to determine binding of clones 14-1, 15, and 17-4 to FMC63 and humanized variants thereof (SS, JS, AS, NS).

DETAILED DESCRIPTION OF THE INVENTION

[0064] The present invention relates to anti-idiotypic antigen binding molecules, including antibodies, which specifically bind to antigen binding molecules that specifically bind the amino acid sequence of the anti-CD19 scFv FMC63 (*see*, *Nicholson et al.*, (1997) *Mol Immunol* 34(16-17):1157-65).

[0065] The anti-CD19 scFv FMC63 has the amino acid sequence:

DIQMTQTTSSLSASLGDRVTISCRASQDISKYLNWYQQKPDGT
VKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYF
CQQGNTLPYTFGGGTKLEITGSTSGSGKPGSGEGSTKGEVKLQ
ESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPRKGLEWL
GVIWGSETTYYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTA
IYYCAKHYYYGGSYAMDYWGQGTSVTVSS (SEQ ID NO: 1)

[0066] Humanized forms of the antigen binding molecules, molecules comprising the anti-CD19 scFv FMC63 and cells presenting a molecule comprising the anti-CD19 scFv FMC63 are also provided. Additionally, polynucleotides encoding the antigen binding molecules, as well as vectors comprising the polynucleotides, and *in vitro* cells comprising the polynucleotides and vectors, are also disclosed.

[0067] 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 moieties comprising the anti-CD19 scFv FMC63, as well as molecules comprising this sequence and cells presenting such molecules, quantifying the amount of a moiety comprising anti-CD19 scFv FMC63, as well as molecules comprising this sequence and cells presenting such molecules, screening for moieties comprising the anti-CD19 scFv FMC63, as well as molecules comprising this sequence and cells presenting such molecules, purifying moieties comprising the anti-CD19 scFv FMC63, as well as molecules comprising this sequence and cells presenting such molecules, and biomarker studies focused on moieties comprising the anti-CD19 scFv FMC63, as well as molecules comprising this sequence and cells presenting such molecules. Therapeutic uses are also provided, for example applications in which the biological activity of a moiety comprising the anti-CD19 scFv FMC63, as well as cells presenting such molecules, is modulated (enhanced or repressed), as well as dose ranging studies related to therapeutics comprising the anti-CD19 scFv FMC63, as well as molecules

comprising this sequence and cells presenting such molecules, and cells presenting such molecules.

[0068] 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 can be generated as described herein.

I. Definitions

[0069] 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 should be understood by reference to the specification as a whole.

[0070] 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.

[0071] 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.

[0072] 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.

[0073] 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), which is

incorporated herein by reference for any purpose. 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.

[0074] As used herein, the term the terms "a" and "an" are used per standard convention and mean one or more, unless context dictates otherwise.

[0075] 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.

[0076] 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.

[0077] As used herein, the term "and/or" is to be understood 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).

[0078] 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.

[0079] 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.

[0080] 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 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). 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.

[0081] 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.

[0082] 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 the anti-CD19 scFv FMC63, as well as molecules comprising this sequence and cells presenting such molecules. 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).

[0083] In various embodiments, an antibody specifically binds the anti-CD19 scFv FMC63 (SEQ ID NO: 1), as well as molecules comprising this sequence and cells presenting such molecules. In some embodiments, the antibody specifically binds to a CAR (or component thereof) comprising SEQ ID NO:1, as well as molecules comprising this sequence, and cells presenting such molecules; cells presenting SEQ ID NO:1 can, but need not be, an immune cell, such as a T cell.

[0084] 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 the anti-CD19 scFv FMC63; SEQ ID NO: 1), as well as 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 the anti-CD19 scFv FMC63, as well as molecules comprising this sequence, which is optionally conjugated to an adjuvant such as keyhole limpet hemocyanin (KLH), or to an Fc to facilitate screening.

[0085] 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.

[0086] 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.

[0087] 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.*, the anti-CD19 scFv FMC63 and a cell surface activator molecule).

[0088] 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 5-21, which specifically bind the anti-CD19 scFv FMC63, as well as molecules comprising the anti-CD19 scFv FMC63, and cells presenting such molecules. In further embodiments, the antigen binding molecule binds to a CAR comprising the anti-CD19 scFv FMC63, as well as molecules comprising the anti-CD19 scFv FMC63, and can be expressed on an immune cell, such as a T cell.

[0089] 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.

[0090] 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.

[0091] 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. 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. Table A defines CDRs using each numbering system. The contact definition is based on an analysis of the available complex crystal structures.

[0092]

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 some embodiments, the

CDRs of the antibodies described herein can be described according to the Kabat numbering scheme, as shown in Figure 6 (although they can readily be construed in other numbering systems using Table A above).

[0093] 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 some embodiments, the CDRs of the antibodies described herein have been determined according to the Chothia numbering scheme, as shown in FIGURE 20.

[0094] 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.

[0095] 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.

[0096] 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

[0097] 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.

[0098] 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).

[0099] 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.

[0100] 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.

[0101] 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.

[0102] 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.

[0103] 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 some embodiments, 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.

[0104] In another embodiment, molecules that specifically bind to an antigen (*e.g.*, the anti-CD19 scFv FMC63; SEQ ID NO: 1), as well as molecules comprising this sequence and cells presenting such molecules) bind with a dissociation constant (K_d) of about 1 x 10^{-7} M. In some embodiments, the antigen binding molecule specifically binds an antigen (*e.g.*, the anti-CD19 scFv FMC63, as well as molecules comprising this sequence and cells presenting such molecules) with "high affinity" when the K_d is about 1 x 10^{-9} M to about 5 x 10^{-9} M. In some embodiments, the antigen binding molecule specifically binds an antigen (*e.g.*, the anti-CD19 scFv FMC63, as well as molecules comprising this sequence and cells presenting such molecules) with "very high affinity" when the K_d is 1 x 10^{-10} M to about 5 x 10^{-10} M.

[0105] In still another embodiment, molecules that specifically bind to an antigen (*e.g.*, the anti-CD19 scFv FMC63, as well as molecules comprising this sequence and cells presenting such molecules) do not cross react with other proteins under similar binding conditions. In some embodiments, molecules that specifically bind to an antigen (*e.g.*, the anti-CD19 scFv FMC63, as well as molecules comprising this sequence and cells presenting such molecules) do not cross react with other proteins that do not comprise the anti-CD19 scFv FMC63, molecules comprising this sequence and cells presenting such molecules. In some embodiments, provided herein is an antibody or fragment thereof that binds to the anti-CD19 scFv FMC63, as well as molecules comprising this sequence 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 the anti-CD19 scFv FMC63, as well 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 some embodiments, the extent of binding of an antigen binding molecule, antibody or antigen binding fragment thereof that specifically binds the anti-CD19 scFv FMC63, as

well as molecules comprising this sequence and cells presenting such molecules, described herein compared to an unrelated protein which does not comprise the anti-CD19 scFv FMC63, as well as molecules comprising this sequence and cells presenting such molecules, is less than 10%, 15%, or 20% of the binding of the antibody to linker fragment protein as measured by, *e.g.*, a radioimmunoassay.

[0106] 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.

[0107] 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.

[0108] 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, Ch. 7 in Fundamental Immunology (Paul, W., ed., Lippincott Williams & Wilkins (2012); which chapter and volume is incorporated by reference in its entirety for all purposes). The variable regions of each light/heavy chain pair form the antibody binding site such that an intact immunoglobulin has two primary binding sites.

[0109] Naturally occurring immunoglobulin chains exhibit the same general structure of relatively conserved framework regions (FR) joined by three hypervariable regions, also called complementarity determining regions or "CDRs." From N-terminus to C-terminus, both light and heavy chains comprise the domains FR1, CDRl, 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 lmmunological 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, IGMT and Abm (Oxford Molecular) numbering systems are described more fully herein.

[0110] 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.

[0111] 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.

[0112] 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 the anti-CD19 scFv FMC63, as well as molecules comprising this sequence and cells presenting such molecules) 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.

[0113] 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.

[0114] As used herein, the terms "peptide," "polypeptide," and "protein" are used interchangeably herein, and mean a compound comprising amino acid residues covalently linked by peptide bonds. A 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 sequence. The term polypeptide encompasses any peptide or protein comprising two or more amino acids joined to each other by peptide bonds. As used herein, the term refers to both short chains, which also commonly are referred to 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.

[0115] 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 SEQ ID NOs: 2-73), deletions, non-naturally occurring amino acids, and chemical analogs of amino acids.

[0116] 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, which are incorporated herein by reference for any purpose.

[0117] Polypeptides, peptides, proteins and analogous molecules comprising the anti-CD19 scFv FMC63, as well as molecules comprising this sequence and cells presenting such molecules, are specifically encompassed by the terms.

[0118] 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 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.

[0119] 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.

[0120] 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.

[0121] 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 is a specific example of a scFv.

[0122] A "therapeutically effective amount," "effective dose," "effective amount," or "therapeutically effective dosage" of a therapeutic agent, (*e.g.*, a moiety comprising the anti-CD19 scFv FMC63, as well as molecules comprising this sequence 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.

[0123] 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.

[0124] 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 about 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 its 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.

[0125] 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).

[0126] 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.

[0127] 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.

[0128] Various aspects of the invention are described in further detail in the following subsections.

II. Antigen Binding Molecules and Polynucleotides Encoding the Same

[0129] The present disclosure is directed to antigen binding molecules, including antibodies, that specifically bind the anti-CD19 scFv FMC63 (SEQ ID NO: 1), as well as molecules comprising this sequence and cells presenting such molecules, and/or those which cross compete with one or more antigen binding molecules described herein (*i.e.*, one or more of those described in FIGURES 5-21 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.

[0130] 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.

[0131] 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 (*e.g.*, 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).

[0132] In some embodiments, the antigen binding molecules of the present invention specifically bind to the anti-CD19 scFv FMC63, as well as molecules comprising this sequence and cells presenting such molecules. In certain embodiments, an antigen binding molecule of the present disclosure specifically binds the anti-CD19 scFv FMC63, as well as molecules comprising this sequence 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 the anti-CD19 scFv FMC63, as well as molecules comprising this sequence 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 the anti-CD19 scFv FMC63, as well as molecules comprising this sequence 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 anti-CD19 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 x 10^{-10} M, or about 5 x 10^{-10} M. K_D can be calculated using standard methodologies, as described herein.

[0133] In specific embodiments, an antigen binding molecule of the instant disclosure is an antibody identified herein as Clone 7, Clone 13, Clone 14-1, Clone 14-7, Clone 15, or Clone 17, and each comprises the following heavy and light chain amino acid, coding, variable, and CDR sequences, as provided and labeled:

Clone 7 VH DNA

ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGT
CCAGTGTCAGGAGCAGCTGGAGGAGTCCGGGGGAGACCTGGTCAAGCCT
GGAGGAACCCTGACAGTCACCTGCAAAGCCTCTGGATTCTCCTTCAGTA
ACAATGGAATTTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTG
GATCGGATGTCTTTATGTTGGTAGTAGTGATACCACTTACTACGCGAGCT
GGGCGAAAGGCCGATTCACCATCTCCAAAAGCTCGTCGACCACGGTGAC
TCTACAAATGACCAGTCTGACAGTCGCGGACACGGCCACCTATTTCTGTA
CGATAAATCTCGGCTTGTGGGGCCCCGGCACCCTGGTCACCGTCTCCTCA
(SEQ ID NO: 2)

Clone 7 VH AA (CDRs underlined)

METGLRWLLLVAVLKGVQCQEQLEESGGDLVKPGGTLTVTCKASGFSFSN
NGICWVRQAPGKGLEWIGCLYVGSSDTTYYASWAKGRFTISKSSSTTVTLQ
MTSLTVADTATYFCTINLGLWGPGTLVTVSS (SEQ ID NO: 3)

Clone 7 HC AA (CDRs underlined)

METGLRWLLLVAVLKGVQCQEQLEESGGDLVKPGGTLTVTCKASGFSFSN
NGICWVRQAPGKGLEWIGCLYVGSSDTTYYASWAKGRFTISKSSSTTVTLQ
MTSLTVADTATYFCTINLGLWGPGTLVTVSSGQPKAPSVFPLAPCCGDTPSS
TVTLGCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSGLYSLSSVVSVTS
SSQPVTCNVAHPATNTKVDKTVAPSTCSKPTCPPPELLGGPSVFIFPPKPKDT
LMISRTPEVTCVVVDVSQDDPEVQFTWYINNEQVRTARPPLREQQFNSTIRV
VSTLPIAHQDWLRGKEFKCKVHNKALPAPIEKTISKARGQPLEPKVYTMGPP
REELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDNYKTTPAVLDSDGSYFL
YSKLSVPTSEWQRGDVFTCSVMHEALHNHYTQKSISRSPGK (SEQ ID NO: 4)

Clone 7 VH CDR1 AA

GFSFSNN (SEQ ID NO: 5)

Clone 7 VH CDR2 AA

YVGSSD (SEQ ID NO: 6)

Clone 7 VH CDR3 AA

NLGL (SEQ ID NO: 7)

Clone 7 VL DNA

ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCT
CCCAGGTGCCACATTTGCCATCGTGGTGACCCAGACTCCATCTTCCAAGT
CTGTCCCTGTGGGAGGCACAGTCACCATCAATTGCCAGGCCAGTGAGAG
TGTTTATAATAGCGACTGGTTAGCCTGGTATCAGCAGAAACCAGGGCAG
CCTCCCAAGCAACTGATCTATGCTGCATCCACTCTGGCATCTGGGGTCCC
ATCGCGCTTCAAAGGCAGTGGATCTGGGACACAGTTCACTCTCACCATC
AGCGATGTGGTGTGTGACGATGCTGCCACTTATTATTGTGCAGGATATAA
AAGTAGTAGTACTGATGGGATTGCTTTCGGCGGAGGGACCGAGGTGGTG
GTCAAA (SEQ ID NO: 8)

Clone 7 VL AA (CDRs underlined)

MDTRAPTQLLGLLLLWLPGATFAIVVTQTPSSKSVPVGGTVTINCQASESVY
NSDWLAWYQQKPGQPPKQLIYAASTLASGVPSRFKGSGSGTQFTLTISDVV
CDDAATYYCAGYKSSSTDGIAFGGGTEVVVK (SEQ ID NO: 9)

Clone 7 LC AA (CDRs underlined)

MDTRAPTQLLGLLLLWLPGATFAIVVTQTPSSKSVPVGGTVTINCQASESVY
NSDWLAWYQQKPGQPPKQLIYAASTLASGVPSRFKGSGSGTQFTLTISDVV
CDDAATYYCAGYKSSSTDGIAFGGGTEVVVKGDPVAPTVLIFPPAADQVAT
GTVTIVCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADCTYNLSSTLT
LTSTQYNSHKEYTCKVTQGTTSVVQSFNRGDC (SEQ ID NO: 10)

Clone 7 VL CDR1 AA

QASESVYNSDWLA (SEQ ID NO: 11)

Clone 7 VL CDR2 AA

AASTLAS (SEQ ID NO: 12)

Clone 7 VL CDR3 AA

AGYKSSSTDGIA (SEQ ID NO: 13)

Clone 13 VH DNA

ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGT
CCAGTGTCAGGAGCAGCTGGAGGAGTCCGGGGGAGACCTGGTCAAGCCT
GGAGGAACCCTGACAGTCACCTGCAAAGCCTCTGGATTCTCCTTCAGTA
ACAATGGAATTTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTG
GATCGGATGTCTTTATGTTGGTAGTAGTGATACCACTTACTACGCGAGCT
GGGCGAAAGGCCGATTCACCATCTCCAAAAGCTCGTCGACCACGGTGAC
TCTACAAATGACCAGTCTGACAGTCGCGGACACGGCCACCTATTTCTGTA
CGATAAATCTCGGCTTGTGGGGCCCCGGCACCCTGGTCACCGTCTCCTCA
(SEQ ID NO: 14)

Clone 13 VH AA (CDRs underlined)

METGLRWLLLVAVLKGVQCQEQLEESGGDLVKPGGTLTVTCKASGFSFSN
NGICWVRQAPGKGLEWIGCLYVGSSDTTYYASWAKGRFTISKSSSTTVTLQ
MTSLTVADTATYFCTINLGLWGPGTLVTVSS (SEQ ID NO: 15)

Clone 13 HC AA (CDRs underlined)

METGLRWLLLVAVLKGVQCQEQLEESGGDLVKPGGTLTVTCKASGFSFSN
NGICWVRQAPGKGLEWIGCLYVGSSDTTYYASWAKGRFTISKSSSTTVTLQ
MTSLTVADTATYFCTINLGLWGPGTLVTVSSGQPKAPSVFPLAPCCGDTPSS
TVTLGCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSGLYSLSSVVSVTS
SSQPVTCNVAHPATNTKVDKTVAPSTCSKPTCPPPELLGGPSVFIFPPKPKDT
LMISRTPEVTCVVVDVSQDDPEVQFTWYINNEQVRTARPPLREQQFNSTIRV

VSTLPIAHQDWLRGKEFKCKVHNKALPAPIEKTISKARGQPLEPKVYTMGPP
REELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDNYKTTPAVLDSDGSYFL
YSKLSVPTSEWQRGDVFTCSVMHEALHNHYTQKSISRSPGK (SEQ ID NO:
16)

Clone 13 VH CDR1 AA
GFSFSNN (SEQ ID NO: 5)

Clone 13 VH CDR2 AA
YVGSSD (SEQ ID NO: 6)

Clone 13 VH CDR3 AA
NLGL (SEQ ID NO: 7)

Clone 13 VL DNA
ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCT
CCCAGGTGCCACACTTGCCATCGTGGTGACCCAGACTCCATCTTCCAAGT
CTGTCCCTGTGGGAGGCACAGTCACCATCAATTGCCAGGCCAGTGAGAG
TGTTTATAATAGCGACTGGTTAGCCTGGTATCAGCAGAAACCAGGGCAG
CCTCCCAAGCAACTGATCTATGCTGCATCCACTCTGGCATCTGGGGTCCC
ATCGCGCTTCAAAGGCAGTGGATCTGGGACACAGTTCACTCTCACCATC
AGCGATGTGGTGTGTGACGATGCTGCCACTTATTATTGTGCAGGATATAA
AAGTAGTAGTACTGATGGGATTGCTTTCGGCGGAGGGACCGAGGTGGTG
GTCAAA (SEQ ID NO: 17)

Clone 13 VL AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGATLAIVVTQTPSSKSVPVGGTVTINCQASESVY
NSDWLAWYQQKPGQPPKQLIYAASTLASGVPSRFKGSGSGTQFTLTISDVV
CDDAATYYCAGYKSSSTDGIAFGGGTEVVVK (SEQ ID NO: 18)

Clone 13 LC AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGATLAIVVTQTPSSKSVPVGGTVTINCQASESVY
NSDWLAWYQQKPGQPPKQLIYAASTLASGVPSRFKGSGSGTQFTLTISDVV

CDDAATYYCAGYKSSSTDGIAFGGGTEVVVKGDPVAPTVLIFPPAADQVAT
GTVTIVCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADCTYNLSSTLT
LTSTQYNSHKEYTCKVTQGTTSVVQSFNRGDC (SEQ ID NO: 19)

Clone 13 VL CDR1 AA

QASESVYNSDWLA (SEQ ID NO: 11)

Clone 13 VL CDR2 AA

AASTLAS (SEQ ID NO: 12)

Clone 13 VL CDR3 AA

AGYKSSSTDGIA (SEQ ID NO: 13)

Clone 14-1 VH DNA

ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGT
CCAGTGTCAGGAGCAGCTGGAGGAGTCCGGGGGAGGCCTGGTCAAGCCT
GGGGCATCCCTGACACTCACCTGCAAAGCCTCTGGATTCGACTTCAGTAT
CAACTACTACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGTTGGAG
TGGATCGCATGCATTTATACTGGTGATGATGACACTTTCTACGCGAGCTG
GGCGAAAGGCCGGTTCACCATCTCCAAAACCTCGTCGACCACGGTGACT
CTACAACTGAACAGTCTGACAGCCGCGGACACGGCCACCTATTTCTGTGT
GAGAGGTCTATATAGTGGTAGTATTAATAACCTGTGGGGCCCAGGCACC
CTGGTCACCGTCTCCTCA (SEQ ID NO: 20)

Clone 14-1 VH AA (CDRs underlined)

METGLRWLLLVAVLKGVQCQEQLEESGGGLVKPGASLTLTCKASGFDFSIN
YYMCWVRQAPGKGLEWIACIYTGDDDTFYASWAKGRFTISKTSSTTVTLQL
NSLTAADTATYFCVRGLYSGSINNLWGPGTLVTVSS (SEQ ID NO: 21)

Clone 14-1 HC AA (CDRs underlined)

METGLRWLLLVAVLKGVQCQEQLEESGGGLVKPGASLTLTCKASGFDFSIN
YYMCWVRQAPGKGLEWIACIYTGDDDTFYASWAKGRFTISKTSSTTVTLQL
NSLTAADTATYFCVRGLYSGSINNLWGPGTLVTVSSGQPKAPSVFPLAPCCG

DTPSSTVTLGCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSGLYSLSSV
VSVTSSSQPVTCNVAHPATNTKVDKTVAPSTCSKPTCPPPELLGGPSVFIFPP
KPKDTLMISRTPEVTCVVVDVSQDDPEVQFTWYINNEQVRTARPPLREQQF
NSTIRVVSTLPIAHQDWLRGKEFKCKVHNKALPAPIEKTISKARGQPLEPKV
YTMGPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDNYKTTPAVLDS
DGSYFLYSKLSVPTSEWQRGDVFTCSVMHEALHNHYTQKSISRSPGK (SEQ
ID NO: 22)

Clone 14-1 VH CDR1 AA

GFDFSINY (SEQ ID NO: 23)

Clone 14-1 VH CDR2 AA

YTGDD (SEQ ID NO: 24)

Clone 14-1 VH CDR3 AA

GLYSGSINNL (SEQ ID NO: 25)

Clone 14-1 VL DNA

ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCT
CCCAGATGCCAGATGTGCGCTTGTGATGACCCAGACTCCATCCCCTGTGT
CTGCAGCTGTGGGAGGCACAGTCACCATCAGTTGCCAGGCCAGTCAGAG
TGTTTATAACAACGACTACTTATCCTGGTATCAGCAGAAACCAGGGCAG
CCTCCCAAACTCCTGATCTATTATGCATCCACTCTGGCATCTGGGGTCTC
ATCGCGGTTCAAAGGCAGTGGATCTGGGACACAGTTCACTCTCACCATC
AGCGACGTGCAGTGTGACGATGCTGCCGCTTACTATTGTGCAGGCGTTA
AAGGTTATAGTAATGATAATAATGGTTTCGGCGGAGGGACCGAGGTGGT
GGTCAAA (SEQ ID NO: 26)

Clone 14-1 VL AA (CDRs underlined)

MDTRAPTQLLGLLLLWLPDARCALVMTQTPSPVSAAVGGTVTISCQASQSV
YNNDYLSWYQQKPGQPPKLLIYYASTLASGVSSRFKGSGSGTQFTLTISDVQ
CDDAAAYYCAGVKGYSNDNNGFGGGTEVVVK (SEQ ID NO: 27)

Clone 14-1 LC AA (CDRs underlined)

MDTRAPTQLLGLLLLWLPDARCALVMTQTPSPVSAAVGGTVTISCQASQSV
YNNDYLSWYQQKPGQPPKLLIYYASTLASGVSSRFKGSGSGTQFTLTISDVQ
CDDAAAYYCAGVKGYSNDNNGFGGGTEVVVKGDPVAPTVLIFPPAADQVA
TGTVTIVCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADCTYNLSSTL
TLTSTQYNSHKEYTCKVTQGTTSVVQSFNRGDC (SEQ ID NO:28)

Clone 14-1 VL CDR1 AA

QASQSVYNNDYLS (SEQ ID NO: 29)

Clone 14-1 VL CDR2 AA

YASTLAS (SEQ ID NO: 30)

Clone 14-1 VL CDR3 AA

AGVKGYSNDNNG (SEQ ID NO: 31)

Clone 14-7 VH DNA

ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGT
CCAATGTCAGTCGCTGGAGGAGTCCGGGGGAGGCCTGGTCAAGCCTGGG
GCATCCCTGACACTCACCTGCAAAGCCTCTGGATTCGACTTCAGTATCAA
CTACTACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGTTGGAGTGG
ATCGCATGCATTTATACTGGTGATGATGACACTTTCTACGCGAGCTGGGC
GAAAGGCCGGTTCACCATCTCCAAAACCTCGTCGACCACGGTGACTCTA
CAACTGAACAGTCTGACAGCCGCGGACACGGCCACCTATTTCTGTGTGA
GAGGTCTATATAGTGGTAGTATTAATAACCTGTGGGGCCCAGGCACCCT
GGTCACCGTCTCCTCA (SEQ ID NO: 32)

Clone 14-7 VH AA (CDRs underlined)

METGLRWLLLVAVLKGVQCQSLEESGGGLVKPGASLTLTCKASGFDFSINY
YMCWVRQAPGKGLEWIACIYTGDDDTFYASWAKGRFTISKTSSTTVTLQLN
SLTAADTATYFCVRGLYSGSINNLWGPGTLVTVSS (SEQ ID NO: 33)

Clone 14-7 HC AA (CDRs underlined)

METGLRWLLLVAVLKGVQCQSLEESGGGLVKPGASLTLTCKASGFDFSINY YMCWVRQAPGKGLEWIACIYTGDDDTFYASWAKGRFTISKTSSTTVTLQLN SLTAADTATYFCVRGLYSGSINNLWGPGTLVTVSSGQPKAPSVFPLAPCCGD TPSSTVTLGCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSGLYSLSSVV SVTSSSQPVTCNVAHPATNTKVDKTVAPSTCSKPTCPPPELLGGPSVFIFPPKP KDTLMISRTPEVTCVVVDVSQDDPEVQFTWYINNEQVRTARPPLREQQFNS TIRVVSTLPIAHQDWLRGKEFKCKVHNKALPAPIEKTISKARGQPLEPKVYT MGPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDNYKTTPAVLDSDG SYFLYSKLSVPTSEWQRGDVFTCSVMHEALHNHYTQKSISRSPGK (SEQ ID NO: 34)

Clone 14-7 VH CDR1 AA

GFDFSINY (SEQ ID NO: 23)

Clone 14-7 VH CDR2 AA

YTGDD (SEQ ID NO: 24)

Clone 14-7 VH CDR3 AA

GLYSGSINNL (SEQ ID NO: 25)

Clone 14-7 VL DNA

ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCT CCCAGATGCCAGATGTGCGCTTGTGATGACCCAGACTCCATCCCCTGTGT CTGCAGCTGTGGGAGGCACAGTCACCATCAGTTGCCAGGCCAGTCAGAG TGTTTATAACAACGACTACTTATCCTGGTATCAGCAGAAACCAGGGCAG CCTCCCAAACTCCTGATCTATTATGCATCCACTCTGGCATCTGGGGTCTC ATCGCGGTTCAAAGGCAGTGGATCTGGGACACAGTTCACTCTCACCATC AGCGACGTGCAGTGTGACGATGCTGCCGCTTACTATTGTGCAGGCGTTA AAGGTTATAGTAATGATAATAATGGTTTCGGCGGAGGGACCGAGGTGGT GGTCAAA (SEQ ID NO: 35)

Clone 14-7 VL AA (CDRs underlined)

MDTRAPTQLLGLLLLWLPDARCALVMTQTPSPVSAAVGGTVTISCQASQSV
YNNDYLSWYQQKPGQPPKLLIYYASTLASGVSSRFKGSGSGTQFTLTISDVQ
CDDAAAYYCAGVKGYSNDNNGFGGGTEVVVK (SEQ ID NO: 36)

Clone 14-7 LC AA (CDRs underlined)

MDTRAPTQLLGLLLLWLPDARCALVMTQTPSPVSAAVGGTVTISCQASQSV
YNNDYLSWYQQKPGQPPKLLIYYASTLASGVSSRFKGSGSGTQFTLTISDVQ
CDDAAAYYCAGVKGYSNDNNGFGGGTEVVVKGDPVAPTVLIFPPAADQVA
TGTVTIVCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADCTYNLSSTL
TLTSTQYNSHKEYTCKVTQGTTSVVQSFNRGDC (SEQ ID NO: 37)

Clone 14-7 VL CDR1 AA

QASQSVYNNDYLS (SEQ ID NO: 29)

Clone 14-7 VL CDR2 AA

YASTLAS (SEQ ID NO: 30)

Clone 14-7 VL CDR3 AA

AGVKGYSNDNNG (SEQ ID NO: 31)

Clone 15 VH DNA

ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGGGT
CCAGTGTCAGTCGTTGGAGGAGTCCGGGGGAGACCTGGTCAAGCCTGGG
GCATCCCTGACACTCACCTGCACAGCCTCTGGATTCTCCTTCACGAGCAA
CTACTACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGG
GTCGCGTGCATTTTTCTTGGTAGTAGTGGTAACACTGTCTACGCGAACTG
GGCGAAAGGCCGATTCACCATCTCCAAAACCTCGTCGACCACGGTGACT
CTGCAAATGACCAGTCTGACAGTCGCGGACACGGCCACCTATTTCTGTGC
GAGAGACTATGTTAATGGTTATGACTACTTTAACTTGTGGGGCCCAGGCA
CCTTGGTCACCGTCTCCTCA (SEQ ID NO: 38)

Clone 15 VH AA (CDRs underlined)

METGLRWLLLVAVLKGVQCQSLEESGGDLVKPGASLTLTCTASGFSFTSNY
YMCWVRQAPGKGLEWVACIFLGSSGNTVYANWAKGRFTISKTSSTTVTLQ
MTSLTVADTATYFCARDYVNGYDYFNLWGPGTLVTVSS (SEQ ID NO: 39)

Clone 15 HC AA (CDRs underlined)

METGLRWLLLVAVLKGVQCQSLEESGGDLVKPGASLTLTCTASGFSFTSNY
YMCWVRQAPGKGLEWVACIFLGSSGNTVYANWAKGRFTISKTSSTTVTLQ
MTSLTVADTATYFCARDYVNGYDYFNLWGPGTLVTVSSGQPKAPSVFPLAP
CCGDTPSSTVTLGCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSGLYSL
SSVVSVTSSSQPVTCNVAHPATNTKVDKTVAPSTCSKPTCPPPELLGGPSVFI
FPPKPKDTLMISRTPEVTCVVVDVSQDDPEVQFTWYINNEQVRTARPPLREQ
QFNSTIRVVSTLPIAHQDWLRGKEFKCKVHNKALPAPIEKTISKARGQPLEPK
VYTMGPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDNYKTTPAVLD
SDGSYFLYSKLSVPTSEWQRGDVFTCSVMHEALHNHYTQKSISRSPGK (SEQ
ID NO: 40)

Clone 15 VH CDR1 AA

GFSFTSNY (SEQ ID NO: 41)

Clone 15 VH CDR2 AA

FLGSSG (SEQ ID NO: 42)

Clone 15 VH CDR3 AA

DYVNGYDYFNL (SEQ ID NO: 43)

Clone 15 VL DNA

ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCT
CCCAGGTGCCACATTTGCCCAAGTGCTGACCCAGACTGCATCCCCCGTGT
CTGCGGCTGTTGGAGGCACAGTCACCATCAATTGCCAGTCCAGTCAGAG
TGTTTATAATAAGAACTTAGCCTGGTATCAGCAGAAACCAGGGCAGCCT
CCCAAAGGCCTGATCTATTCTACATCGACTCTAGATTCTGGGGTCCCATC

GCGGTTCAGCGGCAGTGGATCTGGGACACAGTTCACTCTCACCATCAGC
GACGTGCAGTGTGACGATGCTGCCACTTACTACTGTCTAGGCAGTTATGA
TTGTAGTAGTGCTGATTGTAATGCTTTCGGCGGAGGGACCGAGGTGGTG
GTCAAA (SEQ ID NO: 44)

Clone 15 VL AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGATFAQVLTQTASPVSAAVGGTVTINCQSSQSV
YNKNLAWYQQKPGQPPKGLIYSTSTLDSGVPSRFSGSGSGTQFTLTISDVQC
DDAATYYCLGSYDCSSADCNAFGGGTEVVVK (SEQ ID NO: 45)

Clone 15 LC AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGATFAQVLTQTASPVSAAVGGTVTINCQSSQSV
YNKNLAWYQQKPGQPPKGLIYSTSTLDSGVPSRFSGSGSGTQFTLTISDVQC
DDAATYYCLGSYDCSSADCNAFGGGTEVVVKGDPVAPTVLIFPPAADQVAT
GTVTIVCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADCTYNLSSTLT
LTSTQYNSHKEYTCKVTQGTTSVVQSFNRGDC (SEQ ID NO: 46)

Clone 15 VL CDR1 AA
QSSQSVYNKNLA (SEQ ID NO: 47)

Clone 15 VL CDR2 AA
STSTLDS (SEQ ID NO: 48)

Clone 15 VL CDR3 AA
LGSYDCSSADCNA (SEQ ID NO: 49)

Clone 17 VH DNA
ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGT
CCAATGTCAGTCGCTGGAGGAGTCCGGGGGAGGCCTGGTCAAGCCTGGG
GCATCCCTGACACTCACCTGCACAGCCTCTGGATTCTCCTTCAGTGACAG
TTGGTACTTGTGTTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGG
ATCGCATGCATTTATACTGGTGATGGTGACACTTATTACGCGACCTGGGC
GAAAGGCCGATTCACCATCTCCAAGACCTCGTCGACCACAGTGACTCTA

CAAATGACCAGTCTGACAGCCGCGGACACGGCCACCTATTTCTGTGCGA
GGGGTGCCCAATTTTACTTGTGGGGCCAAGGCACCCTGGTCACCGTCTCC
TCA (SEQ ID NO: 50)

Clone 17 VH AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQSLEESGGGLVKPGASLTLTCTASGFSFSDSW
YLCWVRQAPGKGLEWIACIYTGDGDTYYATWAKGRFTISKTSSTTVTLQMT
SLTAADTATYFCARGAQFYLWGQGTLVTVSS (SEQ ID NO: 51)

Clone 17 HC AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQSLEESGGGLVKPGASLTLTCTASGFSFSDSW
YLCWVRQAPGKGLEWIACIYTGDGDTYYATWAKGRFTISKTSSTTVTLQMT
SLTAADTATYFCARGAQFYLWGQGTLVTVSSGQPKAPSVFPLAPCCGDTPS
STVTLGCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSGLYSLSSVVSVT
SSSQPVTCNVAHPATNTKVDKTVAPSTCSKPTCPPPELLGGPSVFIFPPKPKD
TLMISRTPEVTCVVVDVSQDDPEVQFTWYINNEQVRTARPPLREQQFNSTIR
VVSTLPIAHQDWLRGKEFKCKVHNKALPAPIEKTISKARGQPLEPKVYTMGP
PREELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDNYKTTPAVLDSDGSYF
LYSKLSVPTSEWQRGDVFTCSVMHEALHNHYTQKSISRSPGK (SEQ ID NO:
52)

Clone 17 VH CDR1 AA
GFSFSDSW (SEQ ID NO: 53)

Clone 17 VH CDR2 AA
YTGDG (SEQ ID NO: 54)

Clone 17 VH CDR3 AA
GAQFYL (SEQ ID NO: 55)

Clone 17 VL DNA
ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCT
CCCAGGTGCCACATTTGCCCAGGTGCTGACCCAGACTCCATCCTCCGTGT

CTGCAGCTGTGGGAGGCACAGTCACCATCAATTGCCAGTCCAGTCAGAG
TGTTTATGCCAACACCTACTTATCCTGGTATCAGCAGAAACCAGGGCAGC
CTCCCAAGCAACTGATCTATTCTGCATCCAGTCTGGCATCTGGGGTCCCA
CCGCGGTTCAAAGGCAGTGGATCTGGGACACAGTTCGCTCTCACCATCA
GCGACGTGCAGTGTGACGATGCTGCCACTTACTACTGTCTAGGCAGATAT
AGTTGTGGTCTTGCTGATTGTGCTGCTTTCGGCGGAGGGACCGAGGTGGT
GGTCAAA (SEQ ID NO:56)

Clone 17 VL AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGATFAQVLTQTPSSVSAAVGGTVTINCQSSQSV
YANTYLSWYQQKPGQPPKQLIYSASSLASGVPPRFKGSGSGTQFALTISDVQ
CDDAATYYCLGRYSCGLADCAAFGGGTEVVVK (SEQ ID NO: 57)

Clone 17 LC AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGATFAQVLTQTPSSVSAAVGGTVTINCQSSQSV
YANTYLSWYQQKPGQPPKQLIYSASSLASGVPPRFKGSGSGTQFALTISDVQ
CDDAATYYCLGRYSCGLADCAAFGGGTEVVVKGDPVAPTVLIFPPAADQV
ATGTVTIVCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADCTYNLSS
TLTLTSTQYNSHKEYTCKVTQGTTSVVQSFNRGDC (SEQ ID NO: 58)

Clone 17 VL CDR1 AA
QSSQSVYANTYLS (SEQ ID NO: 59)

Clone 17 VL CDR2 AA
SASSLAS (SEQ ID NO: 60)

Clone 17 VL CDR3 AA
LGRYSCGLADCAA (SEQ ID NO: 61)

[0134] In some embodiments, the antigen binding molecules of the present disclosure are antibodies and antigen binding fragments thereof. In some embodiments, the antibodies of the present disclosure comprise at least one CDR set forth in Figures 5-21. In another aspect, the present disclosure provides hybridomas capable of producing the antibodies

disclosed herein, and also methods of producing antibodies from hybridomas, as described herein and as known in the art.

[0135] Humanized antibodies are described herein and may be prepared by known techniques. In some embodiments, 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 some embodiments, 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.

[0136] 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.

[0137] 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).

[0138] 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.

[0139] 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 anti-CD19 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^{TM}(H) and λImmunoZap^{TM}(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.

[0140] Briefly, mRNA is isolated from a B-cell population, and used to create heavy and light chain immunoglobulin cDNA expression libraries in the λImmunoZap^{TM}(H) and λImmunoZap^{TM}(L) 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*.

[0141] In some embodiments, 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_{Ha}, V_{Hb}, V_{Hc}, V_{Hd}, C_{H1}, V_L and C_L regions). These primers can be used to amplify heavy or light chain variable regions, which can then be inserted into vectors such as λImmunoZap^{TM}(H) and λImmunoZap^{TM}(L) (Stratagene), respectively. 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.

[0142] 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.

[0143] It will be understood by one skilled 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 Harris, (1995) *J Chromatog* 705:129-34.

[0144] An alternative method for production of a murine monoclonal antibody (from which FMC63 can be derived) 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.

[0145] 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.

[0146] The instant disclosure provides antigen binding molecules that specifically bind to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules. Antigen binding molecules that cross compete with the disclosed antigen binding molecules disclosed herein for an aspect of the disclosure. 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: 1-60. 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: 5, 23, 41 and 53. 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: 6, 24, 42 and 54. 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: 7, 25, 43 and 55. In certain 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 NOs: 11, 29, 47 and 59. 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 NOs: 12, 30, 48 and 60. 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 NOs: 13, 31, 49 and 61.

[0147] In some embodiments, the polynucleotides of the present invention encodes an antibody or antigen binding molecule that specifically binds the anti-CD19 scFv FMC63 (SEQ ID NO: 1), as well as molecules comprising these sequences and cells presenting such molecules, wherein the antibody or antigen binding molecule binds the same or an overlapping epitope as a reference antibody disclosed herein (*e.g.*, those comprising sequences presented in Figures 5-21). In certain embodiments, the antibody or antigen binding molecule binds the same or an overlapping epitope as a reference antibody.

II.A. Clone 7

[0148] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence GFSFNN (SEQ ID NO: 5).

[0149] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence YVGSSD (SEQ ID NO: 6).

[0150] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence NLGL (SEQ ID NO: 7).

[0151] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), 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 GFSFNN (SEQ ID NO: 5); and/or (b) a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence YVGSSD (SEQ ID NO: 6); and/or (c) a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence NLGL (SEQ ID NO: 7).

[0152] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 5, 19, 20 and 21. In a particular embodiment, the VH CDRs are those presented in FIGURE 5.

[0153] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence comprising an amino acid sequence of FIGURE 5 (SEQ ID NO: 3).

[0154] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 5 (*e.g.*, one, two, three, or four of the FRs in one sequence of FIGURE 5).

[0155] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain sequence disclosed herein (*e.g.*, SEQ ID NO: 4 in FIGURE 5). In some embodiments, the antibody or antigen binding molecule comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 3.

[0156] 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:3.

[0157] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QASESVYNSDWLA (SEQ ID NO: 11).

[0158] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence AASTLAS (SEQ ID NO: 12).

[0159] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence AGYKSSSTDGIA (SEQ ID NO: 13).

[0160] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), 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 QASESVYNSDWLA (SEQ ID NO: 11); and/or (b) a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence AASTLAS (SEQ ID NO: 12); and/or (c) a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence AGYKSSSTDGIA (SEQ ID NO: 13).

[0161] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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, 19, 20 and 21. In a particular embodiment, the VL CDRs are those presented in FIGURE 6.

[0162] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a light chain variable region sequence comprising an amino acid sequence of FIGURE 6 (SEQ ID NO: 9)

[0163] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 FIGURE 6 (*e.g.*, one, two, three, or four of the FRs in one sequence of FIGURE 6).

[0164] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a light chain sequence disclosed herein (*e.g.*, SEQ ID NO: 10 in FIGURE 6). In some embodiments, the antibody or antigen binding molecule comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 9.

[0165] 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: 9.

[0166] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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.

[0167] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises: (a) a VH CDR1 region comprising

the amino acid sequence of SEQ ID NO: 5; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 6; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 7; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 11; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 12; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 13.

[0168] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (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 5, 6, respectively, and in FIGURES 19, 20 and 21.

[0169] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence disclosed herein (*e.g.*, in FIGURE 5) and a light chain variable region sequence disclosed herein (*e.g.*, in FIGURE 6).

[0170] In some embodiments, the antibody or antigen binding molecule comprises: (a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 3; and (b) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 9. Nucleotide sequences encoding the heavy chain variable region and the light chain variable region are provided in FIGURES 5 and 6, respectively.

[0171] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain sequence disclosed herein (*e.g.*, in FIGURE 5) and a light chain sequence disclosed herein (*e.g.*, in FIGURE 6).

[0172] In some embodiments, the antibody or antigen binding molecule comprises: (a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 4; and (b) a light chain comprising the amino acid sequence of SEQ ID NO: 10.

[0173] In some embodiments, 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: 4; 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: 10.

II.B. Clone 13

[0174] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence GFSFNN (SEQ ID NO: 5).

[0175] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence YVGSSD (SEQ ID NO: 6).

[0176] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence NLGL (SEQ ID NO: 7).

[0177] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), 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 GFSFNN (SEQ ID NO: 5); and/or (b) a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence YVGSSD (SEQ ID NO: 6); and/or (c) a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence NLGL (SEQ ID NO: 7).

[0178] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 7, 19, 20 and 21. In a particular embodiment, the VH CDRs are those presented in FIGURE 7.

[0179] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence comprising an amino acid sequence of FIGURE 7 (SEQ ID NO: 15).

[0180] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 7 (*e.g.*, one, two, three, or four of the FRs in one sequence of FIGURE 7).

[0181] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain sequence disclosed herein (e.g., SEQ ID NO: 16 in FIGURE 7). In some embodiments, the antibody or antigen binding molecule comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 15.

[0182] 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:15.

[0183] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QASESVYNSDWLA (SEQ ID NO: 11).

[0184] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence AASTLAS (SEQ ID NO: 12).

[0185] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR3 comprising, consisting

of, or consisting essentially of the amino acid sequence AGYKSSSTDGIA (SEQ ID NO: 13).

[0186] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), 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 QASESVYNSDWLA (SEQ ID NO: 11); and/or (b) a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence AASTLAS (SEQ ID NO: 12); and/or (c) a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence AGYKSSSTDGIA (SEQ ID NO: 13).

[0187] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 8, 19, 20 and 21. In a particular embodiment, the VL CDRs are those presented in FIGURE 8.

[0188] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a light chain variable region sequence comprising an amino acid sequence of FIGURE 8 (SEQ ID NO: 18)

[0189] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 FIGURE 8 (*e.g.*, one, two, three, or four of the FRs in one sequence of FIGURE 8).

[0190] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a light chain sequence disclosed herein (*e.g.*, SEQ ID NO: 19 in FIGURE 8). In some embodiments, the antibody or antigen binding molecule comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 18.

[0191] 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: 18.

[0192] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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.

[0193] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises: (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 5; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 6; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 7; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 11; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 12; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 13.

[0194] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (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 7, 8, respectively, and in FIGURES 19, 20 and 21.

[0195] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence disclosed herein (*e.g.*, in FIGURE 7) and a light chain variable region sequence disclosed herein (*e.g.*, in FIGURE 8).

[0196] In some embodiments, the antibody or antigen binding molecule comprises: (a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 15; and (b) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 18. Nucleotide sequences encoding the heavy chain variable region and the light chain variable region are provided in FIGURES 7 and 8, respectively.

[0197] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain sequence disclosed herein (*e.g.*, in FIGURE 7) and a light chain sequence disclosed herein (*e.g.*, in FIGURE 8).

[0198] In some embodiments, the antibody or antigen binding molecule comprises: (a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 16; and (b) a light chain comprising the amino acid sequence of SEQ ID NO: 19.

[0199] In some embodiments, 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: 16; 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: 19.

II.C. Clone 14-1

[0200] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence GFDFSINY (SEQ ID NO: 23).

[0201] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence YTGDD (SEQ ID NO: 24).

[0202] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this

sequence and cells presenting such molecules, comprises a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence GLYSGSINNL (SEQ ID NO: 25).

[0203] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), 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 GFDFSINY (SEQ ID NO: 23); and/or (b) a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence YTGDD (SEQ ID NO: 24); and/or (c) a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence GLYSGSINNL (SEQ ID NO: 25).

[0204] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 19, 20, and 21. In a particular embodiment, the VH CDRs are those presented in FIGURE 9.

[0205] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence comprising an amino acid sequence of FIGURE 9 (SEQ ID NO: 21).

[0206] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 9 (*e.g.*, one, two, three, or four of the FRs in one sequence of FIGURE 9).

[0207] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain sequence disclosed herein (*e.g.*, SEQ ID NO: 22 in FIGURE 9). In some embodiments, the antibody or antigen binding molecule comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 21.

[0208] 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:21.

[0209] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QASQSVYNNDYLS (SEQ ID NO: 29).

[0210] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence YASTLAS (SEQ ID NO: 30).

[0211] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence AGVKGYSNDNNG (SEQ ID NO: 31).

[0212] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), 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 QASQSVYNNDYLS (SEQ ID NO: 29); and/or (b) a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence YASTLAS (SEQ ID NO: 30); and/or (c) a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence AGVKGYSNDNNG (SEQ ID NO: 31).

[0213] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 19, 20 and 21. In a particular embodiment, the VL CDRs are those presented in FIGURE 10.

[0214] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a light chain variable region sequence comprising an amino acid sequence of FIGURE 10 (SEQ ID NO: 27).

[0215] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 FIGURE 10 (*e.g.*, one, two, three, or four of the FRs in one sequence of FIGURE 10).

[0216] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a light chain sequence disclosed herein (*e.g.*, SEQ ID NO: 28 in FIGURE 10). In some embodiments, the antibody or antigen binding molecule comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 27.

[0217] 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: 27.

[0218] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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.

[0219] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises: (a) a VH CDR1 region comprising

the amino acid sequence of SEQ ID NO: 23; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 24; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 25; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 29; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 30; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 31.

[0220] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (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 9, 10, respectively, and in FIGURES 19, 20 and 21.

[0221] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence disclosed herein (*e.g.*, in FIGURE 9) and a light chain variable region sequence disclosed herein (*e.g.*, in FIGURE 10).

[0222] In some embodiments, the antibody or antigen binding molecule comprises: (a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 22; and (b) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 28. Nucleotide sequences encoding the heavy chain variable region and the light chain variable region are provided in FIGURES 9 and 10, respectively.

[0223] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain sequence disclosed herein (*e.g.*, in FIGURE 9) and a light chain sequence disclosed herein (*e.g.*, in FIGURE 10).

[0224] In some embodiments, the antibody or antigen binding molecule comprises: (a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 22; and (b) a light chain comprising the amino acid sequence of SEQ ID NO: 28.

[0225] In some embodiments, 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: 22; 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: 28.

II.D. Clone 14-7

[0226] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence GFDFSINY (SEQ ID NO: 23).

[0227] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence YTGDD (SEQ ID NO: 24).

[0228] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence GLYSGSINNL (SEQ ID NO: 25).

[0229] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), 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 GFDFSINY (SEQ ID NO: 23); and/or (b) a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence YTGDD (SEQ ID NO: 24); and/or (c) a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence GLYSGSINNL (SEQ ID NO: 25).

[0230] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 19, 20 and 21. In a particular embodiment, the VH CDRs are those presented in FIGURE 11.

[0231] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence comprising an amino acid sequence of FIGURE 11 (SEQ ID NO: 33).

[0232] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 11 (*e.g.*, one, two, three, or four of the FRs in one sequence of FIGURE 11).

[0233] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain sequence disclosed herein (*e.g.*, in FIGURE 11). In some embodiments, the antibody or antigen binding molecule comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 33.

[0234] 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: 33.

[0235] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QASQSVYNNDYLS (SEQ ID NO: 29).

[0236] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence YASTLAS (SEQ ID NO: 30).

[0237] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR3 comprising, consisting

of, or consisting essentially of the amino acid sequence AGVKGYSNDNNG (SEQ ID NO: 31).

[0238] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), 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 QASQSVYNNDYLS (SEQ ID NO: 29); and/or (b) a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence YASTLAS (SEQ ID NO: 30); and/or (c) a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence AGVKGYSNDNNG (SEQ ID NO: 31).

[0239] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 20, 21 and 22. In a particular embodiment, the VL CDRs are those presented in FIGURE 12.

[0240] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a light chain variable region sequence comprising an amino acid sequence of FIGURE 12 (SEQ ID NO: 36).

[0241] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 FIGURE 12 (*e.g.*, one, two, three, or four of the FRs in one sequence of FIGURE 12).

[0242] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a light chain sequence disclosed herein (*e.g.*, SEQ ID NO: 37 in FIGURE 12). In some embodiments, the antibody or antigen binding molecule comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 36.

[0243] 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: 36.

[0244] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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.

[0245] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises: (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 23; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 24; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 25; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 29; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 30; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 31.

[0246] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (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 11, 12, respectively, and in FIGURES 19, 20 and 21.

[0247] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence disclosed herein (*e.g.*, in FIGURE 11) and a light chain variable region sequence disclosed herein (*e.g.*, in FIGURE 12).

[0248] In some embodiments, the antibody or antigen binding molecule comprises: (a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 33; and (b) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 36. Nucleotide sequences encoding the heavy chain variable region and the light chain variable region are provided in FIGURES 11 and 12, respectively.

[0249] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain sequence disclosed herein (*e.g.*, in FIGURE 11) and a light chain sequence disclosed herein (*e.g.*, in FIGURE 12).

[0250] In some embodiments, the antibody or antigen binding molecule comprises: (a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 34; and (b) a light chain comprising the amino acid sequence of SEQ ID NO: 37.

[0251] In some embodiments, 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: 34; 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: 37.

II.E. Clone 15 (15-7)

[0252] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence GFSFTSNY (SEQ ID NO: 41).

[0253] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence FLGSSG (SEQ ID NO: 42).

[0254] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this

sequence and cells presenting such molecules, comprises a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence DYVNGYDYFNL (SEQ ID NO: 43).

[0255] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), 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 GFSFTSNY (SEQ ID NO: 41); and/or (b) a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence FLGSSG (SEQ ID NO: 42); and/or (c) a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence DYVNGYDYFNL (SEQ ID NO: 43).

[0256] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 19, 20 and 21. In a particular embodiment, the VH CDRs are those presented in FIGURE 13.

[0257] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence comprising an amino acid sequence of FIGURE 13 (SEQ ID NO: 39).

[0258] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 13 (*e.g.*, one, two, three, or four of the FRs in one sequence of FIGURE 13).

[0259] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain sequence disclosed herein (*e.g.*,SEQ ID NO: 40 in FIGURE 13). In some embodiments, the antibody or antigen binding molecule comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 39.

[0260] 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:39.

[0261] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QSSQSVYNKNLA (SEQ ID NO: 47).

[0262] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence STSTLDS (SEQ ID NO: 48).

[0263] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence LGSYDCSSADCNA (SEQ ID NO: 49).

[0264] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), 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 QSSQSVYNKNLA (SEQ ID NO: 47); and/or (b) a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence STSTLDS (SEQ ID NO: 48); and/or (c) a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence LGSYDCSSADCNA (SEQ ID NO: 49).

[0265] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 19, 20 and 21. In a particular embodiment, the VL CDRs are those presented in FIGURE 14.

[0266] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a light chain variable region sequence comprising an amino acid sequence of FIGURE 14 (SEQ ID NO: 45).

[0267] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 FIGURE 14 (*e.g.*, one, two, three, or four of the FRs in one sequence of FIGURE 14).

[0268] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a light chain sequence disclosed herein (*e.g.*, SEQ ID NO: 46 in FIGURE 14). In some embodiments, the antibody or antigen binding molecule comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 45.

[0269] 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: 45.

[0270] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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.

[0271] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises: (a) a VH CDR1 region comprising

the amino acid sequence of SEQ ID NO: 41; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 42; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 43; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 47; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 48; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 49.

[0272] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (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 13, 14, respectively, and in FIGURES 19, 20 and 21.

[0273] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence disclosed herein (*e.g.*, in FIGURE 13) and a light chain variable region sequence disclosed herein (*e.g.*, in FIGURE 14).

[0274] In some embodiments, the antibody or antigen binding molecule comprises: (a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 39; and (b) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 45. Nucleotide sequences encoding the heavy chain variable region and the light chain variable region are provided in FIGURES 13 and 14, respectively.

[0275] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain sequence disclosed herein (*e.g.*, in FIGURE 13) and a light chain sequence disclosed herein (*e.g.*, in FIGURE 14).

[0276] In some embodiments, the antibody or antigen binding molecule comprises: (a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 40; and (b) a light chain comprising the amino acid sequence of SEQ ID NO: 46.

[0277] In some embodiments, 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: 40; 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: 46.

II.F. Clone 17

[0278] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence GFSFSDSW (SEQ ID NO: 53).

[0279] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence YTGDG (SEQ ID NO: 54).

[0280] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence GAQFYL (SEQ ID NO: 55).

[0281] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), 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 GFSFTSNY (SEQ ID NO: 53); and/or (b) a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence FLGSSG (SEQ ID NO: 54); and/or (c) a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence DYVNGYDYFNL (SEQ ID NO: 55).

[0282] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 19, 20 and 21. In a particular embodiment, the VH CDRs are those presented in FIGURE 15.

[0283] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence comprising an amino acid sequence of FIGURE 15 (SEQ ID NO: 51).

[0284] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 15 (*e.g.*, one, two, three, or four of the FRs in one sequence of FIGURE 15).

[0285] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain sequence disclosed herein (*e.g.*, SEQ ID NO: 52 in FIGURE 15). In some embodiments, the antibody or antigen binding molecule comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 51.

[0286] 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:51.

[0287] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QSSQSVYANTYLS (SEQ ID NO: 59).

[0288] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence SASSLAS (SEQ ID NO: 60).

[0289] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence LGRYSCGLADCAA (SEQ ID NO: 61).

[0290] In some embodiments, an antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), 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 QSSQSVYANTYLS (SEQ ID NO: 59); and/or (b) a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence SASSLAS (SEQ ID NO: 60); and/or (c) a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence LGRYSCGLADCAA (SEQ ID NO: 61).

[0291] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 20, 21 and 22. In a particular embodiment, the VL CDRs are those presented in FIGURE 21.

[0292] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a light chain variable region sequence comprising an amino acid sequence of FIGURE 16 (SEQ ID NO: 57).

[0293] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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 FIGURE 16 (*e.g.*, one, two, three, or four of the FRs in one sequence of FIGURE 16).

[0294] In some embodiments, the antigen binding molecule or antibody that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a light chain sequence disclosed

herein (*e.g.*, SEQ ID NO: 58 in FIGURE 16). In some embodiments, the antibody or antigen binding molecule comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO: 57.

[0295] 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:57.

[0296] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, 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.

[0297] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises: (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 53; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 54; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 55; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 59; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 60; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 61.

[0298] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (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 15, 16, respectively, and in FIGURES 19, 20 and 21.

[0299] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this

sequence and cells presenting this sequence, comprises a heavy chain variable region sequence disclosed herein (*e.g.*, in FIGURE 15) and a light chain variable region sequence disclosed herein (*e.g.*, in FIGURE 16).

[0300] In some embodiments, the antibody or antigen binding molecule comprises: (a) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 45; and (b) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 57. Nucleotide sequences encoding the heavy chain variable region and the light chain variable region are provided in FIGURES 15 and 16, respectively.

[0301] In some embodiments, the antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain sequence disclosed herein (*e.g.*, in FIGURE 15) and a light chain sequence disclosed herein (*e.g.*, in FIGURE 16).

[0302] In some embodiments, the antibody or antigen binding molecule comprises: (a) a heavy chain comprising the amino acid sequence of SEQ ID NO: 52; and (b) a light chain comprising the amino acid sequence of SEQ ID NO: 58.

[0303] In some embodiments, 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: 52; 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: 58.

III Polynucleotides Encoding Antibodies and Other Antigen Binding Molecules

[0304] The present invention is also directed to polynucleotides encoding antibodies and other antigen binding molecules that specifically bind to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence.

[0305] 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: 3, 15, 21, 33, 39 and 51.

[0306] 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: 8, 18, 27, 36, 45 and 57.

[0307] In certain embodiments, the polynucleotide comprises a heavy chain coding sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 14, SEQ ID NO: 20, SEQ ID NO: 32, SEQ ID NO: 38 and SEQ ID NO: 50. In another embodiment, the polynucleotide comprises a light chain coding sequence selected from the group consisting of SEQ ID NO: 8, SEQ ID NO: 17, SEQ ID NO: 26, SEQ ID NO: 35, SEQ ID NO: 44 and SEQ ID NO: 56.

[0308] 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 disclose polynucleotide sequences thus form an aspect of the instant disclosure.

IV. Vectors, Cells, and Pharmaceutical Compositions

[0309] In certain aspects, provided herein are vectors comprising a polynucleotide disclosed herein. In some embodiments, the present invention is directed to a vector or a set of vectors comprising a polynucleotide(s) encoding an amino acid sequence of an antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, as described herein.

[0310] Any vector known in the art can be suitable for expressing the antibodies and other 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.

[0311] 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 the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, as disclosed herein.

[0312] Any cell can be used as a host cell for the polynucleotides and vectors encoding all or a fragment of the antibodies and other 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, *Enterobactehaceae* such as *Escherichia*, *e.g.*, *E. coli*; *Enterobacter*; *Erwinia*; *Klebsiella*; *Proteus*; *Salmonella*, e.g., *Salmonella typhimurium*; *Serratia*, e.g., *Serratia marcescans*, and *Shigella*; *Bacilli* such as *B. subtilis* and *B. licheniformis*; *Pseudomonas* such as *P. aeruginosa*; and *Streptomyces*. In some embodiments, a host cell is 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.

[0313] Other aspects of the present invention are directed to compositions comprising a polynucleotide described herein, a vector described herein, an antibody and/or an antigen binding molecule described herein, 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. In some embodiments, the composition comprises a polynucleotide encoding an antibody or antigen binding molecule that specifically binds to that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence. In another embodiment, the composition comprises an antigen binding molecule encoded by a polynucleotide of the present invention, wherein the antigen binding molecule specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1),

molecules comprising this sequence and cells presenting this sequence, as disclosed herein. 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 of the present invention.

[0314] In some embodiments, the composition comprises one antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, as disclosed herein. In some embodiments, the composition comprises more than one antibody or antigen binding molecule that specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, as disclosed herein, 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

[0315] The following section describes various exemplary methods of using the disclosed antigen binding molecules herein. Any antigen binding molecule disclosed herein can be employed in the disclosed methods.

[0316] In various embodiments of the disclosed methods, 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 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.

[0317] 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, which is herein incorporated by references in its entirety.

[0318] In various embodiments of the disclosed methods, an antigen binding molecule specifically binds to the anti-CD19 scFv FMC63 (SEQ ID NO: 1), molecules comprising this sequence and cells presenting this sequence, as disclosed herein. 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, an antigen binding molecule comprises a heavy chain CDR3 comprising one of SEQ ID NOs: 7, 25, 43, 55, or a light chain CDR3 comprising one of SEQ ID NOs: 13, 31, 49, 61, or both the heavy and light chain CDR3s. In other embodiments of the disclosed methods, the antigen binding molecule comprises a heavy chain CDR1 comprising an amino acid sequence comprising one of SEQ ID NOs: 5, 23, 41 and 53, or a heavy chain CDR2 comprising the amino acid sequence of one of SEQ ID NOs: 6, 24, 42 and 54, or a light chain CDR1 comprising the amino acid sequence of one of SEQ ID NOs: 11, 29, 47 and 59 or a light chain CDR2 comprising the amino acid sequence of one of SEQ ID NOs: 12, 30, 48 and 60. Referring to the Figures, in various embodiments of the disclosed methods, 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 5-21.

[0319] In various embodiments of the disclosed methods, an antigen binding molecule comprises a heavy chain (HC), and the HC comprises a heavy chain variable region (VH) sequence comprising one of SEQ ID NOs: 3, 15, 21, 33, 39 and 51. 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 FIGURES 5-21. 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 molecules comprising a variable region (VH) sequence comprising one of SEQ ID NOs: 3, 15, 21, 33, 39 and 51).

[0320] In various embodiments of the disclosed methods, an antigen binding molecule comprises a light chain (LC), and the LC can comprise a heavy chain variable region (VL) sequence comprising one of SEQ ID NOs: 9, 18, 27, 36, 44 and 57. 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 5-21. 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 VL 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: 9, 18, 27, 36, 44 and 57).

[0321] 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

[0322] 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 the anti-CD19 scFv FMC63 (SEQ ID NO: 1), is provided.

[0323] 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.

[0324] 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.

[0325] 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 SEQ ID NO: 1, is provided. In the disclosed method, the number of cells can be determined using any known method. In preferred embodiments the cells are counted using an automated apparatus, such as a cell sorter (*e.g.*, a FACS), however traditional non-automated cell counting methods can also be employed.

[0326] 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). 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. 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*, etc. Gradient purification, cell culture selection and/or cell sorting can also be employed in obtaining T cells.

[0327] 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 SEQ ID NO: 1 component 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.

[0328] 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 CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof.

[0329] Continuing, an aliquot of the sample comprising a population of cells presenting a molecule comprising the anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1) 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.

[0330] Additionally, an antigen binding molecule that specifically binds the anti-CD19 scFv FMC63 (SEQ ID NO: 1) further comprising 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, 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.*, 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). Suitable optical dyes, including fluoro-phores, are described in Johnson, Molecular Probes Handbook:A Guide to Fluorescent Probes and Labeling Techniques, 11th Edition, Life Technologies, (2010), hereby expressly incorporated by reference, 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. Strategies for the labeling of proteins are known in the art and can be employed in the disclosed method.

[0331] 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 SEQ ID NO: 1 (or fragment thereof) 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 5-21.

[0332] 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.

[0333] 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 anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1). 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.

[0334] The fraction of cells present in a binding complex in the aliquot is then 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 known *ab initio* and thus the fraction of cells present in a binding complex can be easily determined.

[0335] Continuing, the concentration of cells in the initial sample expressing a molecule comprising the anti-CD19 scFv FMC63 (SEQ ID NO: 1) 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.

[0336] 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).

[0337] The volume of the sample that comprises the selected number of cells is then determined, by extrapolation based on the concentration of cells bearing therapeutic molecule present in the sample.

[0338] 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.

[0339] 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 overdosed with cells.

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

[0340] There are situations in which it may be desirable to determine the number of cells present in a sample. For example, it may be desirable to determine the number of immune cells present a sample obtained from a subject. Or it may be desirable to determine the number of cells transfected and expressing a construct, 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.

[0341] Thus, a method of determining a number of cells presenting a molecule in a sample wherein the molecule comprising the anti-CD19 scFv FMC63 (SEQ ID NO: 1) is provided.

[0342] In one embodiment, a sample comprising cells known or suspected to be expressing a molecule comprising the amino acid sequence of the anti-CD19 scFv FMC63 (SEQ ID NO: 1) is provided.

[0343] The cell can be of any type, and can be human or non-human (*e.g.*, mouse, rate, rabbit, hamster, etc). In one 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 (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. 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.

[0344] In specific embodiments, the molecule comprising the anti-CD19 scFv FMC63 (SEQ ID NO: 1) is a CAR. When the molecule is a CAR it can comprise a molecule, or fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand

receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof.

[0345] The sample is then contacted with an antigen binding molecule that specifically binds SEQ ID NO: 1 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 SEQ ID NO: 1 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 FIGURE 5-21.

[0346] 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 fluoro-phores, are described in Johnson, Molecular Probes Handbook:A Guide to Fluorescent Probes and Labeling Techniques, 11th Edition, Life Technologies, (2010), hereby expressly incorporated by reference, 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. Strategies for the labeling of proteins are well known in the art and can be employed in the disclosed method. *See*, *e.g.*, Obermaier *et al.*, (2015) Methods Mol Biol 1295:153-65; Strack (2016) *Nature Methods* 13:33; Site-Specific Protein Labeling: Methods and Protocols, (Gautier and Hinner, eds.) 2015, Springer.

[0347] 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 anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1) (or fragment thereof) can be employed, such as those disclosed herein, *e.g.*, those having one or more of the CDRs shown in FIGURES 5-21.

[0348] 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.

[0349] 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.

[0350] 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.

Vc. Method of Isolating a Molecule

[0351] It is of tremendous value to have the ability to separate different populations of 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. Thus, in one aspect of the instant disclosure, a method of isolating a molecule comprising the anti-CD19 scFv FMC63 (SEQ ID NO: 1) is provided.

[0352] In some embodiments, the method comprises providing a sample known or suspected to comprise a molecule comprising the anti-CD19 scFv FMC63 (SEQ ID NO: 1).

[0353] In specific embodiments, the molecule comprising the anti-CD19 scFv FMC63 (SEQ ID NO: 1) is a CAR. When the molecule is a CAR it can comprise a molecule, or fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8),

SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof.

[0354] An antigen binding molecule that specifically binds the anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1) 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), hereby expressly incorporated by reference, 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. *See*, *e.g.*, Obermaier *et al.*, (2015) *Methods Mol Biol* 1295:153-65; Strack (2016) *Nature Methods* 13:33; Site-Specific Protein Labeling: Methods and Protocols, (Gautier and Hinner, eds.) 2015, Springer.

[0355] 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 anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1) (or fragment thereof) can be employed, such as those disclosed herein, *e.g.*, those having one or more of the CDRs shown in FIGURES 5-21.

[0356] 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.

[0357] 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.

[0358] 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 SEQ ID NO: 1 (or one or more molecules comprising SEQ ID NO: 1 bound to an antigen binding molecule) may have formed. Unbound molecules comprising SEQ ID NO: 1 and/or unbound antigen binding molecules may also be present in the local environment of any formed binding complexes.

[0359] 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.

[0360] 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, are preferably avoided when performing this step of the method.

[0361] A formed binding complex is then separated into (a) a molecule comprising SEQ ID NO: 1, 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.

[0362] Following the separation, if the molecule comprising SEQ ID NO: 1 is of primary interest it can be collected; alternatively, if the antigen binding molecule is of primary interest it can be collected.

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

[0363] As disclosed herein, it may sometimes be desirable to isolate a molecule comprising the anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1), as provided herein. In other cases, simply knowing whether a molecule comprising SEQ ID NO: 1 provided herein 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 performed. Thus, the qualitative determination of the presence or absence of a molecule comprising the anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1) of the instant disclosure can be useful in multiple applications. In view thereof, a method of determining the presence or absence of a molecule comprising SEQ ID NO: 1 in a sample is provided.

[0364] In some embodiments, the method comprises providing a sample known or suspected to comprise a molecule comprising SEQ ID NO: 1.

[0365] In some embodiments, the molecule comprising SEQ ID NO: 1 is a CAR. When the molecule is a CAR it can comprise a molecule, or fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof.

[0366] An antigen binding molecule comprising a detectable label that specifically binds the anti-CD19 scFv FMC63 (SEQ ID NO: 1) 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 fluoro-phores, are described in Johnson, Molecular Probes Handbook:A Guide to Fluorescent Probes and Labeling Techniques, 11th Edition, Life Technologies, (2010), hereby expressly incorporated by reference, 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. Strategies for the labeling of proteins are well known in the art and can be employed in the disclosed method. *See*, *e.g.*, Obermaier et al., (2015) *Methods Mol Biol* 1295:153-65; Strack (2016) *Nature Methods* 13:33; Site-Specific Protein Labeling: Methods and Protocols, (Gautier and Hinner, eds.) 2015, Springer.

[0367] 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 anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1 or fragment thereof) can be employed, such as those disclosed herein, *e.g.*, those having one or more of the CDRs shown in FIGURES 5-21.

[0368] Continuing, the sample is contacted with the antigen binding molecule under conditions that permit the formation of a binding complex comprising a molecule comprising SEQ ID NO: 1 (which can be presented on 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.

[0369] 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.

[0370] 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 anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1) (or one or more molecules comprising SEQ ID NO: 1 bound to an antigen binding molecule) may have formed. Unbound molecules comprising SEQ ID NO: 1 and/or unbound antigen binding molecules may also be present in the local environment of any formed binding complexes.

[0371] 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.

[0372] 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.

[0373] Lastly, the presence or absence of a binding complex--which will comprise a molecule comprising SEQ ID NO: 1 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, flow cytometry or 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 SEQ ID NO: 1.

[0374] As is the case with all of the disclosed methods, the molecule comprising the anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1) can be disposed in any environment. In preferred embodiments, the molecule comprising SEQ ID NO: 1 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 one 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 (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. 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.

[0375] In an 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.

Ve. Method of Increasing the Concentration of a Molecule

[0376] 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 sometimes 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 the anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1). 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.

To address this problem, a method of increasing the concentration of cells presenting a molecule comprising the anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1) is provided.

[0377] In some embodiments, the method comprises providing a sample comprising cells known or suspected to present a molecule comprising the anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1).

[0378] In specific embodiments, the molecule comprising the sequence SEQ ID NO: 1 is a CAR. When the molecule is a CAR it can comprise a molecule, or fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof.

[0379] An antigen binding molecule that specifically binds SEQ ID NO: 1, 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 fluoro-phores, are described in Johnson, Molecular Probes Handbook:A Guide to Fluorescent Probes and Labeling Techniques, 11th Edition, Life Technologies, (2010), hereby expressly incorporated by reference, 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. Strategies for the labeling of proteins are well known in the art and can be employed in the disclosed method. *See*, *e.g.*, Obermaier *et al.*, (2015) *Methods Mol Biol* 1295:153-65; Strack (2016) *Nature Methods* 13:33; Site-Specific Protein Labeling: Methods and Protocols, (Gautier and Hinner, eds.) 2015, Springer.

[0380] 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 anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1) (or fragment thereof) can be employed, such as those disclosed herein, *e.g.*, those having one or more of the CDRs shown in FIGURES 5-21.

[0381] 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.

[0382] A cell presenting a molecule comprising SEQ ID NO: 1 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 (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. 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.

[0383] 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 anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1) 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.

[0384] 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 anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1) (or one or more molecules comprising SEQ ID NO: 1 bound to an antigen binding molecule) may have formed. Unbound molecules comprising SEQ ID NO: 1 and/or unbound antigen binding molecules may also be present in the local environment of any formed binding complexes.

[0385] 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.

[0386] 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.

[0387] At this stage of the method, a population of cells presenting a molecule comprising the SEQ ID NO: 1 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 SEQ ID NO: 1 will be absent, and thus the population (or concentration) of cells presenting a molecule comprising SEQ ID NO: 1 will be increased compared to the levels prior to performing the method.

[0388] If the concentration of the molecule comprising the anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1) 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.

Vf. Method of Depleting a Population of Immune Cells

[0389] 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 the anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1) is provided. An antigen binding molecule that specifically recognizes SEQ ID NO: 1, *e.g.*, those having one or more of the CDRs shown in Figure 6, can be employed in the method.

[0390] In some embodiments, the method comprises providing a population of immune cells to be depleted, wherein the cells are known or suspected to be expressing a molecule comprising the anti-CD19 scFv FMC63 sequence (SEQ ID NO: 1).

[0391] In specific embodiments, the molecule comprising SEQ ID NO: 1 is a CAR. When the molecule is a CAR it can comprise a molecule, or fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof.

[0392] An immune cell expressing a molecule comprising the anti-CD19 scFv FMC63 (SEQ ID NO: 1) sequence 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 (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. 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.

[0393] Continuing, the immune cells are contacted with an antigen binding molecule that specifically binds to (a) the molecule comprising SEQ ID NO: 1, and (b) an activating molecule expressed on the surface of the immune cell not expressing the molecule comprising SEQ ID NO: 1, under conditions that permit the formation of a ternary binding complex comprising the molecule comprising SEQ ID NO: 1, 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.

[0394] 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 anti-CD19 scFv FMC63 (SEQ ID NO: 1) sequence, the antigen binding molecule and an activating molecule expressed on the surface of an immune cell not expressing the molecule comprising SEQ ID NO: 1. 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.

[0395] 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 anti-CD19 scFv FMC63 (SEQ ID NO: 1) sequence. 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 anti-CD19 scFv FMC63 (SEQ ID NO: 1) sequence serves to "tag" those cells presenting the molecule comprising SEQ ID NO: 1 (*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 SEQ ID NO: 1, 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 SEQ ID NO: 1. Thus, with multiple binding events occurring throughout the subject the population of immune cells bearing the molecule comprising SEQ ID NO: 1 are depleted and the risk of harm to the subject decreases.

SEQUENCES AND SEQ ID NOs

The instant disclosure comprises a number of nucleic acid and polypeptide sequences. For convenience, the table below correlates each sequence with its appropriate description and SEQ ID NO.

SEQ ID NO	Description	Sequence
1	Anti-CD19 scFv FMC63	DIQMTQTTSSLSASLGDRVTISCRASQDISKYLNWYQQKP DGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQE DIATYFCQQGNTLPYTFGGGTKLEITGSTSGSGKPGSGEGS TKGEVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWI RQPPRKGLEWLGVIWGSETTYYNSALKSRLTIIKDNSKSQ VFLKMNSLQTDDTAIYYCAKHYYYGGSYAMDYWGQGT SVTVSS
2	Clone 7 VH	ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGT GCTCAAAGGTGTCCAGTGTCAGGAGCAGCTGGAGGAGT CCGGGGGAGACCTGGTCAAGCCTGGAGGAACCCTGAC AGTCACCTGCAAAGCCTCTGGATTCTCCTTCAGTAACA ATGGAATTTGCTGGGTCCGCCAGGCTCCAGGGAAGGGG CTGGAGTGGATCGGATGTCTTTATGTTGGTAGTAGTGA TACCACTTACTACGCGAGCTGGGCGAAAGGCCGATTCA CCATCTCCAAAAGCTCGTCGACCACGGTGACTCTACAA ATGACCAGTCTGACAGTCGCGGACACGGCCACCTATTT CTGTACGATAAATCTCGGCTTGTGGGGCCCCGGCACCC TGGTCACCGTCTCCTCA
3	Clone 7 VH	METGLRWLLLVAVLKGVQCQEQLEESGGDLVKPGGTLT VTCKASGFSFSNNGICWVRQAPGKGLEWIGCLYVGSSDT TYYASWAKGRFTISKSSSTTVTLQMTSLTVADTATYFCTI NLGLWGPGTLVTVSS
4	Clone 7 HC	METGLRWLLLVAVLKGVQCQEQLEESGGDLVKPGGTLT VTCKASGFSFSNNGICWVRQAPGKGLEWIGCLYVGSSDT TYYASWAKGRFTISKSSSTTVTLQMTSLTVADTATYFCTI NLGLWGPGTLVTVSSGQPKAPSVFPLAPCCGDTPSSTVTL GCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSGLYSL SSVVSVTSSSQPVTCNVAHPATNTKVDKTVAPSTCSKPTC PPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVVVDVSQDD PEVQFTWYINNEQVRTARPPLREQQFNSTIRVVSTLPIAHQ DWLRGKEFKCKVHNKALPAPIEKTISKARGQPLEPKVYT MGPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDN YKTTPAVLDSDGSYFLYSKLSVPTSEWQRGDVFTCSVMH EALHNHYTQKSISRSPGK
5	Clone 7 VH CDR1	GFSFSNN
6	Clone 7 VH CDR2	YVGSSD
7	Clone 7 VH CDR3	NLGL
8	Clone 7 VL	ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCT GCTGCTCTGGCTCCCAGGTGCCACATTTGCCATCGTGGT GACCCAGACTCCATCTTCCAAGTCTGTCCCTGTGGGAG GCACAGTCACCATCAATTGCCAGGCCAGTGAGAGTGTT TATAATAGCGACTGGTTAGCCTGGTATCAGCAGAAACC AGGGCAGCCTCCCAAGCAACTGATCTATGCTGCATCCA

SEQ ID NO	Description	Sequence
		CTCTGGCATCTGGGGTCCCATCGCGCTTCAAAGGCAGT GGATCTGGGACACAGTTCACTCTCACCATCAGCGATGT GGTGTGTGACGATGCTGCCACTTATTATTGTGCAGGAT ATAAAAGTAGTAGTACTGATGGGATTGCTTTCGGCGGA GGGACCGAGGTGGTGGTCAAA
9	Clone 7 VL	MDTRAPTQLLGLLLLWLPGATFAIVVTQTPSSKSVPVGGT VTINCQASESVYNSDWLAWYQQKPGQPPKQLIYAASTLA SGVPSRFKGSGSGTQFTLTISDVVCDDAATYYCAGYKSSS TDGIAFGGGTEVVVK
10	Clone 7 LC	MDTRAPTQLLGLLLLWLPGATFAIVVTQTPSSKSVPVGGT VTINCQASESVYNSDWLAWYQQKPGQPPKQLIYAASTLA SGVPSRFKGSGSGTQFTLTISDVVCDDAATYYCAGYKSSS TDGIAFGGGTEVVVKGDPVAPTVLIFPPAADQVATGTVTI VCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADCT YNLSSTLTLTSTQYNSHKEYTCKVTQGTTSVVQSFNRGDC
11	Clone 7 VL CDR1	QASESVYNSDWLA
12	Clone 7 VL CDR2	AASTLAS
13	Clone 7 VL CDR3	AGYKSSSTDGIA
14	Clone 13 VH	ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGT GCTCAAAGGTGTCCAGTGTCAGGAGCAGCTGGAGGAGT CCGGGGGAGACCTGGTCAAGCCTGGAGGAACCCTGAC AGTCACCTGCAAAGCCTCTGGATTCTCCTTCAGTAACA ATGGAATTTGCTGGGTCCGCCAGGCTCCAGGGAAGGGG CTGGAGTGGATCGGATGTCTTTATGTTGGTAGTAGTGA TACCACTTACTACGCGAGCTGGGCGAAAGGCCGATTCA CCATCTCCAAAAGCTCGTCGACCACGGTGACTCTACAA ATGACCAGTCTGACAGTCGCGGACACGGCCACCTATTT CTGTACGATAAATCTCGGCTTGTGGGGCCCCGGCACCC TGGTCACCGTCTCCTCA
15	Clone 13 VH	METGLRWLLLVAVLKGVQCQEQLEESGGDLVKPGGTLT VTCKASGFSFSNNGICWVRQAPGKGLEWIGCLYVGSSDT TYYASWAKGRFTISKSSSTTVTLQMTSLTVADTATYFCTI NLGLWGPGTLVTVSS
16	Clone 13 HC	METGLRWLLLVAVLKGVQCQEQLEESGGDLVKPGGTLT VTCKASGFSFSNNGICWVRQAPGKGLEWIGCLYVGSSDT TYYASWAKGRFTISKSSSTTVTLQMTSLTVADTATYFCTI NLGLWGPGTLVTVSSGQPKAPSVFPLAPCCGDTPSSTVTL GCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSGLYSL SSVVSVTSSSQPVTCNVAHPATNTKVDKTVAPSTCSKPTC PPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVVVDVSQDD PEVQFTWYINNEQVRTARPPLREQQFNSTIRVVSTLPIAHQ DWLRGKEFKCKVHNKALPAPIEKTISKARGQPLEPKVYT MGPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDN YKTTPAVLDSDGSYFLYSKLSVPTSEWQRGDVFTCSVMH EALHNHYTQKSISRSPGK
5	Clone 13 VH CDR1	GFSFSNN
6	Clone 13 VH CDR2	YVGSSD
7	Clone 13 VH CDR3	NLGL
17	Clone 13 VL	ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCT GCTGCTCTGGCTCCCAGGTGCCACACTTGCCATCGTGGT

SEQ ID NO	Description	Sequence
		GACCCAGACTCCATCTTCCAAGTCTGTCCCTGTGGGAG GCACAGTCACCATCAATTGCCAGGCCAGTGAGAGTGTT TATAATAGCGACTGGTTAGCCTGGTATCAGCAGAAACC AGGGCAGCCTCCCAAGCAACTGATCTATGCTGCATCCA CTCTGGCATCTGGGGTCCCATCGCGCTTCAAAGGCAGT GGATCTGGGACACAGTTCACTCTCACCATCAGCGATGT GGTGTGTGACGATGCTGCCACTTATTATTGTGCAGGAT ATAAAAGTAGTAGTACTGATGGGATTGCTTTCGGCGGA GGGACCGAGGTGGTGGTCAAA
18	Clone 13 VL	MDTRAPTQLLGLLLLWLPGATLAIVVTQTPSSKSVPVGGT VTINCQASESVYNSDWLAWYQQKPGQPPKQLIYAASTLA SGVPSRFKGSGSGTQFTLTISDVVCDDAATYYCAGYKSSS TDGIAFGGGTEVVVK
19	Clone 13 LC	MDTRAPTQLLGLLLLWLPGATLAIVVTQTPSSKSVPVGGT VTINCQASESVYNSDWLAWYQQKPGQPPKQLIYAASTLA SGVPSRFKGSGSGTQFTLTISDVVCDDAATYYCAGYKSSS TDGIAFGGGTEVVVKGDPVAPTVLIFPPAADQVATGTVTI VCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADCT YNLSSTLTLTSTQYNSHKEYTCKVTQGTTSVVQSFNRGDC
11	Clone 13 VL CDR1	QASESVYNSDWLA
12	Clone 13 VL CDR2	AASTLAS
13	Clone 13 VL CDR3	AGYKSSSTDGIA
20	Clone 14-1 VH	ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGT GCTCAAAGGTGTCCAGTGTCAGGAGCAGCTGGAGGAGT CCGGGGGAGGCCTGGTCAAGCCTGGGGCATCCCTGACA CTCACCTGCAAAGCCTCTGGATTCGACTTCAGTATCAA CTACTACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGG GGTTGGAGTGGATCGCATGCATTTATACTGGTGATGAT GACACTTTCTACGCGAGCTGGGCGAAAGGCCGGTTCAC CATCTCCAAAACCTCGTCGACCACGGTGACTCTACAAC TGAACAGTCTGACAGCCGCGGACACGGCCACCTATTTC TGTGTGAGAGGTCTATATAGTGGTAGTATTAATAACCT GTGGGGCCCAGGCACCCTGGTCACCGTCTCCTCA
21	Clone 14-1VH	METGLRWLLLVAVLKGVQCQEQLEESGGGLVKPGASLTL TCKASGFDFSINYYMCWVRQAPGKGLEWIACIYTGDDDT FYASWAKGRFTISKTSSTTVTLQLNSLTAADTATYFCVRG LYSGSINNLWGPGTLVTVSS
22	Clone 14-1HC	METGLRWLLLVAVLKGVQCQEQLEESGGGLVKPGASLTL TCKASGFDFSINYYMCWVRQAPGKGLEWIACIYTGDDDT FYASWAKGRFTISKTSSTTVTLQLNSLTAADTATYFCVRG LYSGSINNLWGPGTLVTVSSGQPKAPSVFPLAPCCGDTPSS TVTLGCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSG LYSLSSVVSVTSSSQPVTCNVAHPATNTKVDKTVAPSTCS KPTCPPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVVVDVS QDDPEVQFTWYINNEQVRTARPPLREQQFNSTIRVVSTLPI AHQDWLRGKEFKCKVHNKALPAPIEKTISKARGQPLEPK VYTMGPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKA EDNYKTTPAVLDSDGSYFLYSKLSVPTSEWQRGDVFTCS VMHEALHNHYTQKSISRSPGK
23	Clone 14-1VH CDR1	GFDFSINY

SEQ ID NO	Description	Sequence
24	Clone 14-1VH CDR2	YTGDD
25	Clone 14-1VH CDR3	GLYSGSINNL
26	Clone 14-1VL	ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCT GCTGCTCTGGCTCCCAGATGCCAGATGTGCGCTTGTGA TGACCCAGACTCCATCCCCTGTGTCTGCAGCTGTGGGA GGCACAGTCACCATCAGTTGCCAGGCCAGTCAGAGTGT TTATAACAACGACTACTTATCCTGGTATCAGCAGAAAC CAGGGCAGCCTCCCAAACTCCTGATCTATTATGCATCC ACTCTGGCATCTGGGGTCTCATCGCGGTTCAAAGGCAG TGGATCTGGGACACAGTTCACTCTCACCATCAGCGACG TGCAGTGTGACGATGCTGCCGCTTACTATTGTGCAGGC GTTAAAGGTTATAGTAATGATAATAATGGTTTCGGCGG AGGGACCGAGGTGGTGGTCAAA
27	Clone 14-1VL	MDTRAPTQLLGLLLLWLPDARCALVMTQTPSPVSAAVGG TVTISCQASQSVYNNDYLSWYQQKPGQPPKLLIYYASTLA SGVSSRFKGSGSGTQFTLTISDVQCDDAAAYYCAGVKGY SNDNNGFGGGTEVVVK
28	Clone 14-1LC	MDTRAPTQLLGLLLLWLPDARCALVMTQTPSPVSAAVGG TVTISCQASQSVYNNDYLSWYQQKPGQPPKLLIYYASTLA SGVSSRFKGSGSGTQFTLTISDVQCDDAAAYYCAGVKGY SNDNNGFGGGTEVVVKGDPVAPTVLIFPPAADQVATGTV TIVCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADC TYNLSSTLTLTSTQYNSHKEYTCKVTQGTTSVVQSFNRGD C
29	Clone 14-1 VL CDR1	QASQSVYNNDYLS
30	Clone 14-1 VL CDR2	YASTLAS
31	Clone 14-1 VL CDR3	AGVKGYSNDNNG
32	Clone 14-7 VH	ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGT GCTCAAAGGTGTCCAATGTCAGTCGCTGGAGGAGTCCG GGGGAGGCCTGGTCAAGCCTGGGGCATCCCTGACACTC ACCTGCAAAGCCTCTGGATTCGACTTCAGTATCAACTA CTACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGT TGGAGTGGATCGCATGCATTTATACTGGTGATGATGAC ACTTTCTACGCGAGCTGGGCGAAAGGCCGGTTCACCAT CTCCAAAACCTCGTCGACCACGGTGACTCTACAACTGA ACAGTCTGACAGCCGCGGACACGGCCACCTATTTCTGT GTGAGAGGTCTATATAGTGGTAGTATTAATAACCTGTG GGGCCCAGGCACCCTGGTCACCGTCTCCTCA
33	Clone 14-7 VH	METGLRWLLLVAVLKGVQCQSLEESGGGLVKPGASLTLT CKASGFDFSINYYMCWVRQAPGKGLEWIACIYTGDDDTF YASWAKGRFTISKTSSTTVTLQLNSLTAADTATYFCVRGL YSGSINNLWGPGTLVTVSS
34	Clone 14-7 HC	METGLRWLLLVAVLKGVQCQSLEESGGGLVKPGASLTLT CKASGFDFSINYYMCWVRQAPGKGLEWIACIYTGDDDTF YASWAKGRFTISKTSSTTVTLQLNSLTAADTATYFCVRGL YSGSINNLWGPGTLVTVSSGQPKAPSVFPLAPCCGDTPSST

SEQ ID NO	Description	Sequence
		VTLGCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSGL YSLSSVVSVTSSSQPVTCNVAHPATNTKVDKTVAPSTCSK PTCPPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVVVDVSQ DDPEVQFTWYINNEQVRTARPPLREQQFNSTIRVVSTLPIA HQDWLRGKEFKCKVHNKALPAPIEKTISKARGQPLEPKV YTMGPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAE DNYKTTPAVLDSDGSYFLYSKLSVPTSEWQRGDVFTCSV MHEALHNHYTQKSISRSPGK
23	Clone 14-7 VH CDR1	GFDFSINY
24	Clone 14-7 VH CDR2	YTGDD
25	Clone 14-7 VH CDR3	GLYSGSINNL
35	Clone 14-7 VL	ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCT GCTGCTCTGGCTCCCAGATGCCAGATGTGCGCTTGTGA TGACCCAGACTCCATCCCCTGTGTCTGCAGCTGTGGGA GGCACAGTCACCATCAGTTGCCAGGCCAGTCAGAGTGT TTATAACAACGACTACTTATCCTGGTATCAGCAGAAAC CAGGGCAGCCTCCCAAACTCCTGATCTATTATGCATCC ACTCTGGCATCTGGGGTCTCATCGCGGTTCAAAGGCAG TGGATCTGGGACACAGTTCACTCTCACCATCAGCGACG TGCAGTGTGACGATGCTGCCGCTTACTATTGTGCAGGC GTTAAAGGTTATAGTAATGATAATAATGGTTTCGGCGG AGGGACCGAGGTGGTGGTCAAA
36	Clone 14-7 VL	MDTRAPTQLLGLLLLWLPDARCALVMTQTPSPVSAAVGG TVTISCQASQSVYNNDYLSWYQQKPGQPPKLLIYYASTLA SGVSSRFKGSGSGTQFTLTISDVQCDDAAAYYCAGVKGY SNDNNGFGGGTEVVVK
37	Clone 14-7 LC	MDTRAPTQLLGLLLLWLPDARCALVMTQTPSPVSAAVGG TVTISCQASQSVYNNDYLSWYQQKPGQPPKLLIYYASTLA SGVSSRFKGSGSGTQFTLTISDVQCDDAAAYYCAGVKGY SNDNNGFGGGTEVVVKGDPVAPTVLIFPPAADQVATGTV TIVCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADC TYNLSSTLTLTSTQYNSHKEYTCKVTQGTTSVVQSFNRGD C
29	Clone 14-7 VL CDR1	QASQSVYNNDYLS
30	Clone 14-7 VL CDR2	YASTLAS
31	Clone 14-7 VL CDR3	AGVKGYSNDNNG
38	Clone 15 VH	ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGT GCTCAAAGGGGTCCAGTGTCAGTCGTTGGAGGAGTCCG GGGGAGACCTGGTCAAGCCTGGGGCATCCCTGACACTC ACCTGCACAGCCTCTGGATTCTCCTTCACGAGCAACTA CTACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGC TGGAGTGGGTCGCGTGCATTTTTCTTGGTAGTAGTGGTA ACACTGTCTACGCGAACTGGGCGAAAGGCCGATTCACC ATCTCCAAAACCTCGTCGACCACGGTGACTCTGCAAAT GACCAGTCTGACAGTCGCGGACACGGCCACCTATTTCT

SEQ ID NO	Description	Sequence
		GTGCGAGAGACTATGTTAATGGTTATGACTACTTTAAC TTGTGGGGCCCAGGCACCTTGGTCACCGTCTCCTCA
39	Clone 15 VH	METGLRWLLLVAVLKGVQCQSLEESGGDLVKPGASLTLT CTASGFSFTSNYYMCWVRQAPGKGLEWVACIFLGSSGNT VYANWAKGRFTISKTSSTTVTLQMTSLTVADTATYFCAR DYVNGYDYFNLWGPGTLVTVSS
40	Clone 15 HC	METGLRWLLLVAVLKGVQCQSLEESGGDLVKPGASLTLT CTASGFSFTSNYYMCWVRQAPGKGLEWVACIFLGSSGNT VYANWAKGRFTISKTSSTTVTLQMTSLTVADTATYFCAR DYVNGYDYFNLWGPGTLVTVSSGQPKAPSVFPLAPCCGD TPSSTVTLGCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVR QSSGLYSLSSVVSVTSSSQPVTCNVAHPATNTKVDKTVAP STCSKPTCPPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVV VDVSQDDPEVQFTWYINNEQVRTARPPLREQQFNSTIRVV STLPIAHQDWLRGKEFKCKVHNKALPAPIEKTISKARGQP LEPKVYTMGPPREELSSRSVSLTCMINGFYPSDISVEWEKN GKAEDNYKTTPAVLDSDGSYFLYSKLSVPTSEWQRGDVF TCSVMHEALHNHYTQKSISRSPGK
41	Clone 15 VH CDR1	GFSFTSNY
42	Clone 15 VH CDR2	FLGSSG
43	Clone 15 VH CDR3	DYVNGYDYFNL
44	Clone 15 VL	ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCT GCTGCTCTGGCTCCCAGGTGCCACATTTGCCCAAGTGCT GACCCAGACTGCATCCCCCGTGTCTGCGGCTGTTGGAG GCACAGTCACCATCAATTGCCAGTCCAGTCAGAGTGTT TATAATAAGAACTTAGCCTGGTATCAGCAGAAACCAGG GCAGCCTCCCAAAGGCCTGATCTATTCTACATCGACTCT AGATTCTGGGGTCCCATCGCGGTTCAGCGGCAGTGGAT CTGGGACACAGTTCACTCTCACCATCAGCGACGTGCAG TGTGACGATGCTGCCACTTACTACTGTCTAGGCAGTTAT GATTGTAGTAGTGCTGATTGTAATGCTTTCGGCGGAGG GACCGAGGTGGTGGTCAAA
45	Clone 15 VL	MDTRAPTQLLGLLLLWLPGATFAQVLTQTASPVSAAVGG TVTINCQSSQSVYNKNLAWYQQKPGQPPKGLIYSTSTLDS GVPSRFSGSGSGTQFTLTISDVQCDDAATYYCLGSYDCSS ADCNAFGGGTEVVVK
46	Clone 15 LC	MDTRAPTQLLGLLLLWLPGATFAQVLTQTASPVSAAVGG TVTINCQSSQSVYNKNLAWYQQKPGQPPKGLIYSTSTLDS GVPSRFSGSGSGTQFTLTISDVQCDDAATYYCLGSYDCSS ADCNAFGGGTEVVVKGDPVAPTVLIFPPAADQVATGTVTI VCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADCT YNLSSTLTLTSTQYNSHKEYTCKVTQGTTSVVQSFNRGDC
47	Clone 15 VL CDR1	QSSQSVYNKNLA
48	Clone 15 VL CDR2	STSTLDS
49	Clone 15 VL CDR3	LGSYDCSSADCNA
50	Clone 17 VH	ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGT GCTCAAAGGTGTCCAATGTCAGTCGCTGGAGGAGTCCG GGGGAGGCCTGGTCAAGCCTGGGGCATCCCTGACACTC ACCTGCACAGCCTCTGGATTCTCCTTCAGTGACAGTTGG TACTTGTGTTGGGTCCGCCAGGCTCCAGGGAAGGGGCT

SEQ ID NO	Description	Sequence
		GGAGTGGATCGCATGCATTTATACTGGTGATGGTGACA CTTATTACGCGACCTGGGCGAAAGGCCGATTCACCATC TCCAAGACCTCGTCGACCACAGTGACTCTACAAATGAC CAGTCTGACAGCCGCGGACACGGCCACCTATTTCTGTG CGAGGGGTGCCCAATTTTACTTGTGGGGCCAAGGCACC CTGGTCACCGTCTCCTCA
51	Clone 17 VH	METGLRWLLLVAVLKGVQCQSLEESGGGLVKPGASLTLT CTASGFSFSDSWYLCWVRQAPGKGLEWIACIYTGDGDTY YATWAKGRFTISKTSSTTVTLQMTSLTAADTATYFCARG AQFYLWGQGTLVTVSS
52	Clone 17 HC	METGLRWLLLVAVLKGVQCQSLEESGGGLVKPGASLTLT CTASGFSFSDSWYLCWVRQAPGKGLEWIACIYTGDGDTY YATWAKGRFTISKTSSTTVTLQMTSLTAADTATYFCARG AQFYLWGQGTLVTVSSGQPKAPSVFPLAPCCGDTPSSTVT LGCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSGLYS LSSVVSVTSSSQPVTCNVAHPATNTKVDKTVAPSTCSKPT CPPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVVVDVSQD DPEVQFTWYINNEQVRTARPPLREQQFNSTIRVVSTLPIAH QDWLRGKEFKCKVHNKALPAPIEKTISKARGQPLEPKVYT MGPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDN YKTTPAVLDSDGSYFLYSKLSVPTSEWQRGDVFTCSVMH EALHNHYTQKSISRSPGK
53	Clone 17 VH CDR1	GFSFSDSW
54	Clone 17 VH CDR2	YTGDG
55	Clone 17 VH CDR3	GAQFYL
56	Clone 17 VL	ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCT GCTGCTCTGGCTCCCAGGTGCCACATTTGCCCAGGTGCT GACCCAGACTCCATCCTCCGTGTCTGCAGCTGTGGGAG GCACAGTCACCATCAATTGCCAGTCCAGTCAGAGTGTT TATGCCAACACCTACTTATCCTGGTATCAGCAGAAACC AGGGCAGCCTCCCAAGCAACTGATCTATTCTGCATCCA GTCTGGCATCTGGGGTCCCACCGCGGTTCAAAGGCAGT GGATCTGGGACACAGTTCGCTCTCACCATCAGCGACGT GCAGTGTGACGATGCTGCCACTTACTACTGTCTAGGCA GATATAGTTGTGGTCTTGCTGATTGTGCTGCTTTCGGCG GAGGGACCGAGGTGGTGGTCAAA
57	Clone 17 VL	MDTRAPTQLLGLLLLWLPGATFAQVLTQTPSSVSAAVGG TVTINCQSSQSVYANTYLSWYQQKPGQPPKQLIYSASSLA SGVPPRFKGSGSGTQFALTISDVQCDDAATYYCLGRYSCG LADCAAFGGGTEVVVK
58	Clone 17 LC	MDTRAPTQLLGLLLLWLPGATFAQVLTQTPSSVSAAVGG TVTINCQSSQSVYANTYLSWYQQKPGQPPKQLIYSASSLA SGVPPRFKGSGSGTQFALTISDVQCDDAATYYCLGRYSCG LADCAAFGGGTEVVVKGDPVAPTVLIFPPAADQVATGTV TIVCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADC TYNLSSTLTLTSTQYNSHKEYTCKVTQGTTSVVQSFNRGD C
59	Clone 17 VL CDR1	QSSQSVYANTYLS
60	Clone 17 VL CDR2	SASSLAS
61	Clone 17 VL CDR3	LGRYSCGLADCAA

SEQ ID NO	Description	Sequence
11	7 VL CDR1 Kabat	QASESVYNSDWLA
12	7 VL CDR2 Kabat	AASTLAS
13	7 VL CDR3 Kabat	AGYKSSSTDGIA
11	13 VL CDR1 Kabat	QASESVYNSDWLA
12	13 VL CDR2 Kabat	AASTLAS
13	13 VL CDR3 Kabat	AGYKSSSTDGIA
29	14-1 VL CDR1 Kabat	QASQSVYNNDYLS
30	14-1 VL CDR2 Kabat	YASTLAS
31	14-1 VL CDR3 Kabat	AGVKGYSNDNNG
29	14-7 VL CDR1 Kabat	QASQSVYNNDYLS
30	14-7 VL CDR2 Kabat	YASTLAS
31	14-7 VL CDR3 Kabat	AGVKGYSNDNNG
47	15 VL CDR1 Kabat	QSSQSVYNKNLA
48	15 VL CDR2 Kabat	STSTLDS
49	15 VL CDR3 Kabat	LGSYDCSSADCNA
59	17 VL CDR1 Kabat	QSSQSVYANTYLS
60	17 VL CDR2 Kabat	SASSLAS
61	17 VL CDR3 Kabat	LGRYSCGLADCAA
62	7 VH CDR1 Kabat	NNGIC
63	7 VH CDR2 Kabat	CLYVGSSDTTYYASWAK
7	7 VH CDR3 Kabat	NLGL
62	13VH CDR1 Kabat	NNGIC
63	13 VH CDR2 Kabat	CLYVGSSDTTYYASWAK
7	13 VH CDR3 Kabat	NLGL
64	14-1 VH CDR1 Kabat	INYYMC
65	14-1 VH CDR2 Kabat	CIYTGDDDTFYASWAK
25	14-1 VH CDR3 Kabat	GLYSGSINNL
64	14-7 VH CDR1 Kabat	INYYMC
65	14-7 VH CDR2 Kabat	CIYTGDDDTFYASWAK
25	14-7 VH CDR3 Kabat	GLYSGSINNL
66	15 VH CDR1 Kabat	SNYYMC
67	15 VH CDR2 Kabat	CIFLGSSGNTVYANWAK
43	15 VH CDR3 Kabat	DYVNGYDYFNL
68	17 VH CDR1 Kabat	DSWYLC
69	17 VH CDR2 Kabat	CIYTGDGDTYYATWAK
55	17 VH CDR3 Kabat	GAQFYL
11	7 VL CDR1 Chothia	QASESVYNSDWLA
12	7 VL CDR2 Chothia	AASTLAS

SEQ ID NO	Description	Sequence
13	7 VL CDR3 Chothia	AGYKSSSTDGIA
11	13 VL CDR1 Chothia	QASESVYNSDWLA
12	13 VL CDR2 Chothia	AASTLAS
13	13 VL CDR3 Chothia	AGYKSSSTDGIA
29	14-1 VL CDR1 Chothia	QASQSVYNNDYLS
30	14-1 VL CDR2 Chothia	YASTLAS
31	14-1 VL CDR3 Chothia	AGVKGYSNDNNG
29	14-7 VL CDR1 Chothia	QASQSVYNNDYLS
30	14-7 VL CDR2 Chothia	YASTLAS
31	14-7 VL CDR3 Chothia	AGVKGYSNDNNG
47	15 VL CDR1 Chothia	QSSQSVYNKNLA
48	15 VL CDR2 Chothia	STSTLDS
49	15 VL CDR3 Chothia	LGSYDCSSADCNA
59	17 VL CDR1 Chothia	QSSQSVYANTYLS
60	17 VL CDR2 Chothia	SASSLAS
61	17 VL CDR3 Chothia	LGRYSCGLADCAA
5	7 VH CDR1 Chothia	GFSFSNN
6	7 VH CDR2 Chothia	YVGSSD
7	7 VH CDR3 Chothia	NLGL
5	13VH CDR1 Chothia	GFSFSNN
6	13 VH CDR2 Chothia	YVGSSD
7	13 VH CDR3 Chothia	NLGL
23	14-1 VH CDR1 Chothia	GFDFSINY
24	14-1 VH CDR2 Chothia	YTGDD
25	14-1 VH CDR3 Chothia	GLYSGSINNL

SEQ ID NO	Description	Sequence
23	14-7 VH CDR1 Chothia	GFDFSINY
24	14-7 VH CDR2 Chothia	YTGDD
25	14-7 VH CDR3 Chothia	GLYSGSINNL
41	15 VH CDR1 Chothia	GFSFTSNY
42	15 VH CDR2 Chothia	FLGSSG
43	15 VH CDR3 Chothia	DYVNGYDYFNL
53	17 VH CDR1 Chothia	GFSFSDSW
54	17 VH CDR2 Chothia	YTGDG
55	17 VH CDR3 Chothia	GAQFYL
11	7 VL CDR1 IMGT	QASESVYNSDWLA
12	7 VL CDR2 IMGT	AASTLAS
13	7 VL CDR3 IMGT	AGYKSSSTDGIA
11	13 VL CDR1 IMGT	QASESVYNSDWLA
12	13 VL CDR2 IMGT	AASTLAS
13	13 VL CDR3 IMGT	AGYKSSSTDGIA
29	14-1 VL CDR1 IMGT	QASQSVYNNDYLS
30	14-1 VL CDR2 IMGT	YASTLAS
31	14-1 VL CDR3 IMGT	AGVKGYSNDNNG
29	14-7 VL CDR1 IMGT	QASQSVYNNDYLS
30	14-7 VL CDR2 IMGT	YASTLAS
31	14-7 VL CDR3 IMGT	AGVKGYSNDNNG
47	15 VL CDR1 IMGT	QSSQSVYNKNLA
48	15 VL CDR2 IMGT	STSTLDS
49	15 VL CDR3 IMGT	LGSYDCSSADCNA
59	17 VL CDR1 IMGT	QSSQSVYANTYLS
60	17 VL CDR2 IMGT	SASSLAS
61	17 VL CDR3 IMGT	LGRYSCGLADCAA
70	7 VH CDR 1 IMGT	GFSFSNNGIC
63	7 VH CDR 2 IMGT	CLYVGSSDTTYYASWAK
7	7 VH CDR 3 IMGT	NLGL
70	13 VH CDR 1 IMGT	GFSFSNNGIC
63	13 VH CDR 2 IMGT	CLYVGSSDTTYYASWAK

SEQ ID NO	Description	Sequence
7	13 VH CDR 3 IMGT	NLGL
71	14-1 VH CDR 1 IMGT	GFDFSINYYMC
65	14-1 VH CDR 2 IMGT	CIYTGDDDTFYASWAK
25	14-1 VH CDR 3 IMGT	GLYSGSINNL
71	14-7 VH CDR 1 IMGT	GFDFSINYYMC
65	14-7 VH CDR 2 IMGT	CIYTGDDDTFYASWAK
25	14-7 VH CDR 3 IMGT	GLYSGSINNL
72	15 VH CDR 1 IMGT	GFSFTSNYYMC
67	15 VH CDR 2 IMGT	CIFLGSSGNTVYANWAK
43	15 VH CDR 3 IMGT	DYVNGYDYFNL
73	17 VH CDR 1 IMGT	GFSFSDSWYLC
69	17 VH CDR 2 IMGT	CIYTGDGDTYYATWAK
55	17 VH CDR 3 IMGT	GAQFYL
74	HUMANIZED FMC 63 VL CDR1	RASQDISKYLN
75	HUMANIZED FMC 63 VL CDR2	HTSRLHS
76	HUMANIZED FMC 63 VL CDR3	QQGNTLPYT
77	HUMANIZED FMC 63 VH CDR1 Clothia	GVSLPDY
78	HUMANIZED FMC 63 VH CDR2 Clothia	WGSET
79	HUMANIZED FMC 63 VH CDR3	HYYYGGSYAMDY
80	HUMANIZED FMC 63 VH CDR1 Kabat	DYGVS
81	HUMANIZED FMC 63 VH CDR2 Kabat/IMGT	VIWGSETTYYNSALKS
82	HUMANIZED FMC 63 VH CDR1 IMGT	GVSLPDYGVS

INCORPORATION BY REFERENCE

[0396] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference. However, the citation of a reference herein should not be construed as an acknowledgement that such reference is prior art to the present invention. To the extent that any of the definitions or terms provided in the references incorporated by reference differ from the terms and discussion provided herein, the present terms and definitions control.

[0397] The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The foregoing description and Examples that follow detail certain preferred embodiments of the invention and describe the best mode contemplated by the inventors. It will be appreciated, however, that no matter how detailed the foregoing may appear in text, the invention may be practiced in many ways and the invention should be construed in accordance with the appended claims and any equivalents thereof.

EXAMPLES

[0398] The present invention is further illustrated by the following examples, which should not be construed as further limiting. The contents of all references cited throughout this application are expressly incorporated herein by reference.

EXAMPLE 1

Generation and Screening of Antigen Binding Molecules

[0399] Monoclonal antibodies were generated through immunization of rabbits using the anti-CD19 scFv FMC63 (SEQ ID NO: 1), conjugated to Fc as immunogen. Titer was determined via screening polyclonal sera by using Fc as a screen. A secondary screen was performed using CAR T cells assayed via flow cytometry. 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.

[0400] 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 presenting the anti-CD19 scFv FMC63 (SEQ ID NO: 1) 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). Results are shown in Figures 1A-1B and 2.

EXAMPLE 2

Immunohistochemistry (IHC) Studies

[0401] Several antibodies disclosed herein, (Clones 7 and 13) were assessed with respect to their ability to function as reagents in immunohistochemistry (IHC) studies. To create the fixed cell pellets for IHC staining, ~2e6 CAR T cells presenting the anti-CD19 scFv FMC63 (SEQ ID NO: 1) 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. The results of the IHC experiments are shown in Figures 3 and 4A (Figure 4B shows controls), and demonstrate that at least clones 7 and 13 can be useful in these types of experiments.

EXAMPLE 3

Use of an Anti-FMC63 Antibody for Purifying Macromolecules and Cells

[0402] The antigen binding molecules disclosed herein are anti-idiotypic antigen binding molecules, and recognize an epitope on the anti-CD19 scFv FMC63. An antigen binding molecule (*e.g.*, an antibody) disclosed herein can thus be used to purify a molecule, such as the anti-CD19 scFv FMC63, macromolecule, polymer, cell, material, etc., displaying an epitope that is recognized by the antigen binding molecules disclosed herein.

[0403] In some embodiments, an antigen binding molecule disclosed herein (*e.g.*, Clones 7, 13, 14-1, 14-7, 15 and/or 17 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 anti-CD19 scFv FMC63 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 the anti-CD19 scFv FMC63. 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 the anti-CD19 scFv FMC63. The washing can remove unwanted and unbound components of the sample. Following the washing step, the molecule comprising all or a fragment of the anti-CD19 scFv FMC63 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 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. During the elution step, eluted molecules, cells and moieties of interest comprising all or a fragment of the anti-CD19 scFv FMC63 is collected, and purity can be subsequently checked by running a sample on an SDS polyacrylamide gel.

[0404] 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. Subsequently, dialysis can be used to return materials to desired buffer conditions.

[0405] In some embodiments, cells displaying a molecule comprising all or a fragment of the anti-CD19 scFv FMC63 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).

[0406] Cells bound by the beads (which will be presenting molecules comprising the anti-CD19 scFv FMC63) are then separated from cells not displaying a molecule comprising the anti-CD19 scFv FMC63 or fragment thereof. In some embodiments, the beads can be

washed with media, such as RPMI-1640 supplemented with 10% FBS, in the presence of a magnet.

[0407] Selected cells, *i.e.*, those presenting molecules that comprise the anti-CD19 scFv FMC63 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 expressing desired molecule.

[0408] 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.

[0409] In another alternative embodiment, an antigen binding molecule disclosed herein (*e.g.*, Clones 7, 13, 14-1, 14-7, 15 and/or 17 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 expressing SEQ ID NO: 1 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 4

Activating CAR-positive T cells Using an Anti-FMC63 Antigen Binding Molecule

[0410] Also provided is a method of activating CAR-positive T cells presenting a molecule comprising a specific idiotope recognized by a specific antigen binding molecule (*e.g.*, an antigen binding molecule that recognizes the anti-CD19 scFv FMC63 (SEQ ID NO: 1), such as those disclosed herein: Clone 7, 13, 14-1, 14-7, 15 and/or 17, and fragments thereof). This method may 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 SEQ ID NO: 1. 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.

[0411] In some embodiments, the method can be performed as follows: first, a 12-well tissue culture treated plate is coated with 1 mL of a 1.5 µg/mL solution of an anti-CD19 scFv FMC63 antigen binding molecule disclosed herein, which has been diluted in HBSS or other phosphate buffer, and placed in an incubator at 37 C for 2 hours. Next, the plate is washed three times with HBSS or other phosphate buffer having a suitable pH, ionic strength, etc. Continuing, CAR-positive T-cells in OpTmizer media (with supplements) or RPMI-1640 media with 10% FBS are added to the tissue culture treated plate. The cells are then grown at 37 C with 5% CO_2.

[0412] After 2 days, the cells are examined to determine any increase in the percent CAR-positive cells. This determination can be made by identifying any increase in the expression of any cell-surface and/or internal markers, including, but not limited to 4-1BB, CD69, CD25, PD-1, and Ki-67.

EXAMPLE 5

Generation of Humanized Sequences from Rabbit Antibodies

[0413] The Molecular Operating Environment (MOE) software developed by Chemical Computing Group (CCG) can be used to generate alignments between the rabbit antibody Clones 7, 13, 14-1, 14-7, 15 and 17 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.

[0414] 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 can be exported and clustered using kClust (Hauser, Mayer, & Soding, (2013) *BMC Bioinformatics*, 248). Tables for VL and VH sequences for each of the antibodies, can be constructed, with sequences from each of the two databases clustered at 90% and 95%.

EXAMPLE 6

Flow Cytometry of Humanized FMC63 CAR

[0415] Humanized FMC63 CAR constructs were identified comprising conserved CDR loops (e.g., comprising amino acid sequences defined in Table C and D) and bind to CD19. Jurkat cells expressing FMC63 and humanized FMC63 CAR constructs were generated by transduction with lentivirus carrying the respective constructs. Monoclonal antibodies 14-1, 15, and 17-4 were incubated with CAR-expressing Jurkat cells and detected with a FITC-conjugated goat anti-rabbit F(ab')2 antibody (Thermo). An antibody reactive against all of these CAR constructs was used as a control to verify expression (Figure 22, top row). Clone 15 binds to the common amino acids in the CDR loops of FMC63 and all the humanized constructs, but shows no reactivity against mock-transduced Jurkat cells. (Figure 22). Secondary antibody only and mock-transduced controls show no background staining.

Table C. CDRs for the light chain variable (VL) region of the humanized FMC63 anti-CD19

Sequence (Convention)	**CDR1**	**SEQ ID NO**	**CDR2**	**SEQ ID NO**	**CDR3**	**SEQ ID NO**
VL (Chothia)	RASQDISKYL N	74	HTSRLHS	75	QQGNTLPYT	76
VL (Kabat)	RASQDISKYL N	74	HTSRLHS	75	QQGNTLPYT	76
VL (IMGT)	RASQDISKYL N	74	HTSRLHS	75	QQGNTLPYT	76

Table D. CDRs for the heavy chain variable (VH) region of the humanized FMC63 anti-CD19

Sequence (Convention)	**CDR1**	**SEQ ID NO**	**CDR2**	**SEQ ID NO**	**CDR3**	**SEQ ID NO**
VH (Chothia)	GVSLPDY	77	WGSET	78	HYYYGGSYAM DY	79
VH (Kabat)	DYGVS	80	VIWGSETTYYNSAL KS	81	HYYYGGSYAM DY	79
VH (IMGT)	GVSLPDYGV S	82	VIWGSETTYYNSAL KS	81	HYYYGGSYAM DY	79

CLAIMS

What is claimed is:

1. An isolated antigen binding molecule that specifically binds a molecule comprising SEQ ID NO: 1.
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 rabbit antibody, a mouse antibody, a rat antibody, a non-human primate antibody, 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 IgG3 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.
3. The antigen binding molecule of claim 2, wherein the antigen binding molecule comprises a heavy chain (HC).
4. The antigen binding molecule of claim 3, wherein the HC comprises a heavy chain variable region (VH) sequence selected from the group consisting of SEQ ID NOs: 3, 15, 21, 33, 39 and 51.
5. The antigen binding molecule of claim 4, wherein the variable region (VH) and comprises one or more of (a) a CDR1, (b) a CDR2, and (c) a CDR3.
6. The antigen binding molecule of claim 5, wherein the antigen binding molecule comprises a heavy chain CDR1 selected from the group consisting of SEQ ID NOs: 5, 23, 41 and 53.
7. The antigen binding molecule of claim 5, wherein the antigen binding molecule comprises a heavy chain CDR2 selected from the group consisting of SEQ ID NOs: 6, 24, 42 and 54.
8. The antigen binding molecule of claim 5, wherein the antigen binding molecule comprises a heavy chain CDR3 selected from the group consisting of SEQ ID NOs: 7, 25, 43 and 55.

9. The antigen binding molecule of claim 5, wherein 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 5-21.

10. An antigen binding molecule, 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 4.

11. The antigen binding molecule of claim 2, wherein the antigen binding molecule comprises a light chain (LC).

12. The antigen binding molecule of claim 11, wherein the LC comprises a light chain variable region (VL) sequence selected from the group consisting of SEQ ID NOs: 8, 18, 27, 36, 45 and 57.

13. The antigen binding molecule of claim 12, wherein the variable region (VL) and comprises one or more of (a) a CDR1, (b) a CDR2, and (c) a CDR3.

14. The antigen binding molecule of claim 13, wherein the antigen binding molecule comprises a light chain CDR1 selected from the group consisting of SEQ ID NOs: 11, 29, 47 and 59.

15. The antigen binding molecule of claim 13, wherein the antigen binding molecule comprises a light chain CDR2 selected from the group consisting of SEQ ID NOs: 12, 30, 48 and 60.

16. The antigen binding molecule of claim 13, wherein the antigen binding molecule comprises a light chain CDR3 selected from the group consisting of SEQ ID NOs: 13, 31, 49 and 61.

17. The antigen binding molecule of claim 13, wherein 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 one of FIGURES 5-21.

18. An antigen binding molecule, 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 VL of an antigen binding molecule of claim 12.

19. The antigen binding molecule of claim 2, wherein the antigen binding molecule comprises:

(a) a VH comprising the amino acid sequence of SEQ ID NO: 3; and

(b) a VL comprising the amino acid sequence of SEQ ID NO: 9.

20. The antigen binding molecule of claim 19, wherein the antigen binding molecule comprises:

(a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 5;

(b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 6;

(c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 7;

(d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 11;

(e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 12; and

(f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 13.

21. The antigen binding molecule of claim2, wherein the antigen binding molecule comprises:

(a) a VH comprising the amino acid sequence of SEQ ID NO: 15; and

(b) a VL comprising the amino acid sequence of SEQ ID NO: 18.

22. The antigen binding molecule of claim 21, wherein the antigen binding molecule comprises:

(a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 5;

(b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 6;

(c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 7;

(d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 11;

(e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 12; and

(f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 13.

23. The antigen binding molecule of claim 2, wherein the antigen binding molecule comprises:

(a) a VH comprising the amino acid sequence of SEQ ID NO: 21; and

(b) a VL comprising the amino acid sequence of SEQ ID NO: 27.

24. The antigen binding molecule of claim 23, wherein the antigen binding molecule comprises:

(a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 23;

(b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 24;

(c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 25;

(d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 29;

(e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 30; and

(f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 31.

25. The antigen binding molecule of claim 2, wherein the antigen binding molecule comprises:

(a) a VH comprising the amino acid sequence of SEQ ID NO: 33; and

(b) a VL comprising the amino acid sequence of SEQ ID NO: 36.

26. The antigen binding molecule of claim 25, wherein the antigen binding molecule comprises:

(a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 23;

(b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 24;

(c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 25;

(d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 29;

(e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 30; and

(f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 31.

27. The antigen binding molecule of claim 2, wherein the antigen binding molecule comprises:

(a) a VH comprising the amino acid sequence of SEQ ID NO: 39; and

(b) a VL comprising the amino acid sequence of SEQ ID NO: 45.

28. The antigen binding molecule of claim 27, wherein the antigen binding molecule comprises:

(a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 41;

(b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 42;

(c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 43;

(d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 47;

(e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 48; and

(f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 49.

29. The antigen binding molecule of claim 2, wherein the antigen binding molecule comprises:

(a) a VH comprising the amino acid sequence of SEQ ID NO: 51; and

(b) a VL comprising the amino acid sequence of SEQ ID NO: 57.

30. The antigen binding molecule of claim 29, wherein the antigen binding molecule comprises:

(a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 53;

(b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 54;

(c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 55;

(d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 59;

(e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 60; and

(f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 61.

31. The antigen binding molecule of any of claims 1-30, wherein the antigen binding molecule further comprises a detectable label.

32. The antigen binding molecule of claim 31, 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.

33. The antigen binding molecule of claim 32, wherein the fluorescent label is 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-phycoeryhring (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

34. A composition comprising the antigen binding molecule of one of claims 1-30.

35. A polynucleotide encoding the heavy chain of an antigen binding molecule of any of claims 1-30.

36. A polynucleotide encoding the light chain of an antigen binding molecule of any of claims 1-30.

37. A vector comprising the polynucleotide of one of claim 35 and claim 36.

38. A cell comprising one or both of the vectors of claim 37.

39. The cell of claim 38, 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.

40. A method of making an antigen binding molecule of claims 1-30 comprising incubating the cell of claim 39 under suitable conditions.

41. 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 SEQ ID NO: 1, the method comprising:

(a) providing 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 SEQ ID NO: 1;

(b) providing an aliquot of the sample comprising a population of cells presenting a therapeutic molecule comprising SEQ ID NO: 1;

(c) providing an antigen binding molecule that specifically binds the SEQ ID NO: 1, the antigen binding molecule further comprising 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 SEQ ID NO: 1 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.

42. The method of claim 41, wherein (a) the molecule comprising SEQ ID NO: 1 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.

43. The method of claim 42, wherein the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof.

44. The method of claim 41, 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.

45. The method of claim 44, wherein the fluorescent label is 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-phycoeryhring (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

46. The method of claim 42, wherein the immune cell is a T cell.

47. The method of claim 46, wherein the T cell is disposed *in vitro*.

48. The method of claim 46, wherein the T cell is disposed *in vivo*.

49. The method of claim 46, wherein the T cell is in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media.

50. The method of claim 46, wherein the T cell is an autologous T cell.

51. The method of claim 46, wherein the T cell is an allogenic T cell.

52. The method of claim 41, wherein the dose comprises $1.0x10^6$ cells per kg.

53. The method of claim 41, wherein the antigen binding molecule comprises an antigen binding molecule of claims 1-30, and humanized forms thereof.

54. A method of determining a number of cells presenting a molecule comprising SEQ ID NO: 1 in a sample, the method comprising:

(a) providing a sample comprising cells known or suspected to be presenting a molecule comprising SEQ ID NO: 1;

(b) contacting the sample of (a) with an antigen binding molecule that specifically binds the molecule comprising SEQ ID NO: 1, the antigen binding molecule further comprising 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.

55. The method of claim 54, wherein (a) the molecule comprising SEQ ID NO: 1 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.

56. The method of claim 55, wherein the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof.

57. The method of claim 54, 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.

58. The method of claim 57, wherein the fluorescent label is 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-phycoeryhring (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

59. The method of claim 54, wherein the immune cell is a T cell.

60. The method of claim 54, wherein the T cell is disposed *in vitro*.

61. The method of claim 54, wherein the T cell is disposed *in vivo*.

62. The method of claim 54, wherein the T cell is in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media.

63. The method of claim 54, wherein the T cell is an autologous T cell.

64. The method of claim 54, wherein the T cell is an allogenic T cell.

65. The method of claim 54, wherein the antigen binding molecule comprises an antigen binding molecule of claims 1-30, and humanized forms thereof.

66. A method of isolating a molecule comprising SEQ ID NO: 1, the method comprising:

(a) providing a sample known or suspected to comprise a molecule comprising SEQ ID NO: 1;

(b) providing an antigen binding molecule that specifically binds a molecule comprising SEQ ID NO: 1, 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 the molecule comprising SEQ ID NO: 1 and the antigen binding molecule;

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

(e) separating a formed binding complex into: (a) a molecule comprising SEQ ID NO: 1, and (b) an antigen binding molecule.

67. The method of claim 66, wherein the molecule comprising SEQ ID NO: 1 is a CAR.

68. The method of claim 67, wherein the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof.

69. The method of claim 66, wherein 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.

70. The method of claim 69, 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.

71. The method of claim 70, wherein the fluorescent label is 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-phycoeryhring (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

72. The method of claim 66, wherein the antigen binding molecule comprises an antigen binding molecule of claims 1-30, and humanized forms thereof.

73. A method of determining the presence or absence of a molecule comprising SEQ ID NO: 1 in a sample, the method comprising:

(a) providing a sample known or suspected to comprise a molecule comprising SEQ ID NO: 1;

(b) providing an antigen binding molecule comprising a detectable label that specifically binds a molecule comprising SEQ ID NO: 1;

(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.

74. The method of claim 73, wherein the molecule comprising SEQ ID NO: 1 is a CAR.

75. The method of claim 74, wherein the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1,

GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof.

76. The method of claim 73, wherein 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.

77. The method of claim 73, 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.

78. The method of claim 77, wherein the fluorescent label is 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-phycoeryhring (BPE), mCherry,

HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

79. The method of claim 73, wherein the antigen binding molecule comprises an antigen binding molecule of claims 1-30, and humanized forms thereof.

80. A method of increasing the concentration of cells presenting a molecule comprising SEQ ID NO: 1, the method comprising:

(a) providing a sample comprising a cell known or suspected to present a molecule comprising SEQ ID NO: 1;

(b) providing an antigen binding molecule that specifically binds a molecule comprising SEQ ID NO: 1, 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 the molecule comprising SEQ ID NO: 1 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.

81. The method of claim 80, wherein (a) the molecule comprising SEQ ID NO: 1 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.

82. The method of claim 81, wherein the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2,

TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof.

83. The method of claim 80, 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.

84. The method of claim 83, wherein the fluorescent label is 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-phycoeryhring (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

85. The method of claim 81, wherein the immune cell is a T cell.

86. The method of claim 83, wherein the T cell is disposed *in vitro*.

87. The method of claim 83, wherein the T cell is disposed *in vivo*.

88. The method of claim 83, wherein the T cell is in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media.

89. The method of claim 83, wherein the T cell is an autologous T cell.

90. The method of claim 83, wherein the T cell is an allogenic T cell.

91. The method of claim 80, wherein the antigen binding molecule comprises an antigen binding molecule of claims 1-30, and humanized forms thereof.

92. A method of depleting a population of immune cells presenting a molecule comprising SEQ ID NO: 1, the method comprising:

(a) providing a population of immune cells to be depleted, wherein the immune cells are known or suspected to be presenting a molecule comprising SEQ ID NO: 1; and

(b) contacting the immune cells with an antigen binding molecule that specifically binds to (a) the molecule comprising SEQ ID NO: 1, and (b) an activating molecule expressed on the surface of the an immune cell not presenting the molecule comprising SEQ ID NO:1, under conditions that permit the formation of a ternary binding complex comprising the molecule comprising SEQ ID NO: 1, the activating molecule and the antigen binding molecule.

93. The method of claim 92, wherein (a) the molecule comprising SEQ ID NO: 1 is a CAR; and (b) 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.

94. The method of claim 93, wherein the CAR further comprises a molecule, or a fragment thereof, selected from the group consisting of CD28, OX-40, 4-1BB/CD137, CD2, CD7, CD27, CD30, CD40, Programmed Death-1 (PD-1), inducible T cell co-stimulator (ICOS), lymphocyte function-associated antigen-1 (LFA-1, CDl-la/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha (CD79a), DAP-10, Fc gamma receptor, MHC class 1 molecule, TNF receptor proteins, an Immunoglobulin protein, cytokine receptor, integrins, Signaling Lymphocytic Activation Molecules (SLAM proteins), activating NK cell receptors, BTLA, a Toll ligand receptor, ICAM-1, B7-H3, CDS, ICAM-1, GITR, BAFFR, LIGHT, HVEM (LIGHTR), KIRDS2, SLAMF7, NKp80 (KLRF1), NKp44, NKp30, NKp46, CD19, CD4, CD8alpha, CD8beta, IL-2R beta, IL-2R gamma, IL-7R alpha, ITGA4, VLA1, CD49a, ITGA4, IA4, CD49D, ITGA6, VLA-6, CD49f, ITGAD, CDl ld, ITGAE, CD103, ITGAL, CDl la, LFA-1, ITGAM, CDl lb, ITGAX, CDl lc, ITGBl, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRT AM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100

(SEMA4D), CD69, SLAMF6 (NTB-A, Lyl08), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof.

95. The method of claim 93, wherein the immune cell is a T cell.

96. The method of claim 95, wherein the T cell is disposed *in vitro*.

97. The method of claim 95, wherein the T cell is disposed *in vivo*.

98. The method of claim 95, wherein the T cell is in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media.

99. The method of claim 95, wherein the T cell is an autologous T cell.

100. The method of claim 95, wherein the T cell is an allogenic T cell.

101. The method of claim 92, wherein the antigen binding molecule comprises an antigen binding molecule of claims 1-30, and humanized forms thereof.

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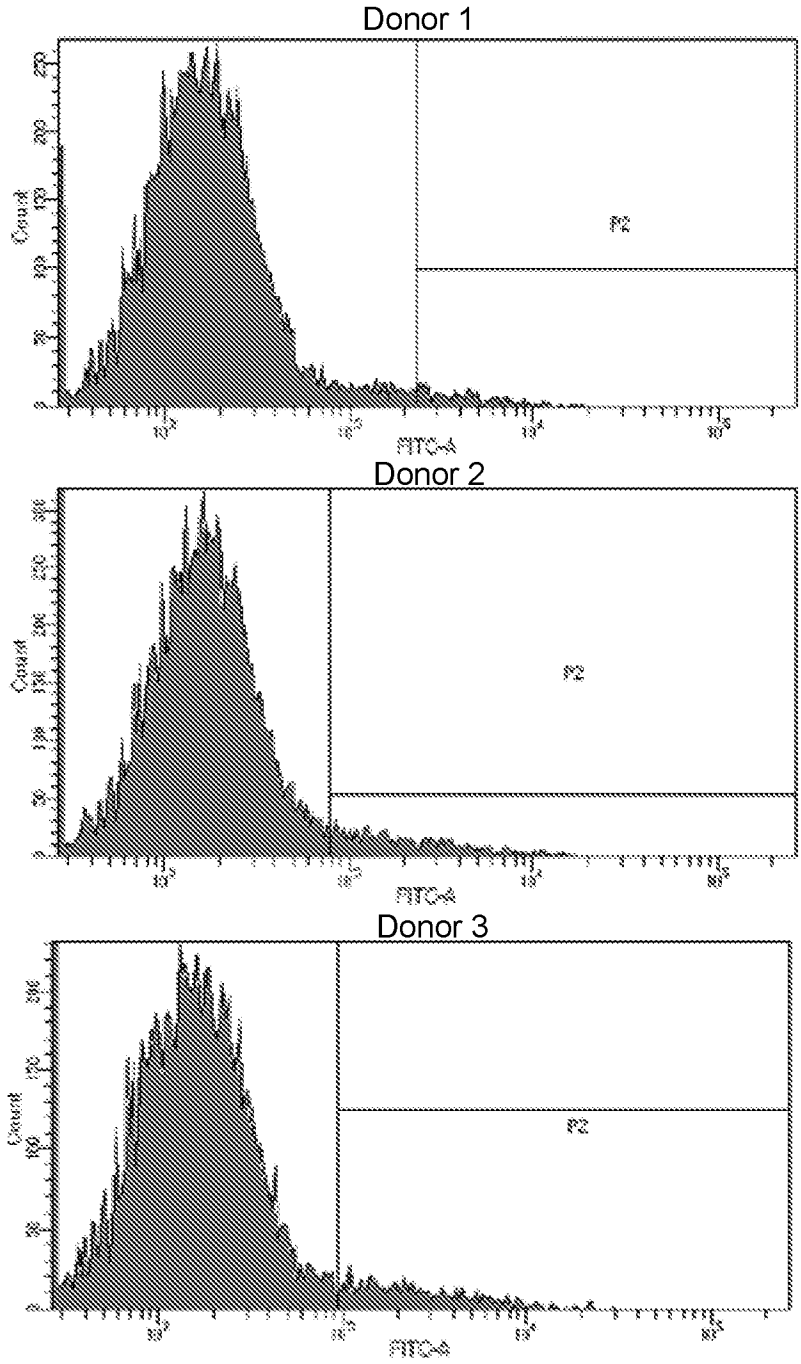
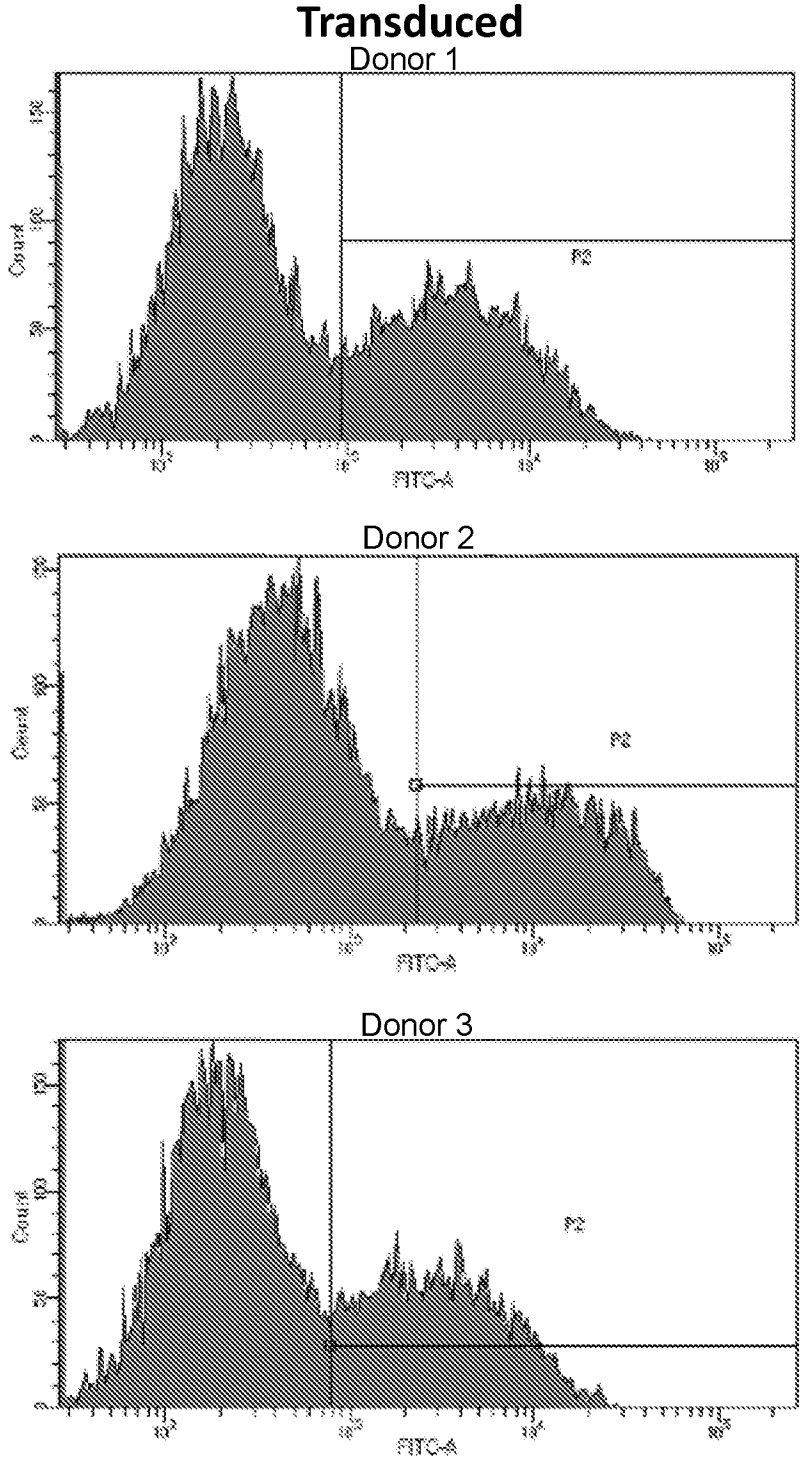


Figure 1A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P2
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P2

Figure 1B

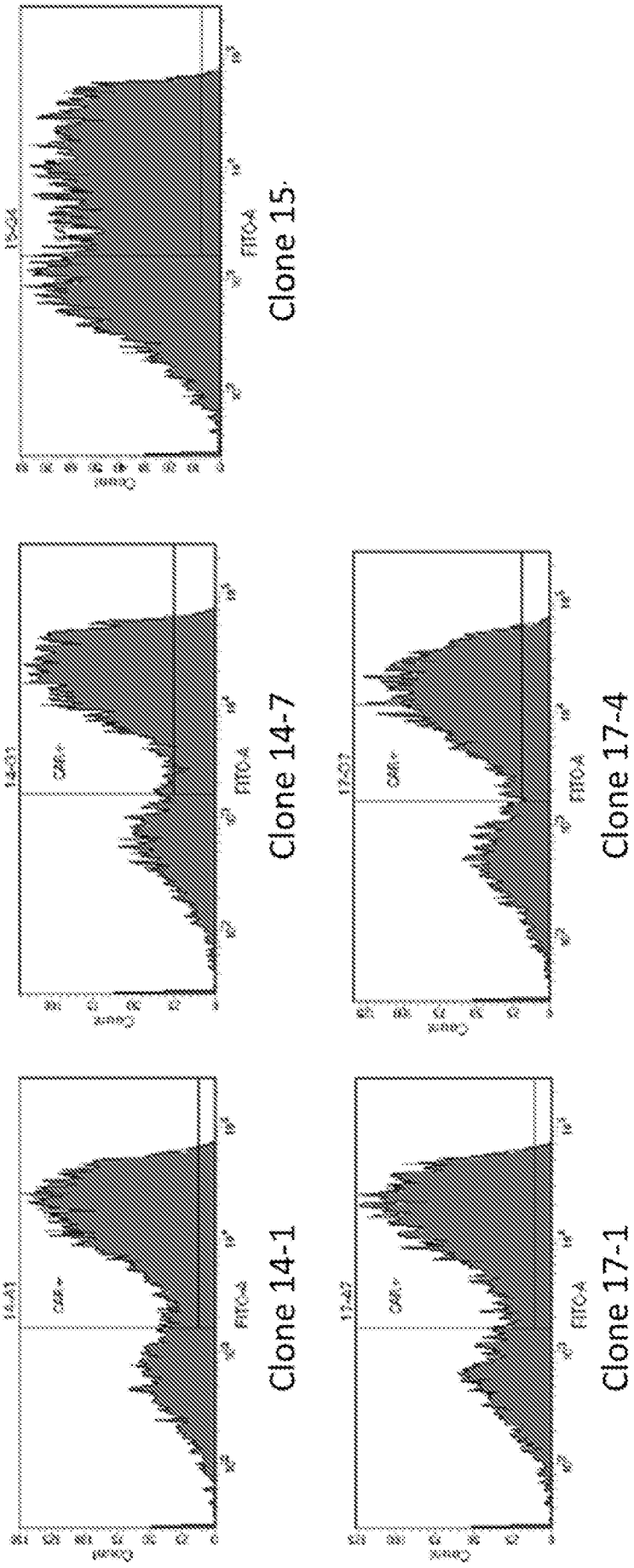
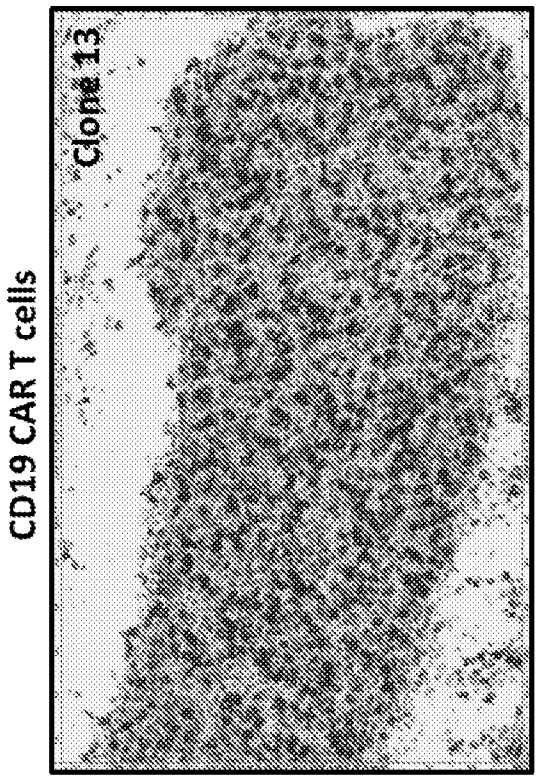


Figure 2



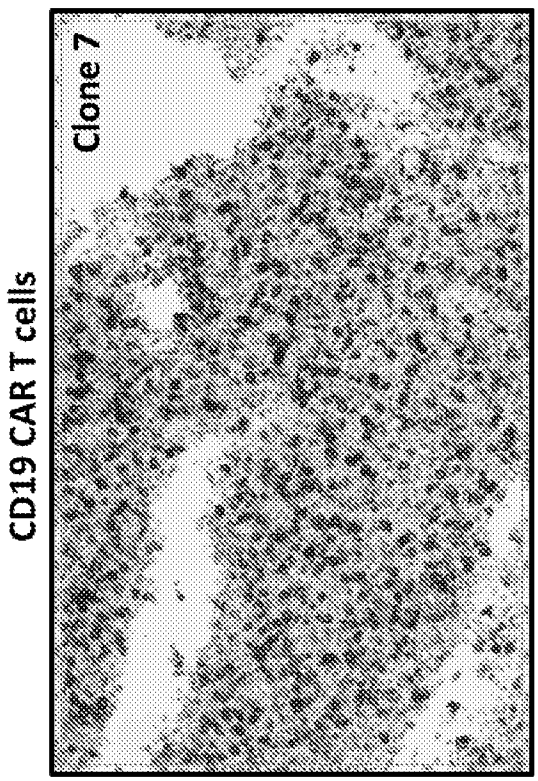


Figure 3

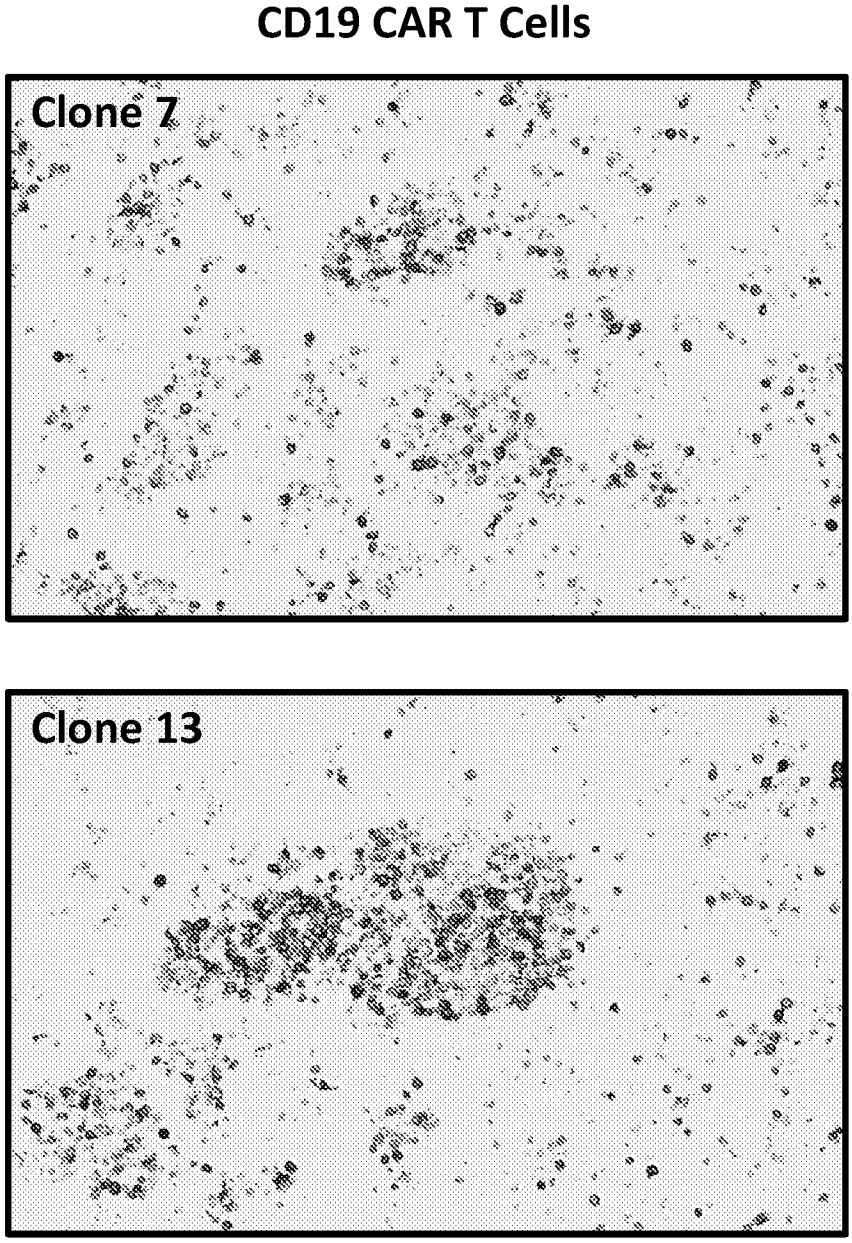


Figure 4A

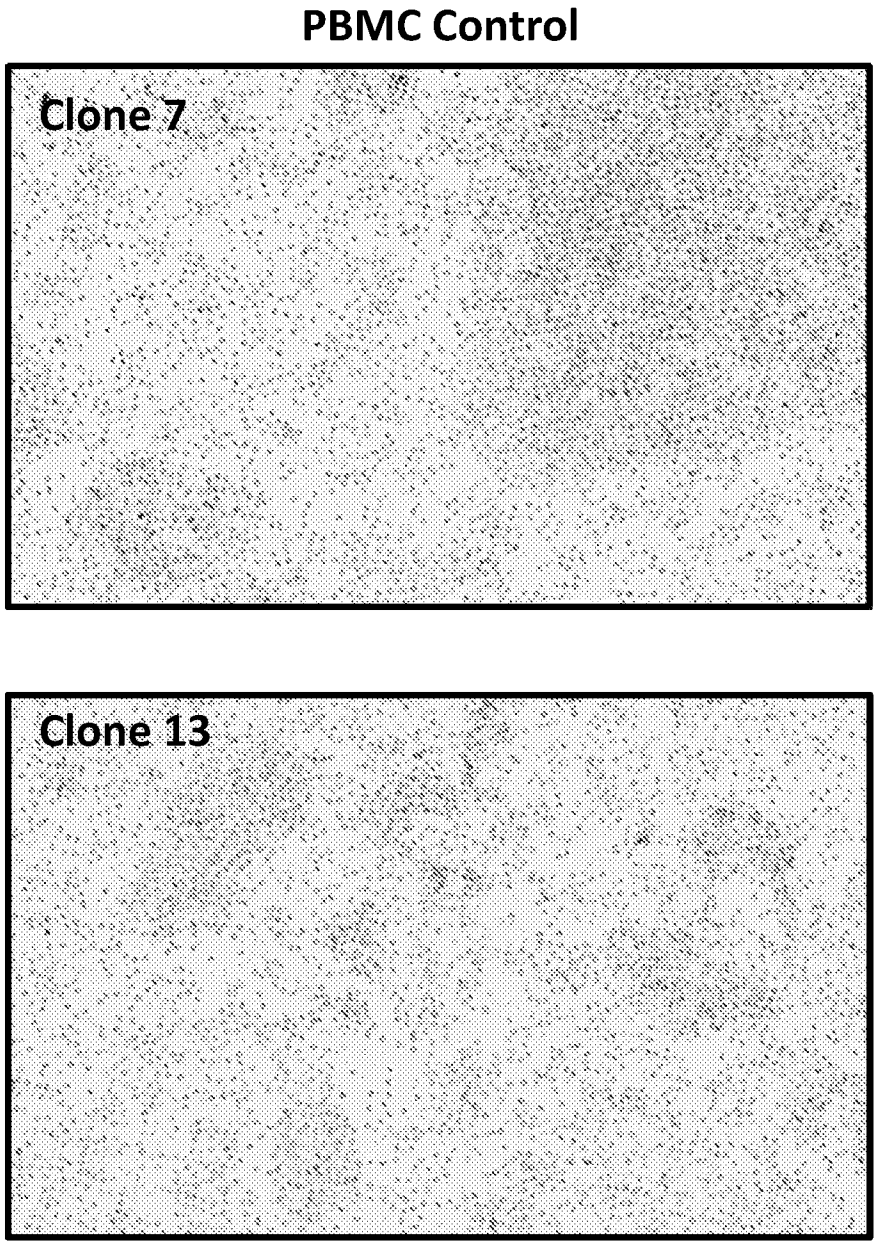


Figure 4B

Clone 7 VH DNA

ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGTCCAGTGTCAGGAGCAGCT
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TTCTCCTTCAGTAACAATGGAATTTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGATCGG
ATGTCTTTATGTTGGTAGTAGTGATACCACTTACTACGCGAGCTGGGCGAAAGGCCGATTCACCATCTC
CAAAAGCTCGTCGACCACGGTGACTCTACAAATGACCAGTCTGACAGTCGCGGACACGGCCACCTATT
TCTGTACGATAAATCTCGGCTTGTGGGGCCCCGGCACCCTGGTCACCGTCTCCTCA (SEQ ID NO: 2)

Clone 7 VH AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQEQLEESGGDLVKPGGTLTVTCKASGFSFSNNGICWVRQAPGKGLEWIGCL
YVGSSDTTYYASWAKGRFTISKSSSTTVTLQMTSLTVADTATYFCTINLGLWGPGTLVTVSS (SEQ ID NO:
3)

Clone 7 HC AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQEQLEESGGDLVKPGGTLTVTCKASGFSFSNNGICWVRQAPGKGLEWIGCL
YVGSSDTTYYASWAKGRFTISKSSSTTVTLQMTSLTVADTATYFCTINLGLWGPGTLVTVSSGQPKAPSVFPL
APCCGDTPSSTVTLGCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSGLYSLSSVVSVTSSSQPVTCNVA
HPATNTKVDKTVAPSTCSKPTCPPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVVVDVSQDDPEVQFTWYI
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GPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDNYKTTPAVLDSDGSYFLYSKLSVPTSEWQRGDVF
TCSVMHEALHNHYTQKSISRSPGK (SEQ ID NO: 4)

Clone 7 VH CDR1 AA
GFSFSNN (SEQ ID NO: 5)

Clone 7 VH CDR2 AA
YVGSSD (SEQ ID NO: 6)

Clone 7 VH CDR3 AA
NLGL (SEQ ID NO: 7)

Figure 5

Clone 7 VL DNA
ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCTCCCAGGTGCCACATTTGCC
ATCGTGGTGACCCAGACTCCATCTTCCAAGTCTGTCCCTGTGGGAGGCACAGTCACCATCAATTGCCAG
GCCAGTGAGAGTGTTTATAATAGCGACTGGTTAGCCTGGTATCAGCAGAAACCAGGGCAGCCTCCCAA
GCAACTGATCTATGCTGCATCCACTCTGGCATCTGGGGTCCCATCGCGCTTCAAAGGCAGTGGATCTGG
GACACAGTTCACTCTCACCATCAGCGATGTGGTGTGTGACGATGCTGCCACTTATTATTGTGCAGGATA
TAAAAGTAGTAGTACTGATGGGATTGCTTTCGGCGGAGGGACCGAGGTGGTGGTCAAA (SEQ ID NO:
8)

Clone 7 VL AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGATFAIVVTQTPSSKSVPVGGTVTINCQASESVYNSDWLAWYQQKPGQPPKQ
LIYAASTLASGVPSRFKGSGSGTQFTLTISDVVCDDAATYYCAGYKSSSTDGIAFGGGTEVVVK (SEQ ID NO:
9)

Clone 7 LC AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGATFAIVVTQTPSSKSVPVGGTVTINCQASESVYNSDWLAWYQQKPGQPPKQ
LIYAASTLASGVPSRFKGSGSGTQFTLTISDVVCDDAATYYCAGYKSSSTDGIAFGGGTEVVVKGDPVAPTVLI
FPPAADQVATGTVTIVCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADCTYNLSSTLTLTSTQYNSH
KEYTCKVTQGTTSVVQSFNRGDC (SEQ ID NO: 10)

Clone 7 VL CDR1 AA
QASESVYNSDWLA (SEQ ID NO: 11)

Clone 7 VL CDR2 AA
AASTLAS (SEQ ID NO: 12)

Clone 7 VL CDR3 AA
AGYKSSSTDGIA (SEQ ID NO: 13)

Figure 6

Clone 13 VH DNA
ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGTCCAGTGTCAGGAGCAGCT
GGAGGAGTCCGGGGGAGACCTGGTCAAGCCTGGAGGAACCCTGACAGTCACCTGCAAAGCCTCTGGA
TTCTCCTTCAGTAACAATGGAATTTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGATCGG
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CAAAAGCTCGTCGACCACGGTGACTCTACAAATGACCAGTCTGACAGTCGCGGACACGGCCACCTATT
TCTGTACGATAAATCTCGGCTTGTGGGGCCCCGGCACCCTGGTCACCGTCTCCTCA (SEQ ID NO: 14)

Clone 13 VH AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQEQLEESGGDLVKPGGTLTVTCKASGFSFSNNGICWVRQAPGKGLEWIGCL
YVGSSDTTYYASWAKGRFTISKSSSTTVTLQMTSLTVADTATYFCTINLGLWGPGTLVTVSS (SEQ ID NO:
15)

Clone 13 HC AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQEQLEESGGDLVKPGGTLTVTCKASGFSFSNNGICWVRQAPGKGLEWIGCL
YVGSSDTTYYASWAKGRFTISKSSSTTVTLQMTSLTVADTATYFCTINLGLWGPGTLVTVSSGQPKAPSVFPL
APCCGDTPSSTVTLGCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSGLYSLSSVVSVTSSSQPVTCNVA
HPATNTKVDKTVAPSTCSKPTCPPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVVVDVSQDDPEVQFTWYI
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GPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDNYKTTPAVLDSDGSYFLYSKLSVPTSEWQRGDVF
TCSVMHEALHNHYTQKSISRSPGK (SEQ ID NO: 16)

Clone 13 VH CDR1 AA
GFSFSNN (SEQ ID NO: 5)

Clone 13 VH CDR2 AA
YVGSSD (SEQ ID NO: 6)

Clone 13 VH CDR3 AA
NLGL (SEQ ID NO: 7)

Figure 7

Clone 13 VL DNA
ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCTCCCAGGTGCCACACTTGC
CATCGTGGTGACCCAGACTCCATCTTCCAAGTCTGTCCCTGTGGGAGGCACAGTCACCATCAATTGCCA
GGCCAGTGAGAGTGTTTATAATAGCGACTGGTTAGCCTGGTATCAGCAGAAACCAGGGCAGCCTCCCA
AGCAACTGATCTATGCTGCATCCACTCTGGCATCTGGGGTCCCATCGCGCTTCAAAGGCAGTGGATCTG
GGACACAGTTCACTCTCACCATCAGCGATGTGGTGTGTGACGATGCTGCCACTTATTATTGTGCAGGAT
ATAAAAGTAGTAGTACTGATGGGATTGCTTTCGGCGGAGGGACCGAGGTGGTGGTCAAA (SEQ ID
NO: 17)

Clone 13 VL AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGATLAIVVTQTPSSKSVPVGGTVTINCQASESVYNSDWLAWYQQKPGQPPKQ
LIYAASTLASGVPSRFKGSGSGTQFTLTISDVVCDDAATYYCAGYKSSSTDGIAFGGGTEVVVK (SEQ ID NO:
18)

Clone 13 LC AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGATLAIVVTQTPSSKSVPVGGTVTINCQASESVYNSDWLAWYQQKPGQPPKQ
LIYAASTLASGVPSRFKGSGSGTQFTLTISDVVCDDAATYYCAGYKSSSTDGIAFGGGTEVVVKGDPVAPTVLI
FPPAADQVATGTVTIVCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADCTYNLSSTLTLTSTQYNSH
KEYTCKVTQGTTSVVQSFNRGDC (SEQ ID NO: 19)

Clone 13 VL CDR1 AA
QASESVYNSDWLA (SEQ ID NO: 11)

Clone 13 VL CDR2 AA
AASTLAS (SEQ ID NO: 12)

Clone 13 VL CDR3 AA
AGYKSSSTDGIA (SEQ ID NO: 13)

Figure 8

Clone 14-1 VH DNA
ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGTCCAGTGTCAGGAGCAGCT
GGAGGAGTCCGGGGGAGGCCTGGTCAAGCCTGGGGCATCCCTGACACTCACCTGCAAAGCCTCTGGA
TTCGACTTCAGTATCAACTACTACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGTTGGAGTGGAT
CGCATGCATTTATACTGGTGATGATGACACTTTCTACGCGAGCTGGGCGAAAGGCCGGTTCACCATCTC
CAAAACCTCGTCGACCACGGTGACTCTACAACTGAACAGTCTGACAGCCGCGGACACGGCCACCTATTT
CTGTGTGAGAGGTCTATATAGTGGTAGTATTAATAACCTGTGGGGCCCAGGCACCCTGGTCACCGTCTC
CTCA
(SEQ ID NO: 20)

Clone 14-1 VH AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQEQLEESGGGLVKPGASLTLTCKASGFDFSINYYMCWVRQAPGKGLEWIAC
IYTGDDDTFYASWAKGRFTISKTSSTTVTLQLNSLTAADTATYFCVRGLYSGSINNLWGPGTLVTVSS
(SEQ ID NO: 21)

Clone 14-1 HC AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQEQLEESGGGLVKPGASLTLTCKASGFDFSINYYMCWVRQAPGKGLEWIAC
IYTGDDDTFYASWAKGRFTISKTSSTTVTLQLNSLTAADTATYFCVRGLYSGSINNLWGPGTLVTVSSGQPKA
PSVFPLAPCCGDTPSSTVTLGCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSGLYSLSSVVSVTSSSQPV
TCNVAHPATNTKVDKTVAPSTCSKPTCPPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVVVDVSQDDPEVQ
FTWYINNEQVRTARPPLREQQFNSTIRVVSTLPIAHQDWLRGKEFKCKVHNKALPAPIEKTISKARGQPLEP
KVYTMGPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDNYKTTPAVLDSDGSYFLYSKLSVPTSEWQ
RGDVFTCSVMHEALHNHYTQKSISRSPGK (SEQ ID NO: 22)

Clone 14-1 VH CDR1 AA
GFDFSINY (SEQ ID NO: 23)

Clone 14-1 VH CDR2 AA
YTGDD (SEQ ID NO: 24)

Clone 14-1 VH CDR3 AA
GLYSGSINNL (SEQ ID NO: 25)

Figure 9

Clone 14-1 VL DNA
ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCTCCCAGATGCCAGATGTGC
GCTTGTGATGACCCAGACTCCATCCCCTGTGTCTGCAGCTGTGGGAGGCACAGTCACCATCAGTTGCCA
GGCCAGTCAGAGTGTTTATAACAACGACTACTTATCCTGGTATCAGCAGAAACCAGGGCAGCCTCCCA
AACTCCTGATCTATTATGCATCCACTCTGGCATCTGGGGTCTCATCGCGGTTCAAAGGCAGTGGATCTG
GGACACAGTTCACTCTCACCATCAGCGACGTGCAGTGTGACGATGCTGCCGCTTACTATTGTGCAGGC
GTTAAAGGTTATAGTAATGATAATAATGGTTTCGGCGGAGGGACCGAGGTGGTGGTCAAA (SEQ ID
NO: 26)

Clone 14-1 VL AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPDARCALVMTQTPSPVSAAVGGTVTISCQASQSVYNNDYLSWYQQKPGQPPK
LLIYYASTLASGVSSRFKGSGSGTQFTLTISDVQCDDAAAYYCAGVKGYSNDNNGFGGGTEVVVK (SEQ ID
NO: 27)

Clone 14-1 LC AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPDARCALVMTQTPSPVSAAVGGTVTISCQASQSVYNNDYLSWYQQKPGQPPK
LLIYYASTLASGVSSRFKGSGSGTQFTLTISDVQCDDAAAYYCAGVKGYSNDNNGFGGGTEVVVKGDPVAP
TVLIFPPAADQVATGTVTIVCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADCTYNLSSTLTLTSTQY
NSHKEYTCKVTQGTTSVVQSFNRGDC (SEQ ID NO:28)

Clone 14-1 VL CDR1 AA
QASQSVYNNDYLS (SEQ ID NO: 29)

Clone 14-1 VL CDR2 AA
YASTLAS (SEQ ID NO: 30)

Clone 14-1 VL CDR3 AA
AGVKGYSNDNNG (SEQ ID NO: 31)

Figure 10

Clone 14-7 VH DNA
ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGTCCAATGTCAGTCGCTGGA
GGAGTCCGGGGGAGGCCTGGTCAAGCCTGGGGCATCCCTGACACTCACCTGCAAAGCCTCTGGATTCG
ACTTCAGTATCAACTACTACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGTTGGAGTGGATCGCA
TGCATTTATACTGGTGATGATGACACTTTCTACGCGAGCTGGGCGAAAGGCCGGTTCACCATCTCCAAA
ACCTCGTCGACCACGGTGACTCTACAACTGAACAGTCTGACAGCCGCGGACACGGCCACCTATTTCTGT
GTGAGAGGTCTATATAGTGGTAGTATTAATAACCTGTGGGGCCCAGGCACCCTGGTCACCGTCTCCTCA
(SEQ ID NO: 32)

Clone 14-7 VH AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQSLEESGGGLVKPGASLTLTCKASGFDFSINYYMCWVRQAPGKGLEWIACIY
TGDDDTFYASWAKGRFTISKTSSTTVTLQLNSLTAADTATYFCVRGLYSGSINNLWGPGTLVTVSS (SEQ ID
NO: 33)

Clone 14-7 HC AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQSLEESGGGLVKPGASLTLTCKASGFDFSINYYMCWVRQAPGKGLEWIACIY
TGDDDTFYASWAKGRFTISKTSSTTVTLQLNSLTAADTATYFCVRGLYSGSINNLWGPGTLVTVSSGQPKAP
SVFPLAPCCGDTPSSTVTLGCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSGLYSLSSVVSVTSSSQPVT
CNVAHPATNTKVDKTVAPSTCSKPTCPPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVVVDVSQDDPEVQF
TWYINNEQVRTARPPLREQQFNSTIRVVSTLPIAHQDWLRGKEFKCKVHNKALPAPIEKTISKARGQPLEPK
VYTMGPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDNYKTTPAVLDSDGSYFLYSKLSVPTSEWQR
GDVFTCSVMHEALHNHYTQKSISRSPGK (SEQ ID NO: 34)

Clone 14-7 VH CDR1 AA
GFDFSINY (SEQ ID NO: 23)

Clone 14-7 VH CDR2 AA
YTGDD (SEQ ID NO: 24)

Clone 14-7 VH CDR3 AA
GLYSGSINNL (SEQ ID NO: 25)

Figure 11

Clone 14-7 VL DNA
ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCTCCCAGATGCCAGATGTGC
GCTTGTGATGACCCAGACTCCATCCCCTGTGTCTGCAGCTGTGGGAGGCACAGTCACCATCAGTTGCCA
GGCCAGTCAGAGTGTTTATAACAACGACTACTTATCCTGGTATCAGCAGAAACCAGGGCAGCCTCCCA
AACTCCTGATCTATTATGCATCCACTCTGGCATCTGGGGTCTCATCGCGGTTCAAAGGCAGTGGATCTG
GGACACAGTTCACTCTCACCATCAGCGACGTGCAGTGTGACGATGCTGCCGCTTACTATTGTGCAGGC
GTTAAAGGTTATAGTAATGATAATAATGGTTTCGGCGGAGGGACCGAGGTGGTGGTCAAA (SEQ ID
NO: 35)

Clone 14-7 VL AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPDARCALVMTQTPSPVSAAVGGTVTISCQASQSVYNNDYLSWYQQKPGQPPK
LLIYYASTLASGVSSRFKGSGSGTQFTLTISDVQCDDAAAYYCAGVKGYSNDNNGFGGGTEVVVK (SEQ ID
NO: 36)

Clone 14-7 LC AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPDARCALVMTQTPSPVSAAVGGTVTISCQASQSVYNNDYLSWYQQKPGQPPK
LLIYYASTLASGVSSRFKGSGSGTQFTLTISDVQCDDAAAYYCAGVKGYSNDNNGFGGGTEVVVKGDPVAP
TVLIFPPAADQVATGTVTIVCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADCTYNLSSTLTLTSTQY
NSHKEYTCKVTQGTTSVVQSFNRGDC (SEQ ID NO: 37)

Clone 14-7 VL CDR1 AA
QASQSVYNNDYLS (SEQ ID NO: 29)

Clone 14-7 VL CDR2 AA
YASTLAS (SEQ ID NO: 30)

Clone 14-7 VL CDR3 AA
AGVKGYSNDNNG (SEQ ID NO: 31)

Figure 12

Clone 15 VH DNA
ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGGGTCCAGTGTCAGTCGTTGGA
GGAGTCCGGGGGAGACCTGGTCAAGCCTGGGGCATCCCTGACACTCACCTGCACAGCCTCTGGATTCT
CCTTCACGAGCAACTACTACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCGC
GTGCATTTTTCTTGGTAGTAGTGGTAACACTGTCTACGCGAACTGGGCGAAAGGCCGATTCACCATCTC
CAAAACCTCGTCGACCACGGTGACTCTGCAAATGACCAGTCTGACAGTCGCGGACACGGCCACCTATTT
CTGTGCGAGAGACTATGTTAATGGTTATGACTACTTTAACTTGTGGGGCCCAGGCACCTTGGTCACCGT
CTCCTCA (SEQ ID NO: 38)

Clone 15 VH AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQSLEESGGDLVKPGASLTLTCTASGFSFTSNYYMCWVRQAPGKGLEWVACI
FLGSSGNTVYANWAKGRFTISKTSSTTVTLQMTSLTVADTATYFCARDYVNGYDYFNLWGPGTLVTVSS
(SEQ ID NO: 39)

Clone 15 HC AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQSLEESGGDLVKPGASLTLTCTASGFSFTSNYYMCWVRQAPGKGLEWVACI
FLGSSGNTVYANWAKGRFTISKTSSTTVTLQMTSLTVADTATYFCARDYVNGYDYFNLWGPGTLVTVSSGQ
PKAPSVFPLAPCCGDTPSSTVTLGCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSGLYSLSSVVSVTSSS
QPVTCNVAHPATNTKVDKTVAPSTCSKPTCPPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVVVDVSQDDP
EVQFTWYINNEQVRTARPPLREQQFNSTIRVVSTLPIAHQDWLRGKEFKCKVHNKALPAPIEKTISKARGQP
LEPKVYTMGPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDNYKTTPAVLDSDGSYFLYSKLSVPTSE
WQRGDVFTCSVMHEALHNHYTQKSISRSPGK (SEQ ID NO: 40)

Clone 15 VH CDR1 AA
GFSFTSNY (SEQ ID NO: 41)

Clone 15 VH CDR2 AA
FLGSSG (SEQ ID NO: 42)

Clone 15 VH CDR3 AA
DYVNGYDYFNL (SEQ ID NO: 43)

Figure 13

Clone 15 VL DNA
ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCTCCCAGGTGCCACATTTGCC
CAAGTGCTGACCCAGACTGCATCCCCCGTGTCTGCGGCTGTTGGAGGCACAGTCACCATCAATTGCCA
GTCCAGTCAGAGTGTTTATAATAAGAACTTAGCCTGGTATCAGCAGAAACCAGGGCAGCCTCCCAAAG
GCCTGATCTATTCTACATCGACTCTAGATTCTGGGGTCCCATCGCGGTTCAGCGGCAGTGGATCTGGGA
CACAGTTCACTCTCACCATCAGCGACGTGCAGTGTGACGATGCTGCCACTTACTACTGTCTAGGCAGTT
ATGATTGTAGTAGTGCTGATTGTAATGCTTTCGGCGGAGGGACCGAGGTGGTGGTCAAA (SEQ ID NO:
44)

Clone 15 VL AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGATFAQVLTQTASPVSAAVGGTVTINCQSSQSVYNKNLAWYQQKPGQPPKG
LIYSTSTLDSGVPSRFSGSGSGTQFTLTISDVQCDDAATYYCLGSYDCSSADCNAFGGGTEVVVK (SEQ ID
NO: 45)

Clone 15 LC AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGATFAQVLTQTASPVSAAVGGTVTINCQSSQSVYNKNLAWYQQKPGQPPKG
LIYSTSTLDSGVPSRFSGSGSGTQFTLTISDVQCDDAATYYCLGSYDCSSADCNAFGGGTEVVVKGDPVAPT
VLIFPPAADQVATGTVTIVCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADCTYNLSSTLTLTSTQYN
SHKEYTCKVTQGTTSVVQSFNRGDC (SEQ ID NO: 46)

Clone 15 VL CDR1 AA
QSSQSVYNKNLA (SEQ ID NO: 47)

Clone 15 VL CDR2 AA
STSTLDS (SEQ ID NO: 48)

Clone 15 VL CDR3 AA
LGSYDCSSADCNA (SEQ ID NO: 49)

Figure 14

Clone 17 VH DNA
ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGTCCAATGTCAGTCGCTGGA
GGAGTCCGGGGGAGGCCTGGTCAAGCCTGGGGCATCCCTGACACTCACCTGCACAGCCTCTGGATTCT
CCTTCAGTGACAGTTGGTACTTGTGTTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGATCGC
ATGCATTTATACTGGTGATGGTGACACTTATTACGCGACCTGGGCGAAAGGCCGATTCACCATCTCCAA
GACCTCGTCGACCACAGTGACTCTACAAATGACCAGTCTGACAGCCGCGGACACGGCCACCTATTTCTG
TGCGAGGGGTGCCCAATTTTACTTGTGGGGCCAAGGCACCCTGGTCACCGTCTCCTCA (SEQ ID NO:
50)

Clone 17 VH AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQSLEESGGGLVKPGASLTLTCTASGFSFSDSWYLCWVRQAPGKGLEWIACIY
TGDGDTYYATWAKGRFTISKTSSTTVTLQMTSLTAADTATYFCARGAQFYLWGQGTLVTVSS (SEQ ID
NO: 51)

Clone 17 HC AA (CDRs underlined)
METGLRWLLLVAVLKGVQCQSLEESGGGLVKPGASLTLTCTASGFSFSDSWYLCWVRQAPGKGLEWIACIY
TGDGDTYYATWAKGRFTISKTSSTTVTLQMTSLTAADTATYFCARGAQFYLWGQGTLVTVSSGQPKAPSVF
PLAPCCGDTPSSTVTLGCLVKGYLPEPVTVTWNSGTLTNGVRTFPSVRQSSGLYSLSSVVSVTSSSQPVTCNV
AHPATNTKVDKTVAPSTCSKPTCPPPELLGGPSVFIFPPKPKDTLMISRTPEVTCVVVDVSQDDPEVQFTWYI
NNEQVRTARPPLREQQFNSTIRVVSTLPIAHQDWLRGKEFKCKVHNKALPAPIEKTISKARGQPLEPKVYTM
GPPREELSSRSVSLTCMINGFYPSDISVEWEKNGKAEDNYKTTPAVLDSDGSYFLYSKLSVPTSEWQRGDVF
TCSVMHEALHNHYTQKSISRSPGK (SEQ ID NO: 52)

Clone 17 VH CDR1 AA
GFSFSDSW (SEQ ID NO: 53)

Clone 17 VH CDR2 AA
YTGDG (SEQ ID NO: 54)

Clone 17 VH CDR3 AA
GAQFYL (SEQ ID NO: 55)

Figure 15

Clone 17 VL DNA
ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCTCCCAGGTGCCACATTTGCC
CAGGTGCTGACCCAGACTCCATCCTCCGTGTCTGCAGCTGTGGGAGGCACAGTCACCATCAATTGCCA
GTCCAGTCAGAGTGTTTATGCCAACACCTACTTATCCTGGTATCAGCAGAAACCAGGGCAGCCTCCCAA
GCAACTGATCTATTCTGCATCCAGTCTGGCATCTGGGGTCCCACCGCGGTTCAAAGGCAGTGGATCTG
GGACACAGTTCGCTCTCACCATCAGCGACGTGCAGTGTGACGATGCTGCCACTTACTACTGTCTAGGCA
GATATAGTTGTGGTCTTGCTGATTGTGCTGCTTTCGGCGGAGGGACCGAGGTGGTGGTCAAA (SEQ ID
NO:56)

Clone 17 VL AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGATFAQVLTQTPSSVSAAVGGTVTINCQSSQSVYANTYLSWYQQKPGQPPKQ
LIYSASSLASGVPPRFKGSGSGTQFALTISDVQCDDAATYYCLGRYSCGLADCAAFGGGTEVVVK (SEQ ID
NO: 57)

Clone 17 LC AA (CDRs underlined)
MDTRAPTQLLGLLLLWLPGATFAQVLTQTPSSVSAAVGGTVTINCQSSQSVYANTYLSWYQQKPGQPPKQ
LIYSASSLASGVPPRFKGSGSGTQFALTISDVQCDDAATYYCLGRYSCGLADCAAFGGGTEVVVKGDPVAPT
VLIFPPAADQVATGTVTIVCVANKYFPDVTVTWEVDGTTQTTGIENSKTPQNSADCTYNLSSTLTLTSTQYN
SHKEYTCKVTQGTTSVVQSFNRGDC (SEQ ID NO: 58)

Clone 17 VL CDR1 AA
QSSQSVYANTYLS (SEQ ID NO: 59)

Clone 17 VL CDR2 AA
SASSLAS (SEQ ID NO: 60)

Clone 17 VL CDR3 AA
LGRYSCGLADCAA (SEQ ID NO: 61)

Figure 16

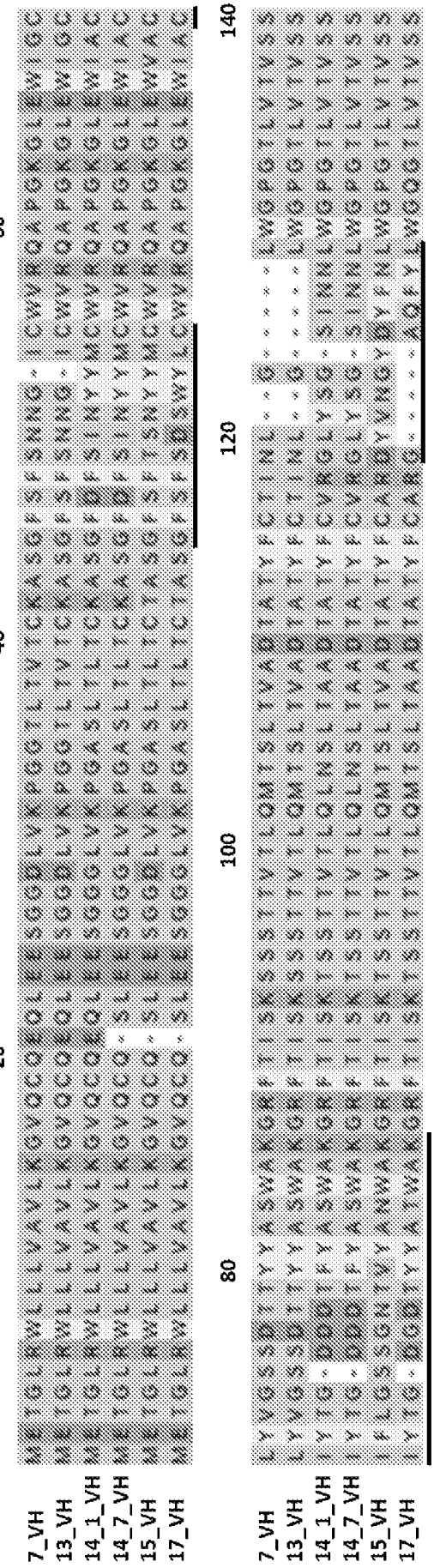

Figure 17A

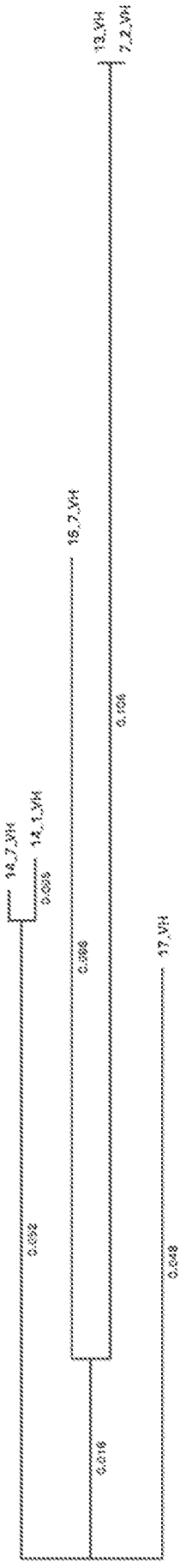

Figure 17B

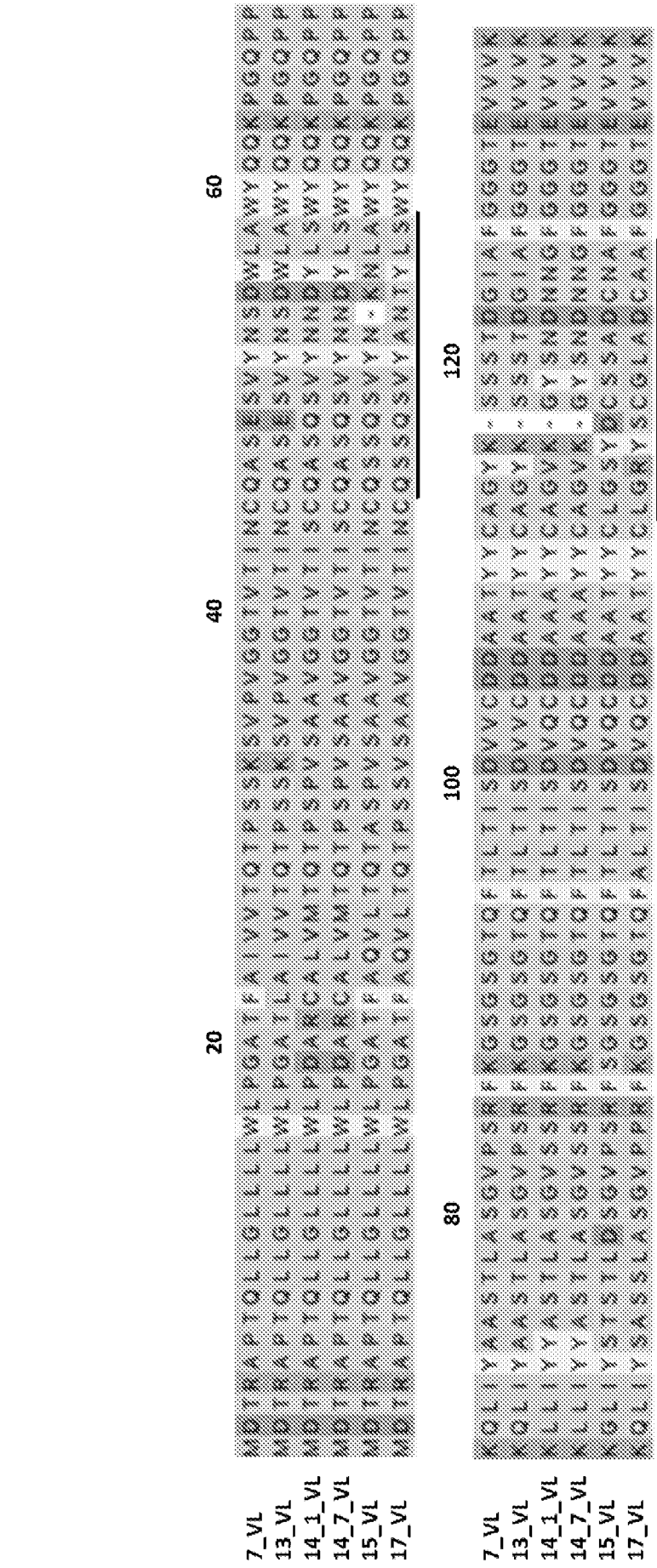

Figure 18A

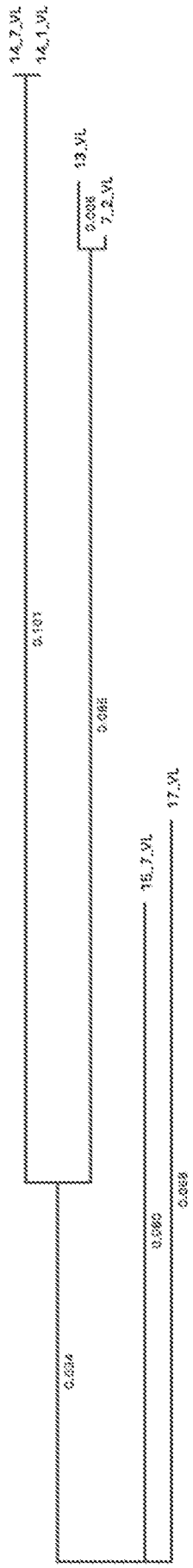

Figure 18B

Table 1. CDR Table (Kabat)

Sequence	CDR1	SEQ ID NO.	CDR2	SEQ ID NO.	CDR3	SEQ ID NO.
7_VL	QASESVYNSDWLA	11	AASTLAS	12	AGYKSSSTDGIA	13
13_VL	QASESVYNSDWLA	11	AASTLAS	12	AGYKSSSTDGIA	13
14-1_VL	QASQSVYNNDYLS	29	YASTLAS	30	AGVKGYSNDNNG	31
14-7_VL	QASQSVYNNDYLS	29	YASTLAS	30	AGVKGYSNDNNG	31
15_VL	QSSQSVYNKNLA	47	STSTLDS	48	LGSYDCSSADCNA	49
17_VL	QSSQSVYANTYLS	59	SASSLAS	60	LGRYSCGLADCAA	61
7_VH	NNGIC	62	CLYVGSSDTTYYASWAK	63	NLGL	7
13_VH	NNGIC	62	CLYVGSSDTTYYASWAK	63	NLGL	7
14-1_VH	INYYMC	64	CIYTGDDDTFYASWAK	65	GLYSGSINNL	25
14-7_VH	INYYMC	64	CIYTGDDDTFYASWAK	65	GLYSGSINNL	25
15_VH	SNYYMC	66	CIFLGSSGNTVYANWAK	67	DYVNGYDYFNL	43
17_VH	DSWYLC	68	CIYTGDGDTYYATWAK	69	GAQFYL	55

Figure 19

Table 2. CDR Table (Chothia)

Sequence	CDR1	SEQ ID NO	CDR2	SEQ ID NO	CDR3	SEQ ID NO.
7_VL	QASESVYNSDWLA	11	AASTLAS	12	AGYKSSSTDGIA	13
13_VL	QASESVYNSDWLA	11	AASTLAS	12	AGYKSSSTDGIA	13
14-1_VL	QASQSVYNNDYLS	29	YASTLAS	30	AGVKGYSNDNNG	31
14-7_VL	QASQSVYNNDYLS	29	YASTLAS	30	AGVKGYSNDNNG	31
15_VL	QSSQSVYNKNLA	47	STSTLDS	48	LGSYDCSSADCNA	49
17_VL	QSSQSVYANTYLS	59	SASSLAS	60	LGRYSCGLADCAA	61
7_VH	GFSFSNN	5	YVGSSD	6	NLGL	7
13_VH	GFSFSNN	5	YVGSSD	6	NLGL	7
14-1_VH	GFDFSINY	23	YTGDD	24	GLYSGSINNL	25
14-7_VH	GFDFSINY	23	YTGDD	24	GLYSGSINNL	25
15_VH	GFSFTSNY	41	FLGSSG	42	DYVNGYDYFNL	43
17_VH	GFSFSDSW	53	YTGDG	54	GAQFYL	55

Figure 20

Table 3. CDR Table (IMGT)

Sequence	CDR1	SEQ ID NO.	CDR2	SEQ ID NO.	CDR3	SEQ ID NO.
7_VL	QASESVYNSDWLA	11	AASTLAS	12	AGYKSSSTDGIA	13
13_VL	QASESVYNSDWLA	11	AASTLAS	12	AGYKSSSTDGIA	13
14-1_VL	QASQSVYNNDYLS	29	YASTLAS	30	AGVKGYSNDNNG	31
14-7_VL	QASQSVYNNDYLS	29	YASTLAS	30	AGVKGYSNDNNG	31
15_VL	QSSQSVYNKNLA	47	STSTLDS	48	LGSYDCSSADCNA	49
17_VL	QSSQSVYANTYLS	59	SASSLAS	60	LGRYSCGLADCAA	61
7_VH	GFSFSNNGIC	70	CLYVGSSDTTYYASWAK	63	NLGL	7
13_VH	GFSFSNNGIC	70	CLYVGSSDTTYYASWAK	63	NLGL	7
14-1_VH	GFDFSINYYMC	71	CIYTGDDDTFYASWAK	65	GLYSGSINNL	25
14-7_VH	GFDFSINYYMC	71	CIYTGDDDTFYASWAK	65	GLYSGSINNL	25
15_VH	GFSFTSNYYMC	72	CIFLGSSGNTVYANWAK	67	DYVNGYDYFNL	43
17_VH	GFSFSDSWYLC	73	CIYTGDGDTYYATWAK	69	GAQFYL	55

Figure 21

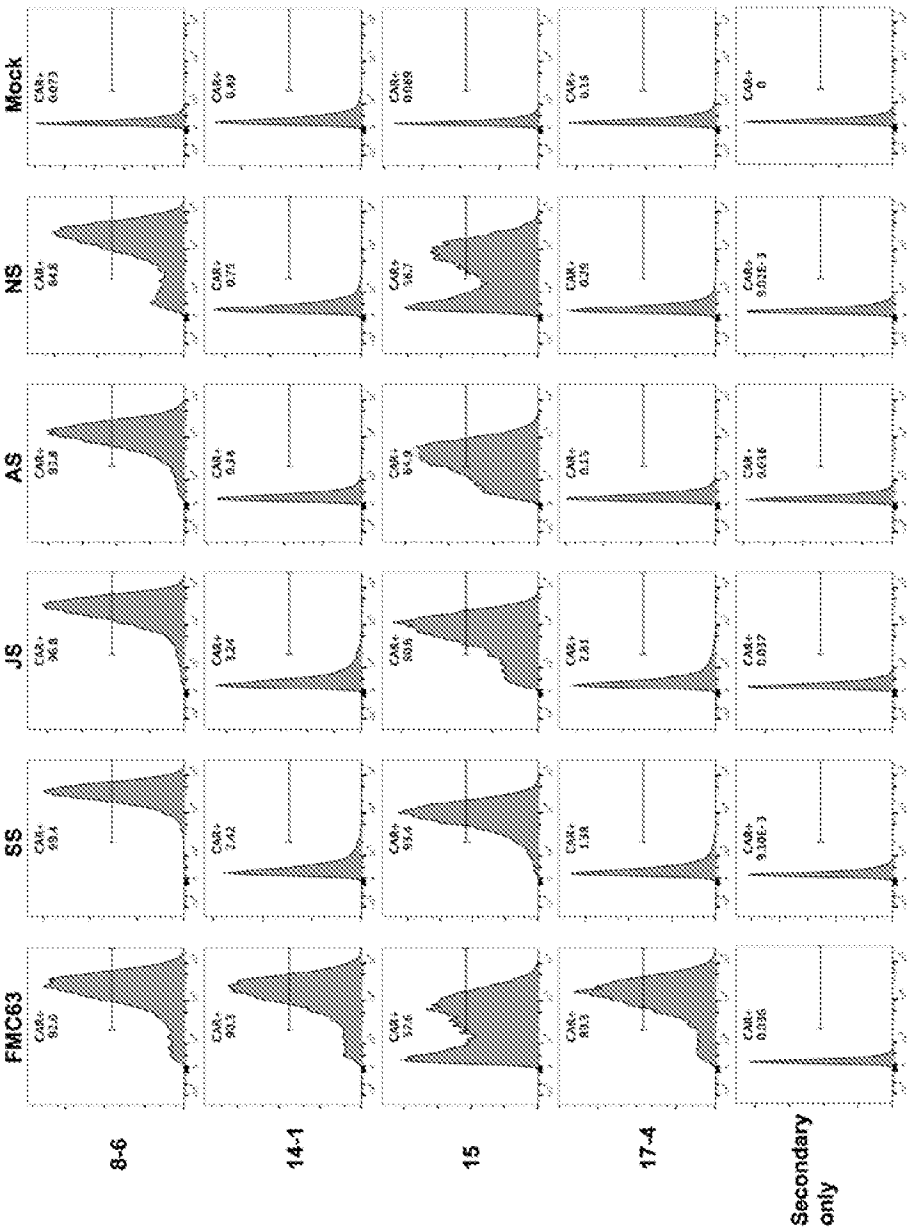

Figure 22

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/053790

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 39/395; C07K 14/705; C07K 16/28; C07K 16/42; C07K 16/46; C12N 5/07 (2018.01)

CPC - C07K 14/70503; C07K 14/70517; C07K 16/2803; C07K 16/42; C07K 16/4208; C07K 16/4258; C07K 16/4266; C07K 16/4283; C07K 2317/622; C07K 2317/74; C07K 2317/75; C07K 2317/76; C07K 2319/02; C07K 2319/31; C07K 2319/33; C12N 5/0636; C12N 2510/00; G01N 33/566 (2018.02)

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See Search History document

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

USPC - 424/178.1; 435/327; 435/7.92; 435/69.6; 435/252.3; 435/254.2; 530/387.2; 530/391.1; 530/391.7; 536/23.53 (keyword delimited)

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

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2014/190273 A1 (BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM) 27 November 2014 (27.11.2014) entire document	1-3, 11, 31-36
A	JENA et al. "Chimeric Antigen Receptor (CAR)-Specific Monoclonal Antibody to Detect CD19-Specific T Cells in Clinical Trials," PLoS ONE, 01 March 2013 (01.03.2013), Vol. 8, Iss. 3, e57838, Pgs. 1-12. entire document	1-8, 11-16, 19, 20, 31-36
A	TORIKAI et al. "A foundation for universal T-cell based immunotherapy: T cells engineered to express a CD19-specific chimeric-antigen-receptor and eliminate expression of endogenous TCR," Blood, 14 June 2012 (14.06.2012), Vol. 119, No. 24, Pgs. 5697-5705. entire document	1-8, 11-16, 19, 20, 31-36
A	DE OLIVEIRA et al. "A CD19/Fc fusion protein for detection of anti-CD19 chimeric antigen receptors," Journal of Translational Medicine, 29 January 2013 (29.01.2013), Vol. 11, Pgs. 1-9. entire document	1-8, 11-16, 19, 20, 31-36
A	ZHENG et al. "Protein L: a novel reagent for the detection of Chimeric Antigen Receptor (CAR) expression by flow cytometry," Journal of Translational Medicine, 13 February 2012 (13.02.2012), Vol. 10, Pgs. 1-6. entire document	1-8, 11-16, 19, 20, 31-36
A	KIEBACK et al. "A safeguard eliminates T cell receptor gene-modified autoreactive T cells after adoptive transfer," Proceedings of the National Academy of Sciences, 15 January 2008 (15.01.2008), Vol. 105, No. 2, Pgs. 623-628. entire document	1-8, 11-16, 19, 20, 31-36

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

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

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

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

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

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
14 February 2018	05 MAR 2018
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300	Authorized officer Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/053790

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:

   a. ☒ forming part of the international application as filed:

      ☒ in the form of an Annex C/ST.25 text file.

      ☐ on paper or in the form of an image file.

   b. ☐ furnished together with the international application under PCT Rule 13*ter*.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.

   c. ☐ furnished subsequent to the international filing date for the purposes of international search only:

      ☐ in the form of an Annex C/ST.25 text file (Rule 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.1(b) and Administrative Instructions, Section 713).

2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

SEQ ID NOs: 3, 5, 6, 7, 9, 11, 12, and 13 were searched.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/053790

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

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

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 37-40
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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

This International Searching Authority found multiple inventions in this international application, as follows:
See extra sheet(s).

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-8, 11-16, 19, 20, and 31-36 to the extent that they read on an antigen binding molecules comprising SEQ ID NOs: 3, 5, 6, 7, 9, 11, 12, and/or 13.

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/053790

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	KAWALEKAR et al. "Distinct Signaling of Coreceptors Regulates Specific Metabolism Pathways and Impacts Memory Development in CAR T Cells," Immunity, 16 February 2016 (16.02.2016), Vol. 44, Pgs. 380-390. entire document	1-8, 11-16, 19, 20, 31-36

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/053790

Continued from Box No. III Observations where unity of invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees need to be paid.

Group I+: claims 1-36 are drawn to isolated antigen binding molecules that specifically bind anti-CD19 scFv FMC63.

Group II: claims 41-101 are drawn to methods comprising a molecule of SEQ ID NO:1.

The first invention of Group I+ is restricted to an isolated antigen binding molecule that specifically bind anti-CD19 scFv FMC63, and methods comprising the same, wherein the antigen binding molecule comprises a heavy chain variable region, wherein in the heavy chain variable region is selected to be SEQ ID NO:3, the heavy chain variable region further comprising heavy chain complementary determining regions CDR1, CDR2, and CDR3, where CDR1 is selected to be SEQ ID NO:5, CDR2 is selected to be SEQ ID NO:6, and CDR3 is selected to be SEQ ID NO:7; and a light chain variable region, wherein the light chain variable region is selected to be SEQ ID NO:9, the light chain variable region further comprising light chain complementary determining regions CDR1, CDR2, and CDR3, where CDR1 is selected to be SEQ ID NO:11, CDR2 is selected to be SEQ ID NO:12, and CDR3 is selected to be SEQ ID NO:13. It is believed that claims 1-8, 11-16, 19, 20, and 31-36 read on this first named invention and thus these claims will be searched without fee to the extent that they read on an antigen binding molecules that specifically bind anti-CD19 scFv FMC63 comprising SEQ ID NOs: 3, 5, 6, 7, 9, 11, 12, and/or 13.

Applicant is invited to elect additional antigen binding molecules that specifically bind anti-CD19 scFv FMC63 with specified SEQ ID NO for each heavy and light chain CDR1, 2, and 3 to be searched in a specific combination by paying an additional fee for each set of election. An exemplary election would be an isolated antigen binding molecule that specifically bind anti-CD19 scFv FMC63, and methods comprising the same, wherein the antigen binding molecule comprises a heavy chain variable region, wherein in the heavy chain variable region is selected to be SEQ ID NO:21, the heavy chain variable region further comprising heavy chain complementary determining regions CDR1, CDR2, and CDR3, where CDR1 is selected to be SEQ ID NO:23, CDR2 is selected to be SEQ ID NO:24, and CDR3 is selected to be SEQ ID NO:25; and a light chain variable region, wherein the light chain variable region is selected to be SEQ ID NO:27, the light chain variable region further comprising light chain complementary determining regions CDR1, CDR2, and CDR3, where CDR1 is selected to be SEQ ID NO:29, CDR2 is selected to be SEQ ID NO:30, and CDR3 is selected to be SEQ ID NO:31. Additional antigen binding molecules that specifically bind anti-CD19 scFv FMC63 will be searched upon the payment of additional fees. Applicants must specify the claims that read on any additional elected inventions. Applicants must further indicate, if applicable, the claims which read on the first named invention if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined.

The Inventions listed in Groups I+ and II do not relate to a single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2 they lack the same or corresponding special technical features for the following reasons:

The special technical features of Groups I+, an antibody comprising a heavy chain variable region (VH) sequence selected from the group consisting of SEQ ID NOs: 3, 15, 21, 33, 39 and 51; or a light chain
variable region (VL) sequence selected from the group consisting of SEQ ID NOs: 8, 18, 27, 36, 45 and 57, are not found in Group II; the special technical features of Groups II, a method of administering a dose of a medicament to a subject, a method of determining a number of cells presenting a molecule, a method of isolating a molecule, a method of determining the presence or absence of a molecule, a method of increasing the concentration of cells presenting a molecule, and a method of depleting a population of immune cells presenting a molecule, are not found in Groups I+.

Even If Groups I+ and II were considered to share the technical features of an antigen molecule comprising anti-CD19 scFv FMC63; and an isolated antigen binding molecule that specifically binds anti-CD19 scFv FMC63, wherein the antigen binding molecule further comprises a detectable label, these shared technical features do not represent a contribution over the prior art.

Specifically, WO 2014/190273 A1 to Board of Regents, the University of Texas System discloses an antigen molecule comprising anti-CD19 scFv FMC63 (mAb clone FMC63, Para. [0005]); and an isolated antigen binding molecule that specifically binds anti-CD19 scFv FMC63 (specific anti-idiotype (anti-Id) mAbs are provided with specificity for... anti-human CD19 mAb (clone FMC63), Para. [0055]), wherein the antigen binding molecule further comprises a detectable label (antibodies were labeled with monomaleimido Nanogold, Para. [00113]).

The inventions listed in Groups I+ do not relate to a single general inventive concept under PCT Rule 13.1, because under PCT Rule 13.2 they lack the same or corresponding special technical features for the following reasons:

The Groups I+ formulas do not share a significant structural element responsible for recognizing and binding an anti-CD19 scFv FMC63 molecule, requiring the selection of alternatives for the light and heavy chain variable regions of the binding molecule, where "the HC comprises a heavy chain
variable region (VH) sequence selected from the group consisting of SEQ ID NOs:3, 15, 21, 33, 39 and 51" and "the LC comprises a light chain variable region (VL) sequence selected from the group consisting of SEQ ID NOs:8, 18, 27, 36, 45 and 57".

Additionally, even if Groups I+ were considered to share the technical features of an isolated antigen binding molecule that specifically binds anti-CD19 scFv FMC63, these shared technical features do not represent a contribution over the prior art.

Specifically, WO 2014/190273 A1 to Board of Regents, the University of Texas System discloses an isolated antigen binding molecule that specifically binds anti-CD19 scFv FMC63 (specific anti-idiotype (anti-Id) mAbs are provided with specificity for... anti-human CD19 mAb (clone FMC63), Para. [0055]).

The inventions listed in Groups I+ and II therefore lack unity under Rule 13 because they do not share a same or corresponding special technical features.