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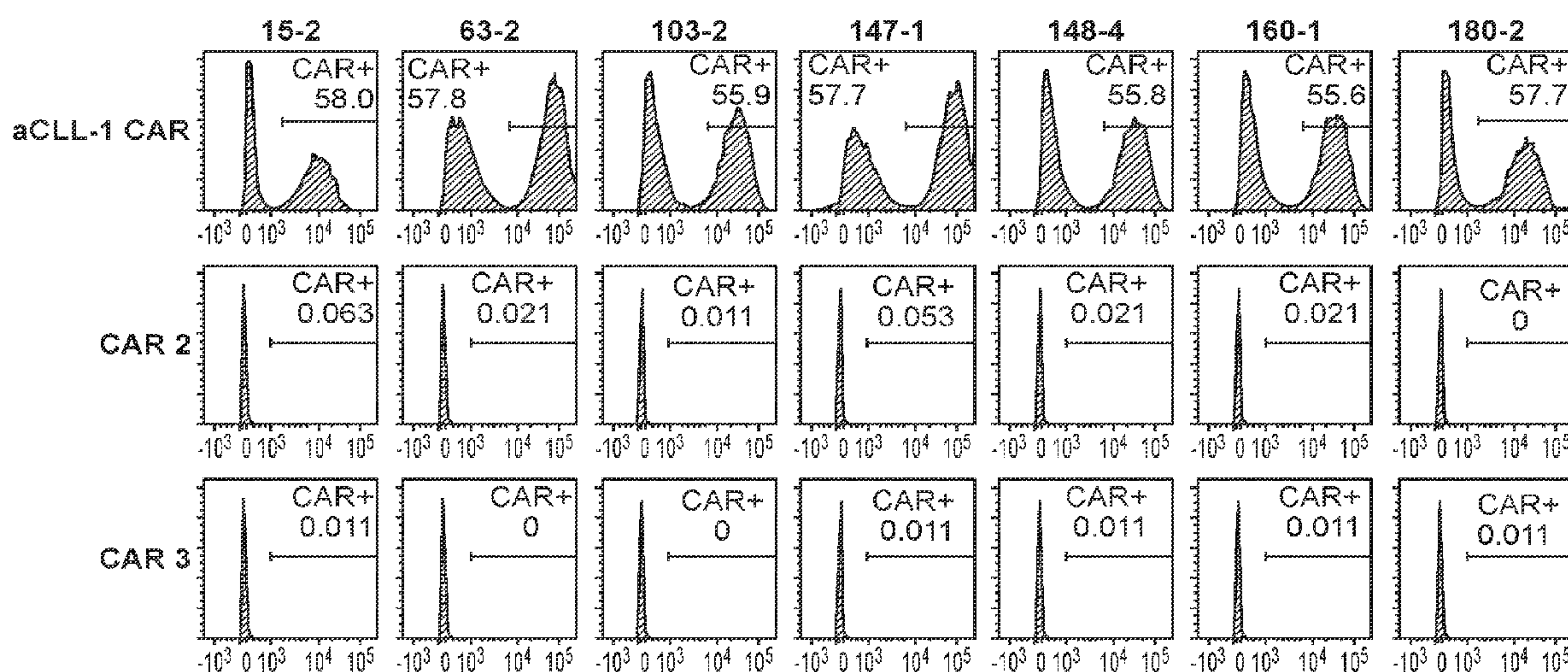


FIG. 1

(57) Abstract: Isolated antigen binding molecules that specifically bind to a CLL-1 binding molecule are provided. The antigen binding molecules may be used in the methods provided herein.

ANTI-IDIOTYPIC ANTIGEN BINDING MOLECULES AND METHODS OF USE THEREOF

CROSS-REFERENCE TO RELATED PATENT APPLICATION

[0001] This application claims priority under 35 U.S.C. § 119(e) to U.S. Provisional Patent Application No. 62/924,843, filed October 23, 2019, the contents of which is hereby incorporated by reference in its entirety.

[0002] SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on October 15, 2020, is named 124493-0114_SL.txt and is 43,173 bytes in size.

TECHNICAL FIELD

[0003] This disclosure relates to antigen binding molecules 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.

TECHNICAL FIELD

[0004] This disclosure relates to antigen binding molecules 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

[0005] 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.

[0006] 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 may 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*).

SUMMARY

[0007] Disclosed herein are rabbit antibodies that specifically bind to a C-type lectin-like molecule-1 (CLL-1) binding molecule as well as molecules comprising these sequences and cells presenting such molecules.

[0008] In one aspect, the present disclosure provides an isolated antigen binding molecule that specifically binds a molecule comprising a CLL-1 binding molecule. In some embodiments, the CLL-1 binding molecule binds human CLL-1.

[0009] In some embodiments, the isolated antigen binding molecule is humanized.

[0010] 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.

[0011] In some embodiments, the antigen binding molecule comprises a heavy chain (HC).

[0012] In some embodiments, the HC comprises a heavy chain variable region (VH) sequence selected from the group consisting of SEQ ID NOs: 1-7 and 15-21.

[0013] In some embodiments, the variable region (VH) and comprises one or more of (a) a CDR1, (b) a CDR2, and (c) a CDR3.

[0014] In some embodiments, the antigen binding molecule comprises a heavy chain CDR1 selected from the group consisting of SEQ ID NOs: 49, 52, 55, 58, 61, 64, and 67.

[0015] In some embodiments, the antigen binding molecule comprises a heavy chain CDR2 selected from the group consisting of SEQ ID NOs: 50, 53, 56, 59, 62, 65, and 68.

[0016] In some embodiments, the antigen binding molecule comprises a heavy chain CDR3 selected from the group consisting of SEQ ID NOs: 51, 54, 57, 60, 63, 66, and 69.

[0017] In some embodiments, the heavy chain comprises a heavy chain CDR1, a heavy chain CDR2, and a heavy chain CDR3, each CDR comprising an amino acid sequence shown in Table C and D.

[0018] In some embodiments, the antigen binding molecule comprises a VH amino acid sequence that is at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or about 100% identical to SEQ ID NOs: 15-21.

[0019] In some embodiments, the antigen binding molecule comprises a light chain (LC).

[0020] In some embodiments, the LC comprises a light chain variable region (VL) sequence selected from the group consisting of SEQ ID NOs: 22-28.

[0021] In some 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: 29, 32, 35, 37, 40, 43, and 46. In some embodiments, the antigen binding molecule comprises a light chain CDR2 selected from the group consisting of SEQ ID NOs: 30, 33, 38, 44, and 47. In some embodiments, the antigen binding molecule comprises a light chain CDR3 selected from the group consisting of SEQ ID NOs: 31, 34, 36, 39, 42, 45, and 48.

[0022] 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 Table C or D.

[0023] In some embodiments, the antigen binding molecule comprises a VL amino acid sequence that is at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or about 100% identical to a VL comprising SEQ ID NOs: 22-28.

[0024] In some embodiments, 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: 22.

[0025] In some embodiments, the antigen binding molecule comprises:

- (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 49;
- (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 50;
- (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 51;
- (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.

[0026] In some embodiments, the antigen binding molecule comprises: (a) a VH comprising the amino acid sequence of SEQ ID NO: 16; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 23.

[0027] In some embodiments, the antigen binding molecule comprises:

- (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 52;
- (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 53;
- (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 54;
- (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 32;
- (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 33;

and

- (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 34.

[0028] In some embodiments, the antigen binding molecule comprises: (a) a VH comprising the amino acid sequence of SEQ ID NO: 17; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 24.

[0029] In some embodiments, the antigen binding molecule comprises:

- (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 55;
- (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 56;
- (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 57;
- (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 35;
- (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 33;

and

- (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 36.

[0030] In some embodiments, the antigen binding molecule comprises: (a) a VH comprising the amino acid sequence of SEQ ID NO: 18; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 25.

[0031] In some embodiments, the antigen binding molecule comprises:

- (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 58;
- (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 59;
- (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 60;
- (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 37;
- (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 38;

and

- (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 39.

[0032] In some embodiments, the antigen binding molecule comprises: (a) a VH comprising the amino acid sequence of SEQ ID NO: 19; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 26.

[0033] In some embodiments, the antigen binding molecule comprises:

- (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 61;
- (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 62;
- (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 63;
- (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 40;
- (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: 42.

[0034] In some embodiments, the antigen binding molecule comprises: (a) a VH comprising the amino acid sequence of SEQ ID NO: 20; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 27.

[0035] In some embodiments, the antigen binding molecule comprises:

- (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 64;
- (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 65;
- (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 66;
- (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 43;
- (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 44;

and

- (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 45.

[0036] In some embodiments, 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: 28.

[0037] In some embodiments, the antigen binding molecule comprises:

- (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 46;
 - (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 47;
 - (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 48;
 - (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 67;
 - (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 68;
- and
- (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 69.

[0038] In some embodiments, the antigen binding molecule further comprises a detectable label. 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.

[0039] In some embodiments, the fluorescent label is selected from the group consisting of an Atto dye, an Alexafluor dye, quantum dots, Hydroxycoumarin, Aminocouramin, 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 Rhocamine B, Texas Red, Allophycocyanin (APC), APC-Cy7 conjugates, Indo-1, Fluo-3, Fluo-4, DCFH, DHR, SNARF, GFP (Y66H mutation), GFP (Y66F mutation), EBFP, EBFP2, Azurite, GFPuv, T-Sapphire, Cerulean, mCFP, mTurquoise2, ECFP, CyPet, GFP (Y66W mutation), mKeima-Red, TagCFP, AmCyan1, mTFP1, GFP (S65A mutation), Midorishi Cyan, Wild Type GFP, GFP (S65C mutation), TurboGFP, TagGFP, GFP (S65L mutation), Emerald, GFP (S65T mutation), EGFP, Azami Green, ZsGreen1, TagYFP, EYFP, Topaz, Venus, mCitrine, YPet, TurboYFP, ZsYellow1, Kusabira Orange, mOrange, Allophycocyanin (APC), mKO, TurboRFP, tdTomato, TagRFP, DsRed monomer, DsRed2 ("RFP"), mStrawberry, TurboFP602, AsRed2, mRFP1, J-Red, R-phycoerythrin (RPE), B-phycoerythrin (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

[0040] In one aspect, the present disclosure provides a composition comprising the antigen binding molecule that specifically binds a molecule comprising a CLL-1 binding molecule described herein.

[0041] In one aspect, the present disclosure provides a polynucleotide encoding the heavy chain of an antigen binding molecule that specifically binds a molecule comprising a CLL-1 binding molecule described herein.

[0042] In one aspect, the present disclosure provides a polynucleotide encoding the light chain of an antigen binding molecule that specifically binds a molecule comprising a CLL-1 binding molecule described herein.

[0043] In one aspect, the present disclosure provides a vector comprising the polynucleotide encoding the heavy chain and/or the light chain of an antigen binding molecule described herein.

[0044] In one aspect, the present disclosure provides a cell comprising one or both of the vectors encoding the heavy chain and/or the light chain of an antigen binding molecule that specifically binds a molecule comprising a CLL-1 binding molecule described herein.

[0045] In some 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.

[0046] In one aspect, the present disclosure provides a method of making an antigen binding molecule described herein, comprising incubating the cell comprising the vector encoding an antigen binding molecule that specifically binds a molecule comprising a CLL-1 binding molecule under suitable conditions.

[0047] In one aspect, the present disclosure provides 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 a CLL-1 binding molecule, 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 a CLL-1 binding molecule; (b) providing an aliquot of the sample comprising a population of cells presenting a therapeutic molecule comprising a CLL-1 binding molecule; (c) providing an antigen binding molecule that specifically binds the a CLL-1 binding molecule, 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 a CLL-1 binding molecule 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.

[0048] In some embodiments, the molecule comprising a CLL-1 binding molecule is a CAR. In some embodiments, 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.

[0049] 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, CD11a/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, BAFR, 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, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, 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, Ly108), 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.

[0050] 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.

[0051] In some embodiments, the fluorescent label is selected from the group consisting of an Atto dye, an Alexafluor dye, quantum dots, Hydroxycoumarin, Aminocouramin, 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 Rhocamine B, Texas Red, Allophycocyanin (APC), APC-Cy7 conjugates, Indo-1, Fluo-3, Fluo-4, DCFH, DHR, SNARF, GFP (Y66H mutation), GFP (Y66F mutation), EBFP, EBFP2, Azurite, GFPuv, T-Sapphire, Cerulean, mCFP, mTurquoise2, ECFP, CyPet, GFP (Y66W mutation), mKeima-Red, TagCFP, AmCyan1,

mTFP1, GFP (S65A mutation), Midorishi Cyan, Wild Type GFP, GFP (S65C mutation), TurboGFP, TagGFP, GFP (S65L mutation), Emerald, GFP (S65T mutation), EGFP, Azami Green, ZsGreen1, TagYFP, EYFP, Topaz, Venus, mCitrine, YPet, TurboYFP, ZsYellow1, Kusabira Orange, mOrange, Allophycocyanin (APC), mKO, TurboRFP, tdTomato, TagRFP, DsRed monomer, DsRed2 ("RFP"), mStrawberry, TurboFP602, AsRed2, mRFP1, J-Red, R-phycoerythrin (RPE), B-phycoerythrin (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

[0052] In some embodiments, the immune cell is a T cell. In some embodiments, the T cell is disposed *in vitro*. In some embodiments, the T cell is disposed *in vivo*. In some embodiments, the T cell is in one of blood, extracted tissue, tissue grown ex vivo, and cell culture media.

[0053] In some embodiments, the T cell is an autologous T cell.

[0054] In some embodiments, the T cell is an allogenic T cell.

[0055] In some embodiments, the dose comprises 1.0×10^6 cells per kg.

[0056] In some embodiments, the antigen binding molecule comprises an antigen binding molecule of described herein and humanized forms thereof.

[0057] In one aspect, the present disclosure provides a method of determining a number of cells presenting a molecule comprising a CLL-1 binding molecule in a sample, the method comprising: (a) providing a sample comprising cells known or suspected to be presenting a molecule comprising a CLL-1 binding molecule; (b) contacting the sample of (a) with an antigen binding molecule that specifically binds the molecule comprising a CLL-1 binding molecule, 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.

[0058] In some embodiments, the molecule comprising a CLL-1 binding molecule is a CAR. In some embodiments, 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.

[0059] 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, CD11a/CD18), CD3 gamma, CD3 delta, CD3 epsilon, CD3 zeta, CD247, CD276 (B7-H3), LIGHT, (TNFSF14), NKG2C, Ig alpha

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[0060] 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.

[0061] In some embodiments, the fluorescent label is selected from the group consisting of an Atto dye, an Alexafluor dye, quantum dots, Hydroxycoumarin, Aminocoumarin, Methoxycoumarin, Cascade Blue, Pacific Blue, Pacific Orange, Lucifer Yellow, NBD, R-Phycoerythrin (PE), PE-Cy5 conjugates, PE-Cy7 conjugates, Red 613, PerCP, TruRed, FluorX, Fluorescein, BODIPY-FL, Cy2, Cy3, Cy3B, Cy3.5, Cy5, Cy5.5, Cy7, TRITC, X-Rhodamine, Lissamine Rhocamine B, Texas Red, Allophycocyanin (APC), APC-Cy7 conjugates, Indo-1, Fluo-3, Fluo-4, DCFH, DHR, SNARF, GFP (Y66H mutation), GFP (Y66F mutation), EBFP, EBFP2, Azurite, GFPuv, T-Sapphire, Cerulean, mCFP, mTurquoise2, ECFP, CyPet, GFP (Y66W mutation), mKeima-Red, TagCFP, AmCyan1, mTFP1, GFP (S65A mutation), Midorishi Cyan, Wild Type GFP, GFP (S65C mutation), TurboGFP, TagGFP, GFP (S65L mutation), Emerald, GFP (S65T mutation), EGFP, Azami Green, ZsGreen1, TagYFP, EYFP, Topaz, Venus, mCitrine, YPet, TurboYFP, ZsYellow1, Kusabira Orange, mOrange, Allophycocyanin (APC), mKO, TurboRFP, tdTomato, TagRFP, DsRed monomer, DsRed2 ("RFP"), mStrawberry, TurboFP602, AsRed2, mRFP1, J-Red, R-phycoerythrin (RPE), B-phycoerythrin (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

[0062] In some embodiments, the immune cell is a T cell. In some embodiments, the T cell is disposed *in vitro*. In some embodiments, the T cell is disposed *in vivo*. In some

embodiments, the T cell is in one of blood, extracted tissue, tissue grown ex vivo, and cell culture media.

[0063] In some embodiments, the T cell is an autologous T cell.

[0064] In some embodiments, the T cell is an allogenic T cell.

[0065] In some embodiments, the dose comprises 1.0×10^6 cells per kg.

[0066] In some embodiments, the antigen binding molecule comprises an antigen binding molecule of described herein and humanized forms thereof.

[0067] In one aspect, the present disclosure provides a method of isolating a cell comprising a CLL-1 binding molecule, the method comprising: (a) providing a sample known or suspected to comprise a molecule comprising a CLL-1 binding molecule; (b) providing an antigen binding molecule that specifically binds a molecule comprising a CLL-1 binding molecule, 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 a CLL-1 binding molecule 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 a CLL-1 binding molecule, and (b) an antigen binding molecule.

[0068] In some embodiments, the molecule comprising a CLL-1 binding molecule is a CAR.

[0069] 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, CD11a/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, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, 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, Ly108), 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.

[0070] 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 well plate, a glass well plate, a ceramic well plate and a cell culture bag.

[0071] 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.

[0072] In some embodiments, the fluorescent label is selected from the group consisting of an Atto dye, an Alexafluor dye, quantum dots, Hydroxycoumarin, Aminocoumarin, Methoxycoumarin, Cascade Blue, Pacific Blue, Pacific Orange, Lucifer Yellow, NBD, R-Phycoerythrin (PE), PE-Cy5 conjugates, PE-Cy7 conjugates, Red 613, PerCP, TruRed, FluorX, Fluorescein, BODIPY-FL, Cy2, Cy3, Cy3B, Cy3.5, Cy5, Cy5.5, Cy7, TRITC, X-Rhodamine, Lissamine Rhocamine B, Texas Red, Allophycocyanin (APC), APC-Cy7 conjugates, Indo-1, Fluo-3, Fluo-4, DCFH, DHR, SNARF, GFP (Y66H mutation), GFP (Y66F mutation), EBFP, EBFP2, Azurite, GFPuv, T-Sapphire, Cerulean, mCFP, mTurquoise2, ECFP, CyPet, GFP (Y66W mutation), mKeima-Red, TagCFP, AmCyan1, mTFP1, GFP (S65A mutation), Midorishi Cyan, Wild Type GFP, GFP (S65C mutation), TurboGFP, TagGFP, GFP (S65L mutation), Emerald, GFP (S65T mutation), EGFP, Azami Green, ZsGreen1, TagYFP, EYFP, Topaz, Venus, mCitrine, YPet, TurboYFP, ZsYellow1, Kusabira Orange, mOrange, Allophycocyanin (APC), mKO, TurboRFP, tdTomato, TagRFP, DsRed monomer, DsRed2 ("RFP"), mStrawberry, TurboFP602, AsRed2, mRFP1, J-Red, R-phycoerythrin (RPE), B-phycoerythrin (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

[0073] In some embodiments, the antigen binding molecule comprises an antigen binding molecule of described herein and humanized forms thereof.

[0074] In one aspect, the present disclosure provides a method of determining the presence or absence of a molecule comprising a CLL-1 binding molecule in a sample, the method comprising: (a) providing a sample known or suspected to comprise a molecule comprising a CLL-1 binding molecule; (b) providing an antigen binding molecule comprising a detectable label that specifically binds a molecule comprising a CLL-1 binding molecule; (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.

[0075] In some embodiments, the molecule comprising a CLL-1 binding molecule is a CAR.

[0076] 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, CD11a/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, BAFR, 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, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, 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, Ly108), 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.

[0077] 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 well plate, a glass well plate, a ceramic well plate and a cell culture bag.

[0078] 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.

[0079] In some embodiments, the fluorescent label is selected from the group consisting of an Atto dye, an Alexafluor dye, quantum dots, Hydroxycoumarin, Aminocoumarin, Methoxycoumarin, Cascade Blue, Pacific Blue, Pacific Orange, Lucifer Yellow, NBD, R-Phycoerythrin (PE), PE-Cy5 conjugates, PE-Cy7 conjugates, Red 613, PerCP, TruRed, FluorX, Fluorescein, BODIPY-FL, Cy2, Cy3, Cy3B, Cy3.5, Cy5, Cy5.5, Cy7, TRITC, X-Rhodamine, Lissamine Rhocamine B, Texas Red, Allophycocyanin (APC),

APC-Cy7 conjugates, Indo-1, Fluo-3, Fluo-4, DCFH, DHR, SNARF, GFP (Y66H mutation), GFP (Y66F mutation), EBFP, EBFP2, Azurite, GFPuv, T-Sapphire, Cerulean, mCFP, mTurquoise2, ECFP, CyPet, GFP (Y66W mutation), mKeima-Red, TagCFP, AmCyan1, mTFP1, GFP (S65A mutation), Midorishi Cyan, Wild Type GFP, GFP (S65C mutation), TurboGFP, TagGFP, GFP (S65L mutation), Emerald, GFP (S65T mutation), EGFP, Azami Green, ZsGreen1, TagYFP, EYFP, Topaz, Venus, mCitrine, YPet, TurboYFP, ZsYellow1, Kusabira Orange, mOrange, Allophycocyanin (APC), mKO, TurboRFP, tdTomato, TagRFP, DsRed monomer, DsRed2 ("RFP"), mStrawberry, TurboFP602, AsRed2, mRFP1, J-Red, R-phycoerythrin (RPE), B-phycoerythrin (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

[0080] In some embodiments, the antigen binding molecule comprises an antigen binding molecule of described herein and humanized forms thereof.

[0081] In one aspect, the present disclosure provides a method of increasing the concentration of cells presenting a molecule comprising a CLL-1 binding molecule, the method comprising: (a) providing a sample comprising a cell known or suspected to present a molecule comprising a CLL-1 binding molecule; (b) providing an antigen binding molecule that specifically binds a molecule comprising a CLL-1 binding molecule, 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 a CLL-1 binding molecule 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.

[0082] In some embodiments, the molecule comprising a CLL-1 binding molecule is a CAR. In some embodiments, 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.

[0083] 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, CD11a/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, BAFR, 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, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, 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, Ly108), 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.

[0084] 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.

[0085] In some embodiments, the fluorescent label is selected from the group consisting of an Atto dye, an Alexafluor dye, quantum dots, Hydroxycoumarin, Aminocoumarin, Methoxycoumarin, Cascade Blue, Pacific Blue, Pacific Orange, Lucifer Yellow, NBD, R-Phycoerythrin (PE), PE-Cy5 conjugates, PE-Cy7 conjugates, Red 613, PerCP, TruRed, FluorX, Fluorescein, BODIPY-FL, Cy2, Cy3, Cy3B, Cy3.5, Cy5, Cy5.5, Cy7, TRITC, X-Rhodamine, Lissamine Rhocamine B, Texas Red, Allophycocyanin (APC), APC-Cy7 conjugates, Indo-1, Fluo-3, Fluo-4, DCFH, DHR, SNARF, GFP (Y66H mutation), GFP (Y66F mutation), EBFP, EBFP2, Azurite, GFPuv, T-Sapphire, Cerulean, mCFP, mTurquoise2, ECFP, CyPet, GFP (Y66W mutation), mKeima-Red, TagCFP, AmCyan1, mTFP1, GFP (S65A mutation), Midorishi Cyan, Wild Type GFP, GFP (S65C mutation), TurboGFP, TagGFP, GFP (S65L mutation), Emerald, GFP (S65T mutation), EGFP, Azami Green, ZsGreen1, TagYFP, EYFP, Topaz, Venus, mCitrine, YPet, TurboYFP, ZsYellow1, Kusabira Orange, mOrange, Allophycocyanin (APC), mKO, TurboRFP, tdTomato, TagRFP, DsRed monomer, DsRed2 ("RFP"), mStrawberry, TurboFP602, AsRed2, mRFP1, J-Red, R-phycoerythrin (RPE), B-phycoerythrin (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

[0086] In some embodiments, the immune cell is a T cell. In some embodiments, the T cell is disposed *in vitro*. In some embodiments, the T cell is disposed *in vivo*. In some embodiments, the T cell is in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media.

[0087] In some embodiments, the T cell is an autologous T cell.

- [0088]** In some embodiments, the T cell is an allogenic T cell.
- [0089]** In some embodiments, the dose comprises 1.0×10^6 cells per kg.
- [0090]** In some embodiments, the antigen binding molecule comprises an antigen binding molecule of described herein and humanized forms thereof.
- [0091]** In one aspect, the present disclosure provides a method of depleting a population of immune cells presenting a molecule comprising a CLL-1 binding molecule, 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 a CLL-1 binding molecule; and (b) contacting the immune cells with an antigen binding molecule that specifically binds to the molecule comprising a CLL-1 binding molecule, and an activating molecule expressed on the surface of the an immune cell not presenting the molecule comprising a CLL-1 binding molecule, under conditions that permit the formation of a ternary binding complex comprising the molecule comprising a CLL-1 binding molecule, the activating molecule and the antigen binding molecule.
- [0092]** In some embodiments, the molecule comprising a CLL-1 binding molecule is a CAR. In some embodiments, the immune cell selected from the group consisting of CD8+ T cells, CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells.
- [0093]** 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, CD11a/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, BAFR, 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, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, 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, Ly108), 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.

[0094] In some embodiments, the immune cell is a T cell. In some embodiments, the T cell is disposed *in vitro*. In some embodiments, the T cell is disposed *in vivo*. In some embodiments, the T cell is in one of blood, extracted tissue, tissue grown ex vivo, and cell culture media.

[0095] In some embodiments, the T cell is an autologous T cell.

[0096] In some embodiments, the T cell is an allogenic T cell.

[0097] In some embodiments, the dose comprises 1.0×10^6 cells per kg.

[0098] In some embodiments, the antigen binding molecule comprises an antigen binding molecule of described herein and humanized forms thereof.

[0099] 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

[0100] Figure 1 depicts a series of histograms using CAR-expressing T cells demonstrating that KIP-10 clonal supernatants (Clones 15-2, 63-2, 103-2, 147-1, 148-4, 160-1 and 180-2) bind anti-CLL-1 CAR-expressing T cells (top row), but not two control CAR-expressing T cells; the plots demonstrate specific, selective binding of the antibodies to the expressed anti-CLL-1 CAR.

DETAILED DESCRIPTION

[0101] The present invention relates to anti-idiotypic antigen binding molecules, including antibodies, which specifically bind to antigen binding molecules that specifically bind CLL-1. 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.

[0102] Methods of using the disclosed antigen binding molecules are provided. The antigen binding molecules, polynucleotides, vectors, *in vitro* cells and methods described herein may be used in a range of applications, *e.g.*, as reagents to detect the presence of moieties comprising the CLL-1 binding molecule, as well as molecules comprising this

sequence and cells presenting such molecules, quantifying the amount of a moiety comprising CLL-1 binding molecule, as well as molecules comprising this sequence and cells presenting such molecules, screening for moieties comprising the CLL-1 binding molecule, as well as molecules comprising this sequence and cells presenting such molecules, purifying moieties comprising a CLL-1 binding molecule, as well as molecules comprising this sequence and cells presenting such molecules, and biomarker studies focused on moieties comprising a CLL-1 binding molecule, 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 a CLL-1 binding molecule, as well as cells presenting such molecules, is modulated (enhanced or repressed), as well as dose ranging studies related to therapeutics comprising a CLL-1 binding molecule, as well as molecules comprising this sequence and cells presenting such molecules, and cells presenting such molecules.

[0103] The antigen binding molecules (antibodies) disclosed herein were generated from hybridomas generated using B-cells of rabbit origin, but may 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 may be generated as described herein.

I. Definitions

[0104] 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.

[0105] 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.

[0106] 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.

[0107] 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.

[0108] 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 may 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.

[0109] As used herein, the term the terms “a” and “an” are used per standard convention and mean one or more, unless context dictates otherwise.

[0110] 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” may mean within one or more than one standard deviation per the practice in the art. Alternatively, “about” or “comprising essentially of” may mean a range of up to 10% (*i.e.*, $\pm 10\%$). For example, about 5mg may include any number between 4.5 mg and 5.5 mg. Furthermore, particularly with respect to biological systems or processes, the terms may 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.

[0111] 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.

[0112] 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).

[0113] 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.

[0114] 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.

[0115] As used herein, the term “antibody” (Ab) includes, without limitation, a glycoprotein immunoglobulin which binds specifically to an antigen. In general, an antibody may 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 may 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 may 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.

[0116] 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.

[0117] A non-human antibody may be humanized using recombinant methods to reduce its immunogenicity in humans, as disclosed herein, with respect to antibodies that specifically bind a CLL-1 binding molecule, 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 (*e.g.*, a scFv).

[0118] In various embodiments, an antibody specifically binds a CLL-1 binding molecule, 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 a CLL-1 binding molecule, as well as molecules comprising this sequence, and cells presenting such molecules; cells presenting a CLL-1 binding molecule may, but need not be, an immune cell, such as a T cell.

[0119] 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 may 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 a CLL-1 binding molecule, as well as molecules comprising this sequence and cells presenting such molecules), may serve as an antigen. Generally, an antigen may be endogenously expressed, *i.e.* expressed by genomic DNA, or it may be recombinantly expressed, or it may be chemically synthesized. In one particular embodiment, an antigen comprises all or a portion of a CLL-1 binding molecule a CLL-1 binding molecule, 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.

[0120] 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 IgG1 antibody; an IgG2 anti-body; an IgG3 antibody; or an IgG4 antibody, and fragments thereof.

[0121] An antigen binding molecule may 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”) may be used, as well as scaffolds based on antibody mimetics utilizing various components (*e.g.*, fibronectin) as a scaffold. An antigen binding molecule may have, for example, the structure of a naturally occurring immunoglobulin.

[0122] An antigen binding molecule may have one or more binding sites. If there is more than one binding site, the binding sites may be identical to one another or they may 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.*, a CLL-1 binding molecule and a cell surface activator molecule).

[0123] 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 (*e.g.*, Table C and D), which specifically bind a CLL-1 binding molecule, as well as molecules comprising a CLL-1 binding molecule, and cells presenting such molecules. In further embodiments, the antigen binding molecule binds to a CAR comprising a CLL-1 binding molecule, as well as molecules comprising a CLL-1 binding molecule, and may be expressed on an immune cell, such as a T cell.

[0124] 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.

[0125] 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 may generally be represented by the dissociation constant (K_D). Affinity may 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} may be determined by standard techniques known to one of ordinary skill in the art, such as BIAcore[®] or KinExA or surface plasmon resonance.

[0126] 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 may 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.

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 may 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 may 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 may be described according to the Kabat numbering scheme, as shown in Table C (although they may readily be construed in other numbering systems using Table A above).

[0127] In certain aspects, the CDRs of an antibody may 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 Table D.

[0128] 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) may be replaced with an amino acid residue with a similar side chain.

[0129] Conservative amino acid substitutions, which are encompassed by the present disclosure, may 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 may 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.

[0130] Non-conservative substitutions may involve the exchange of a member of one of these classes for a member from another class. Such substituted residues may 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

<u>Original Residues</u>	<u>Exemplary Substitutions</u>	<u>Specific Exemplary Substitutions</u>
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

[0131] 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 may 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.

[0132] 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 may 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 may 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 may 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 I¹²⁵ 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).

[0133] 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) may 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.

[0134] 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) *Structure* 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 may 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 may be the same or different.

[0135] As used herein, an “epitope” is a term in the art and refers to a localized region of an antigen to which an antibody may specifically bind. An epitope may be, for example, contiguous amino acids of a polypeptide (linear or contiguous epitope) or an epitope may, 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 may 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 may may 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 may may 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.

[0136] As used herein, the term “Fab fragment” 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.

[0137] 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.

[0138] In another embodiment, molecules that specifically bind to an antigen (*e.g.*, a CLL-1 binding molecule), as well as molecules comprising this sequence and cells presenting such molecules) bind with a dissociation constant (K_d) of about 1×10^{-7} M. In some embodiments, the antigen binding molecule specifically binds an antigen (*e.g.*, a CLL-1 binding molecule, as well as molecules comprising this sequence and cells presenting such molecules) with “high affinity” when the K_d is about 1×10^{-9} M to about 5×10^{-9} M. In some embodiments, the antigen binding molecule specifically binds an antigen (*e.g.*, an anti-CLL-1 binding molecule, as well as molecules comprising this sequence and cells presenting such molecules) with “very high affinity” when the K_d is 1×10^{-10} M to about 5×10^{-10} M.

[0139] In still another embodiment, molecules that specifically bind to an antigen (*e.g.*, a CLL-1 binding molecule, 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.*, a CLL-1 binding molecule, as well as molecules comprising this sequence and cells presenting such molecules) do not cross react with other proteins that do not comprise a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules. In some embodiments, provided herein is an antibody or fragment thereof that binds to a CLL-1 binding molecule, 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 a CLL-1 binding molecule, 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 a CLL-1 binding molecule, as well as molecules comprising this sequence and cells presenting such molecules, described herein compared to an unrelated protein which does not comprise a CLL-1 binding molecule, 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.

[0140] As used herein, the term “heavy chain” when used in reference to an antibody may 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.*, IgG₁, IgG₂, IgG₃ and IgG₄.

[0141] 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.

[0142] 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.

[0143] 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, CDR1, FR2, CDR2, FR3, CDR3 and FR4. The assignment of amino acids to each domain may be done in accordance with the definitions of Kabat (*see, e.g., Kabat et al. in Sequences of Proteins of Immunological Interest*, 5th Ed., NIH Publication 91-3242, Bethesda MD (1991)) or Chothia (Chothia, used herein, (*see, e.g., Chothia & Lesk (1987), J. Mol. Biol. 196:901-917; Chothia et al., 1989, Nature 342:878-883 or Honegger & Pluckthun (2001), J Mol Biol 309:657-670*). The Kabat, Chothia, IGMT and Abm (Oxford Molecular) numbering systems are described more fully herein.

[0144] As used herein, the term “*in vitro* cell” refers to any cell that is cultured *ex vivo*. An *in vitro* cell may include a human cell such as a T cell or dendritic cell, or it may include CHO, sP2/0, rabbit and other non-human cells.

[0145] As used herein, the term “light chain” when used in reference to an antibody may 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.

[0146] 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 a CLL-1 binding molecule, 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.

[0147] 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.

[0148] 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 may 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.

[0149] 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 may 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: 1-82), deletions, non-naturally occurring amino acids, and chemical analogs of amino acids.

[0150] 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.

[0151] Polypeptides, peptides, proteins and analogous molecules comprising a CLL-1 binding molecule, as well as molecules comprising this sequence and cells presenting such molecules, are specifically encompassed by the terms.

[0152] 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 may 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.

[0153] 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 may be, *e.g.*, MOE (Chemical Computing Group) or DNASTAR (University of Wisconsin, Madison, WI). The computer algorithm GAP may 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.

[0154] Certain alignment schemes for aligning two amino acid sequences may result in matching of only a short region of the two sequences, and this small aligned region may 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) may be adjusted if desired to result in an alignment that spans at least 50 contiguous amino acids of the target polypeptide.

[0155] 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).*

[0156] Sample: As used herein, the term “sample” encompasses any sample obtained from a biological source. The terms “biological sample” and “sample” are used interchangeably. A biological sample may, by way of non-limiting example, include skin tissue, liver tissue, kidney tissue, lung tissue, cerebrospinal fluid (CSF), blood, amniotic fluid, sera, urine, feces, epidermal sample, skin sample, cheek swab, sperm, amniotic fluid, cultured cells, bone marrow sample and/or chorionic villi. Cell cultures of any biological samples may also be used as biological samples. A biological sample may also be, e.g., a sample obtained from any organ or tissue (including a biopsy or autopsy specimen), may comprise cells (whether primary cells or cultured cells), medium conditioned by any cell, tissue or organ, tissue culture. In some embodiments, biological samples suitable for the invention are samples which have been processed to release or otherwise make available a peptide for detection as described herein. Fixed or frozen tissues also may be used.

[0157] A “therapeutically effective amount,” “effective dose,” “effective amount,” or “therapeutically effective dosage” of a therapeutic agent, (*e.g., a moiety comprising a CLL-1 binding molecule, 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 may 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.

[0158] 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, an 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.

[0159] 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.

[0160] 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).

[0161] 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.

[0162] 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.

[0163] Various aspects of the invention are described in further detail in the following subsections.

II. Antigen Binding Molecules and Polynucleotides Encoding the Same

[0164] The present disclosure is directed to antigen binding molecules, including antibodies, that specifically bind a CLL-1 binding molecule, 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. Polynucleotides encoding the antigen binding molecules are also provided, and form an aspect of the instant disclosure.

[0165] An antibody or antigen binding molecule encoded of the present invention may 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.

[0166] 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).

[0167] In some embodiments, the antigen binding molecules of the present invention specifically bind to a CLL-1 binding molecule, 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 a CLL-1 binding molecule, 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 a CLL-1 binding molecule, 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 a CLL-1 binding molecule, 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 a CLL-1 binding molecule, as well as molecules comprising this sequence and cells presenting such molecules, with a K_D of about 1×10^{-7} M, about 2×10^{-7} M, about 3×10^{-7} M, about 4×10^{-7} M, about 5×10^{-7} M, about 6×10^{-7} M, about 7×10^{-7} M, about 8×10^{-7} M, about 9×10^{-7} M, about 1×10^{-8} M, about 2×10^{-8} M, about 3×10^{-8} M, about 4×10^{-8} M, about 5×10^{-8} M, about 6×10^{-8} M, about 7×10^{-8} M, about 8×10^{-8} M, about 9×10^{-8} M, about 1×10^{-9} M, about 2×10^{-9} M, about 3×10^{-9} M, about 4×10^{-9} M, about 5×10^{-9} M, about 6×10^{-9} M, about 7×10^{-9} M, about 8×10^{-9} M, about 9×10^{-9} M, about 1×10^{-10} M, or about 5×10^{-10} M. K_D may be calculated using standard methodologies, as described herein.

[0168] In specific embodiments, an antigen binding molecule of the instant disclosure is an antibody identified herein as Clones 15-2, 63-2, 103-2, 147-1, 148-4, 160-1 and 180-2 and each comprises the heavy and light chain amino acid, coding, variable, and CDR sequences, as provided and labeled herein.

[0169] 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 Tables C and D below. 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.

Table C. CDR Table (Kabat)

Sequence	CDR1	CDR2	CDR3
KIP-10_15-2_Vk	QASQTIGSALA SEQ ID NO: 29	TASNLAS SEQ ID NO: 30	QHTFYGTSYVDA SEQ ID NO: 31
KIP-10_63-2_Vk	QASESVSRWL A SEQ ID NO: 32	SASTLAS SEQ ID NO: 33	QGGYYSGGETYHNS SEQ ID NO: 34
KIP-10_103-2_Vk	QASEDIESYLA SEQ ID NO: 35	SASTLAS SEQ ID NO: 33	QQGASSNDVEEP SEQ ID NO: 36
KIP-10_147-1_Vk	QASQSISTVLA SEQ ID NO: 37	WASTLAS SEQ ID NO: 38	AGYKSYSNDDGA SEQ ID NO: 39
KIP-10_148-4_Vk	QASQSIGSALA SEQ ID NO: 40	TASNLAS SEQ ID NO: 30	QCTYYGSSYINA SEQ ID NO: 42
KIP-10_160-1_Vk	QASESIGSSLA SEQ ID NO: 43	AASTLAS SEQ ID NO: 44	QCSYYLNTYVGNP SEQ ID NO: 45
KIP-10_180-2_Vk	QASQSISNLLA SEQ ID NO: 46	GASNLES SEQ ID NO: 47	QQGDSSSNLDNT SEQ ID NO: 48
KIP-10_15-2_Vh	VGYDMC SEQ ID NO: 49	CIDTDSSSRTWNASWA K	NDDTSGWGSKL SEQ ID NO: 51

		SEQ ID NO: 50	
KIP-10_63-2_Vh	SDYDMC SEQ ID NO: 52	CIYAGSSDNTYYATWAK SEQ ID NO: 53	DTADINFYFKL SEQ ID NO: 54
KIP-10_103-2_Vh	SYYMS SEQ ID NO: 55	IYYQSGNTDYASWAK SEQ ID NO: 56	EGYAGYVGYSYNI SEQ ID NO: 57
KIP-10_147-1_Vh	GDYYMC SEQ ID NO: 58	CIYVGSYIYSFYASWAK SEQ ID NO: 59	DPFATDSDVVSL SEQ ID NO: 60
KIP-10_148-4_Vh	GSFDVC SEQ ID NO: 61	CIVVDSSDRTWYASWAK SEQ ID NO: 62	NDDTSGWGFINL SEQ ID NO: 63
KIP-10_160-1_Vh	SNYFVC SEQ ID NO: 64	CINPGSGRTYSASWAK SEQ ID NO: 65	DRPGSDDYYMRDL SEQ ID NO: 66
KIP-10_180-2_Vh	DNYYMC SEQ ID NO: 67	CIYGGHIDTTYASWVS SEQ ID NO: 68	RTIYDDNDDYSYALHL SEQ ID NO: 69

Table D. CDR Table (Clothia)

Sequence	CDR1	CDR2	CDR3
KIP-10_15-2_Vk	QASQTIGSALA SEQ ID NO: 29	TASNLAS SEQ ID NO: 30	QHTFYGTSYVDA SEQ ID NO: 31
KIP-10_63-2_Vk	QASESVSRWLA SEQ ID NO: 32	SASTLAS SEQ ID NO: 33	QGGYYSGGETYHNS SEQ ID NO: 34
KIP-10_103-2_Vk	QASEDIESYLA SEQ ID NO: 35	SASTLAS SEQ ID NO: 33	QQGASSNDVEEP SEQ ID NO: 36
KIP-10_147-1_Vk	QASQSISTVLA SEQ ID NO: 37	WASTLAS SEQ ID NO: 38	AGYKSYSNDDGA SEQ ID NO: 39
KIP-10_148-4_Vk	QASQSIGSALA SEQ ID NO: 40	TASNLAS SEQ ID NO: 30	QCTYYGSSYINA SEQ ID NO: 42
KIP-10_160-1_Vk	QASESIGSSLA SEQ ID NO: 43	AASTLAS SEQ ID NO: 44	QCSYYLNTYVGNP SEQ ID NO: 45
KIP-10_180-2_Vk	QASQSISNLLA SEQ ID NO: 46	GASNLES SEQ ID NO: 47	QQGDSSSNLDNT SEQ ID NO: 48
KIP-10_15-2_Vh	GFSFSVGY SEQ ID NO: 76	DTDSSS SEQ ID NO: 77	NDDTSGWGSKL SEQ ID NO: 51
KIP-10_63-2_Vh	GFSFSSDY SEQ ID NO: 78	YAGSSD SEQ ID NO: 79	DTADINFYFKL SEQ ID NO: 54
KIP-10_103-2_Vh	GFSLGSY SEQ ID NO: 80	YQSG SEQ ID NO: 81	EGYAGYVGYSYNI SEQ ID NO: 57
KIP-10_147-1_Vh	GFSFSGDY SEQ ID NO: 82	YVGSYI SEQ ID NO: 75	DPFATDSDVVSL SEQ ID NO: 60
KIP-10_148-4_Vh	GFSFSGSF SEQ ID NO: 74	VVDSSD SEQ ID NO: 73	NDDTSGWGFINL SEQ ID NO: 63
KIP-10_160-1_Vh	GFSFSSNY SEQ ID NO: 72	NPGSG SEQ ID NO: 71	DRPGSDDYYMRDL SEQ ID NO: 66
KIP-10_180-2_Vh	GFIFSDNY SEQ ID NO: 41	YGGHID SEQ ID NO: 70	RTIYDDNDDYSYALHL SEQ ID NO: 69

[0170] 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.

[0171] An antigen binding molecule of the present invention may also be a fully human monoclonal antibody. Fully human monoclonal antibodies may 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.

[0172] 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).

[0173] 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.

[0174] 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 may be created in phage vectors that may be screened to select Ig fragments (Fab, Fv, sFv, or multimers thereof) that bind a CLL-1 binding molecule, 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 may be inserted into the genome of a filamentous bacteriophage, such as M13 or lambda phage (λ ImmunoZapTM(H) and λ ImmunoZapTM(L) vectors (Stratagene, La Jolla, Calif) may also be used in this approach) or a variant thereof, in frame with the sequence encoding a phage coat protein.

[0175] Briefly, mRNA is isolated from a B-cell population, and used to create heavy and light chain immunoglobulin cDNA expression libraries in the λ ImmunoZapTM(H) and λ ImmunoZapTM(L) vectors. These vectors may be screened individually or co-expressed to form Fab fragments or antibodies. Positive plaques may subsequently be converted to a non-lytic plasmid that allows high level expression of monoclonal antibody fragments from *E. coli*.

[0176] 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 may be synthesized by one of ordinary skill in the art, or may 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 may be used to amplify heavy or light chain variable regions, which may then be inserted into vectors such as λ ImmunoZapTM(H) and λ ImmunoZapTM(L) (Stratagene), respectively. These vectors may 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 may be produced using these methods.

[0177] 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 may be cloned by isolating and amplifying DNA or mRNA therefrom according to standard procedures as described herein. The antibodies produced therefrom may be sequenced and the CDRs identified and the DNA coding for the CDRs may be manipulated as described previously to generate other antibodies according to the invention.

[0178] It will be understood by one skilled in the art that some proteins, such as antibodies, may 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 may include variations in glycosylation, methionine oxidation, diketopiperazine 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).

[0179] An alternative method for production of a murine monoclonal antibody is to inject the hybridoma cells into the peritoneal cavity of a syngeneic mouse, for example, a

mouse that has been treated (*e.g.*, pristane-primed) to promote formation of ascites fluid containing the monoclonal antibody. Monoclonal antibodies may 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 may 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-idiotypic antibody.

[0180] 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 may be prepared as described herein and form an aspect of the instant disclosure.

[0181] In some embodiments, the antibody or antigen binding molecule that specifically binds to a CLL-1 binding molecule, 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.

[0182] In some embodiments, the antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, 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 Table C or D.

[0183] The instant disclosure provides antigen binding molecules that specifically bind to a CLL-1 binding molecule and subsequences thereof, 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 some embodiments, the polynucleotides of the present invention encodes an antibody or antigen binding molecule that specifically binds a CLL-1 binding molecule, 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. In certain embodiments, the antibody or antigen binding molecule binds the same or an overlapping epitope as a reference antibody.

Clone 15-2

[0184] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence VGYDMC (SEQ ID NO: 49).

[0185] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence CIDTDSSSRRTWNASWAK (SEQ ID NO: 50).

[0186] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence NDDTSGWGSKL (SEQ ID NO: 51).

[0187] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, 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 VGYDMC (SEQ ID NO: 49); and/or (b) a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence CIDTDSSSRRTWNASWAK (SEQ ID NO: 50); and/or (c) a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence NDDTSGWGSKL (SEQ ID NO: 51).

[0188] In some embodiments, the antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence comprising an amino acid sequence of SEQ ID NO: 15.

METGLRWLLLVAVLKGVCQEQLVESGGGLVKPGASLTLTCKASGFSFSVG
YDMCWVRQAPGKGLEWIACTDSSSRTWNASWAKGRFTISKPSSTTVTLQM
TSLTAADTATYFCARNDDTSGWGSKLWGPGLVTVSS (SEQ ID NO: 15)

[0189] 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.

[0190] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QASQTIGSALA (SEQ ID NO: 29).

[0191] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence TASNLAS (SEQ ID NO: 30).

[0192] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence QHTFYGTSYVDA (SEQ ID NO: 31).

[0193] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, 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 QASQTIGSALA (SEQ ID NO: 29); and/or (b) a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence TASNLAS (SEQ ID NO: 30); and/or (c) a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence QHTFYGTSYVDA (SEQ ID NO: 31).

[0194] In some embodiments, the antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells

presenting this sequence, comprises a light chain variable region sequence comprising an amino acid sequence of SEQ ID NO: 22.

MDTRAPTQLLGLLLLWLPGARCDVVMTPASVSEPVGGTVTIKCQASQTIG
SALAWYQQKPGQPPKLLIYTASNLASGVSSRFKGSRSRGTEFTLTISDLECADA
ATYYCQHTFYGTSYVDAFGGGTEVVVK (SEQ ID NO: 22)

[0195] 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: 22.

[0196] 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: 22. In some embodiments, an antigen binding molecule comprises: (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 49; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 50; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 51; (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.

[0197] 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: 22.

[0198] The nucleotide sequence encoding the heavy chain variable region of clone 15-2 comprises:

ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGTC
CAGTGTCAGGAGCAGCTGGTGGAGTCCGGGGGAGGCCTGGTCAAGCCTGG
GGCATCCCTGACACTCACCTGCAAAGCCTCTGGATTCTCCTTCAGTGTCGG
CTACGACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGA
TCGCATGCATTGATACTGATAGTAGTAGTAGGACATGGAACGCGAGCTGG
GCGAAAGGCCGATTCACCATCTCCAAACCCTCGTCGACCACGGTGACTCT
GCAAATGACCAGTCTGACAGCCGCGGACACGGCCACCTATTTCTGTGCGA
GGAATGACGATACTAGTGGCTGGGGTTCTAAGTTGTGGGGCCCAGGCACC
CTGGTCACCGTCTCCTCA (SEQ ID NO: 1)

[0199] The nucleotide sequences encoding the light chain variable region of clone 15-2 comprises:

ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCTCCCA
GGTGCCAGATGTGATGTTGTGATGACCCAGACTCCAGCCTCCGTGTCTGAACCT
GTGGGAGGCACAGTCACCATCAAGTGCCAGGCCAGTCAGACCATTGGTAGTGC
TTAGCCTGGTATCAGCAGAAACCAGGGCAGCCTCCCAAGCTCCTGATCTATAC
TGCATCCAATCTGGCATCTGGGGTCTCATCGCGGTTCAAAGGTAGTAGATCTGG
GACAGAGTTCACTCTCACCATCAGCGACCTGGAGTGTGCCGATGCTGCCACTTA
CTACTGTCAACATACTTTTTATGGTACTAGTTATGTTGATGCATTCGGCGGAGGG
ACCGAGGTGGTGGTCAAA (SEQ ID NO: 8)

[0200] In some embodiments, the antibody or antigen binding molecule comprises: (a) a heavy chain variable region 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: 15; and (b) a light chain variable region 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.

Clone 63-2

[0201] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence SDYDMC (SEQ ID NO: 52).

[0202] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence CIYAGSSDNTYYATWAK (SEQ ID NO: 53).

[0203] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence DTADINFYFKL (SEQ ID NO: 54).

[0204] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, 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 SDYDMC (SEQ ID NO: 52); and/or (b) a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence CIYAGSSDNTYYATWAK (SEQ ID NO: 53); and/or (c) a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence DTADINFYFKL (SEQ ID NO: 54).

[0205] In some embodiments, the antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence comprising an amino acid sequence of SEQ ID NO: 16.

METGLRWLLLVAVLKGVCQCCQLEESGGGLVKPGGTLTLTCKASGFSFSSDY
DMCWVRQAPGKGLEWIACIYAGSSDNTYYATWAKGRFTISKTSSTTVTLQM
TSLTAADTATYFCARDTADINFYFKLWGPGLVTVSS (SEQ ID NO: 16)

[0206] 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: 16.

[0207] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QASESVRWLA (SEQ ID NO: 32).

[0208] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence SASTLAS (SEQ ID NO: 33).

[0209] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence QGGYYSGGETYHNS (SEQ ID NO: 34).

[0210] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, 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

QASESVSRWLA (SEQ ID NO: 32); and/or (b) a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence SASTLAS (SEQ ID NO: 33); and/or (c) a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence QGGYYSGGETYHNS (SEQ ID NO: 34).

[0211] In some embodiments, the antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting this sequence, comprises a light chain variable region sequence comprising an amino acid sequence of SEQ ID NO: 23.

MDTRAPTQLLGLLLLWLPGARCAIVMTQTPASVSAAVGGTVTIKCQASESVSRW
LAWYQQKPGQPPNLLIYSASTLASGVPSRFRGSGSGTEYTLTISDLECADAATYYCQ
GGYYSGGETYHNSFGGGTEVVVK (SEQ ID NO: 23)

[0212] In various embodiments, the light chain variable region is 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to the light chain variable region sequence of SEQ ID NO: 23.

[0213] In some embodiments, an antigen binding molecule comprises (a) a VH comprising the amino acid sequence of SEQ ID NO: 16; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 23. In some embodiments, an antigen binding molecule comprises: (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 52; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 53; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 54; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 32; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 33; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 34.

[0214] 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: 16; and (b) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 23.

[0215] The nucleotide sequence encoding the heavy chain variable region of clone 63-2 is:

ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGTC
CAGTGTCAGCAGCAGTTGGAGGAGTCCGGGGGAGGCCTGGTCAAGCCTGG
AGGAACCCTGACACTCACCTGCAAAGCCTCTGGATTCTCCTTCAGTAGCGA
CTACGACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGA

TCGCATGCATTTACGCTGGTAGTAGTGACAATACTTACTACGCGACCTGGG
CGAAAGGCCGATTCACCATCTCCAAAACCTCGTCGACCACGGTGACTCTG
CAAATGACCAGTCTGACAGCCGCGGACACGGCCACCTATTTCTGTGCGAG
AGATACTGCTGATATTAATTTTTACTTTAAGTTGTGGGGCCCAGGCACCCT
AGTCACCGTCTCCTCA (SEQ ID NO: 2)

[0216] The nucleotide sequence encoding the light chain variable region of clone 63-2 is:

ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTACTGCTCTGGCTC
CCAGGTGCCAGATGTGCTGACATTGTGATGACCCAGACTCCAGCCTCCGTG
TCTGCAGCTGTGGGAGGCACAGTCACCATCAAGTGCCAGGCCAGTGAGAG
CGTTAGTCGTTGGTTAGCCTGGTATCAGCAGAAACCAGGGCAGCCTCCCA
ACCTCCTGATCTATTCTGCATCAACTCTGGCATCTGGGGTCCCATCGCGGT
TCAGAGGCAGTGGATCTGGGACAGAGTACACTCTCACCATCAGCGACCTG
GAGTGTGCCGATGCTGCCACTTACTACTGTCAAGGCGGTTATTATAGTGGT
GGTGAGACTTACCATAATAGTTTCGGCGGAGGGACCGAGGTGGTGGTCAA
A (SEQ ID NO: 9)

[0217] In some embodiments, the antibody or antigen binding molecule comprises:
(a) a heavy chain variable region 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 variable region 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: 23.

Clone 103-2

[0218] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence SYYS (SEQ ID NO: 55).

[0219] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence IYQSGNTDYASWAK (SEQ ID NO: 56).

[0220] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence EGYAGYVGYSYNI (SEQ ID NO: 57).

[0221] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, 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 SYYS (SEQ ID NO: 55); and/or (b) a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence IYQSGNTDYASWAK (SEQ ID NO: 56); and/or (c) a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence EGYAGYVGYSYNI (SEQ ID NO: 57).

[0222] In some embodiments, the antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence comprising an amino acid sequence of SEQ ID NO: 17.

METGLRWLLLVAVLKGVCQSVEESGGRLVTPGTPLTLTCTVSGFSLGSYYM
SWVRQAPGKGLEWIGIIYQSGNTDYASWAKGRFTISKTSSTTVDLKMTSLTTE
DTATYFCAREGYAGYVGYSYNIWGPGLVTVSS (SEQ ID NO: 17)

[0223] In various embodiments, the heavy chain variable region is 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to the heavy chain variable region sequence of SEQ ID NO: 17.

[0224] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QASEDIESYLA (SEQ ID NO: 35).

[0225] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence SASTLAS (SEQ ID NO: 33).

[0226] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells

presenting such molecules, comprises a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence QQGASSNDVEEP (SEQ ID NO: 36).

[0227] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, 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 QASEDIESYLA (SEQ ID NO: 35); and/or (b) a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence SASTLAS (SEQ ID NO: 33); and/or (c) a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence QQGASSNDVEEP (SEQ ID NO: 36).

[0228] In some embodiments, the antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting this sequence, comprises a light chain variable region sequence comprising an amino acid sequence of SEQ ID NO: 24.

MDTRAPTQLLGLLLLWLPGARCAYDMTQTPASVSAAVGGTVSINCQASEDIE
SYLAWYQQRPGQPPKLLIYSASTLASGVSSRFKGS GSGTQFTLTISDLECADAA
TYYCQQGASSNDVEEPFGGGTEVVVK (SEQ ID NO: 24)

[0229] 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: 24.

[0230] In some embodiments, an antigen binding molecule comprises (a) a VH comprising the amino acid sequence of SEQ ID NO: 17; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 24. In some embodiments, an antigen binding molecule comprises: (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 52; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 53; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 54; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 35; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 33; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 36.

[0231] 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: 17; and (b) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 24.

[0232] The nucleotide sequence encoding the heavy chain variable region of clone 103-2 comprises:

ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGTC
 CAGTGTCAGTCGGTGGAGGAGTCCGGGGGGTCGCCTGGTCACGCCTGGGAC
 ACCCCTGACACTCACCTGCACAGTCTCTGGATTCTCCCTCGGTAGCTACTA
 CATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGGCTGGAATGGATCGGAA
 TCATTTATCAGAGTGGTAACACGGACTACGCGAGCTGGGCGAAAGGCCGA
 TTCACCATCTCCAAAACCTCGTCGACCACGGTGGATCTGAAAATGACCAGT
 CTGACAACCGAGGACACGGCCACCTATTTCTGTGCCAGAGAGGGGGTATGC
 TGGTTATGTTGGTTATAGTTATAACATCTGGGGGCCAGGCACCCTGGTCAC
 CGTCTCCTCA (SEQ ID NO: 3)

[0233] The nucleotide sequence encoding the light chain variable region of clone 103-2 comprises:

ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCTCCC
 AGGTGCCAGATGTGCCTATGATATGACCCAGACTCCAGCCTCCGTGTCTGC
 AGCTGTGGGAGGCACAGTCAGCATCAATTGCCAGGCCAGTGAGGACATTG
 AAAGCTATTTAGCCTGGTATCAGCAGAGACCAGGGCAGCCTCCCAAGCTC
 CTGATCTATTCTGCATCCACTCTGGCATCTGGGGTCTCATCGCGGTTCAAA
 GGCAGTGGATCTGGGACGCAGTTCACTCTCACCATCAGCGACCTGGAGTG
 TGCCGATGCTGCCACTTACTACTGTCAACAGGGCGCTAGTAGTAATGATGT
 TGAGGAGCCTTTCGGCGGAGGGACCGAGGTGGTGGTCAAA (SEQ ID NO:
 10)

[0234] In some embodiments, the antibody or antigen binding molecule comprises:
 (a) a heavy chain variable region 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: 17; and (b) a light chain variable region comprising an amino acid sequence that is 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to the amino acid sequence of SEQ ID NO: 24.

Clone 147-1

[0235] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells

presenting such molecules, comprises a VH CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence GDYYMC (SEQ ID NO: 58).

[0236] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence CIYVGSIYISFYASWAK (SEQ ID NO: 59).

[0237] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence DPFATDSDVVSL (SEQ ID NO: 60).

[0238] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, 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 GDYYMC (SEQ ID NO: 58); and/or (b) a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence CIYVGSIYISFYASWAK (SEQ ID NO: 59); and/or (c) a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence DPFATDSDVVSL (SEQ ID NO: 60).

[0239] In some embodiments, the antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence comprising an amino acid sequence of SEQ ID NO: 18.

METGLRWLLLVAVLKGVCQEQLEESGGDLVKPEGSLTLTCTASGFSFSGDY
YMCWVRQAPGKGLEWIACIYVGSIYISFYASWAKGRFTISRTSSTTVTLQMT
SLTAADTATYFCARDPFATDSDVVSLWGPGLVTVSS (SEQ ID NO: 18)

[0240] 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: 18.

[0241] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QASQSISTVLA (SEQ ID NO: 37).

[0242] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence WASTLAS (SEQ ID NO: 38).

[0243] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence AGYKSYSNDDGA (SEQ ID NO: 39).

[0244] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, 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 QASQSISTVLA (SEQ ID NO: 37); and/or (b) a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence WASTLAS (SEQ ID NO: 38); and/or (c) a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence AGYKSYSNDDGA (SEQ ID NO: 39).

[0245] In some embodiments, the antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting this sequence, comprises a light chain variable region sequence comprising an amino acid sequence of SEQ ID NO: 25.

MDTRAPTQLLGLLLLWLPGARCAVVLTPASVSAAVGGTVTINCQASQSIST
VLA WYQQKPGQRPKLLIYWASTLASGVPSRFGSGSGTQFTLTISGVECDDA
ATYYCAGYKSYSNDDGA FGGGTEVVVK (SEQ ID NO: 25)

[0246] 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: 25.

[0247] In some embodiments, an antigen binding molecule comprises (a) a VH comprising the amino acid sequence of SEQ ID NO: 18; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 25. In some embodiments, an antigen binding molecule comprises: (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 55; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 56; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 57; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 37; (e) a VL CDR2 region comprising

the amino acid sequence of SEQ ID NO: 38; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 39.

[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: 18; and (b) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 25.

[0249] The nucleotide sequence encoding the heavy chain variable region of clone 147-1 comprises:

ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGTC
CAGTGTCAGGAGCAGCTGGAGGAGTCCGGGGGAGACCTGGTCAAGCCTGA
GGGATCCCTGACACTCACCTGCACAGCCTCTGGATTCTCCTTCAGTGGCGA
CTACTACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGA
TCGCATGCATTTATGTTGGTAGTTATATTTACAGTTTCTACGCGAGCTGGG
CGAAAGGCCGATTCACCATCTCCAGAACCTCGTCGACCACGGTGACTCTG
CAAATGACCAGTCTGACAGCCGCGGACACGGCCACCTATTTCTGTGCGAG
AGATCCATTTGCTACTGATAGTGATGTTGTCAGCTTGTGGGGCCCAGGCAC
CCTGGTCACCGTCTCCTCA (SEQ ID NO: 4)

[0250] The nucleotide sequence encoding the light chain variable region of clone 147-1 comprises:

ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCTC
CCAGGTGCCAGATGTGCCGTCGTGCTGACCCAGACTCCAGCCTCCGTGTCT
GCAGCTGTGGGAGGCACAGTCACCATCAATTGCCAGGCCAGTCAGAGCAT
TAGTACTGTATTAGCCTGGTATCAGCAGAAACCAGGGCAGCGTCCCAAGC
TCCTGATCTACTGGGCATCCACTCTGGCATCTGGGGTCCCATCGCGGTTCA
AAGGCAGTGGATCTGGGACACAGTTCACTCTCACCATCAGTGGCGTGGAG
TGTGACGATGCTGCCACTTACTACTGTGCAGGCTATAAAAGTTATAGTAAT
GATGATGGTGCTTTTCGGCGGAGGGACCGAGGTGGTGGTCAAA (SEQ ID NO:
11)

[0251] In some embodiments, the antibody or antigen binding molecule comprises: (a) a heavy chain variable region comprising an amino acid sequence that is 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to the amino acid sequence of SEQ ID NO: 18; and (b) a light chain variable region 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: 25.

Clone 148-4

[0252] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence GSFDVC (SEQ ID NO: 61).

[0253] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence CIVVDSSDRTWYASWAK (SEQ ID NO: 62).

[0254] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence NDDTSGWGFNL (SEQ ID NO: 63).

[0255] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, 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 GSFDVC (SEQ ID NO: 61); and/or (b) a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence CIVVDSSDRTWYASWAK (SEQ ID NO: 62); and/or (c) a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence NDDTSGWGFNL (SEQ ID NO: 63).

[0256] In some embodiments, the antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence comprising an amino acid sequence of SEQ ID NO: 19.

METGLRWLLLVAVLKGVCQEQLEESGGDLVKPEGSLTLTCTASGFSFSGSF
DVCWVRQAPGKGLEWIA CIVVDSSDRTWYASWAKGRFTISKPSSTTVTLQMT
SLTAADTATYFCARNDDTSGWGFNLWGPGTLVTVSS (SEQ ID NO: 19)

[0257] 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: 19.

[0258] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QASQSIGSALA (SEQ ID NO: 40).

[0259] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence TASNLAS (SEQ ID NO: 30).

[0260] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence QCTYYGSSYINA (SEQ ID NO: 42).

[0261] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, 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 QASQSIGSALA (SEQ ID NO: 40); and/or (b) a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence TASNLAS (SEQ ID NO: 30); and/or (c) a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence QCTYYGSSYINA (SEQ ID NO: 42).

[0262] In some embodiments, the antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting this sequence, comprises a light chain variable region sequence comprising an amino acid sequence of SEQ ID NO: 26.

MDTRAPTQLLGLLLLWLPGARCDVTMTQTPASVSEPVGGTVTIKCQASQSIGS
ALAWYQQKPGQPPKLLIWTASNLASGVSSRFKGSRSRGTDFTLTISDLECADAA
TYYCQCTYYGSSYINAFGGGTEVVVK (SEQ ID NO: 26)

[0263] 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: 26.

[0264] In some embodiments, an antigen binding molecule comprises (a) a VH comprising the amino acid sequence of SEQ ID NO: 19; and (b) a VL comprising the amino acid sequence of SEQ ID NO: 26. In some embodiments, an antigen binding molecule comprises: (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 61; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 62; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 63; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 40; (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: 42.

[0265] 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: 19; and (b) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 26.

[0266] The nucleotide sequence encoding the heavy chain variable region of clone 148-4 comprises:

ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGTC
CAGTGTCAGGAGCAGCTGGAGGAGTCCGGGGGAGACCTGGTCAAGCCTGA
GGGATCCCTGACACTCACCTGCACAGCCTCTGGATTCTCCTTCAGTGGCAG
CTTTGACGTGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGA
TCGCGTGCATTGTTGTTGATAGTAGTGATAGGACATGGTACGCGAGCTGG
GCGAAAGGCCGATTCACCATCTCCAAACCCTCGTCGACTACGGTGACTCTA
CAAATGACCAGTCTGACAGCCGCGGACACGGCCACCTATTTCTGTGCGAG
GAATGACGATACTAGTGGCTGGGGTTTTTAATTTGTGGGGCCCAGGCACCCT
GGTCACCGTCTCCTCA (SEQ ID NO: 5)

[0267] The nucleotide sequence encoding the light chain variable region of clone 148-4 comprises:

ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCTC
CCAGGTGCCAGATGTGATGTTACGATGACCCAGACTCCAGCCTCCGTGTCT
GAACCTGTGGGAGGCACAGTCACCATCAAGTGCCAGGCCAGTCAGAGCAT
TGGTAGTGCTTTAGCCTGGTATCAGCAGAAACCAGGGCAGCCTCCCAAGC
TCCTGATCTGGACTGCATCCAATCTGGCATCTGGGGTCTCATCGCGGTTCA

AAGGCAGTAGATCTGGGACAGATTTCCTCTCACCATCAGCGACCTGGAG
 TGTGCCGATGCTGCCACTTACTACTGTCAGTGTACTTATTATGGTAGTAGT
 TATATTAATGCATTCGGCGGAGGGACCGAGGTGGTGGTCAAA (SEQ ID NO:
 12)

[0268] In some embodiments, the antibody or antigen binding molecule comprises:
 (a) a heavy chain variable region 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; and (b) a light chain variable region 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: 26.

Clone 160-1

[0269] In some embodiments, an antigen binding molecule or antibody that
 specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells
 presenting such molecules, comprises a VH CDR1 comprising, consisting of, or consisting
 essentially of the amino acid sequence SNYFVC (SEQ ID NO: 64).

[0270] In some embodiments, an antigen binding molecule or antibody that
 specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells
 presenting such molecules, comprises a VH CDR2 comprising, consisting of, or consisting
 essentially of the amino acid sequence CINPGSGRTYSASWAK (SEQ ID NO: 65).

[0271] In some embodiments, an antigen binding molecule or antibody that
 specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells
 presenting such molecules, comprises a VH CDR3 comprising, consisting of, or consisting
 essentially of the amino acid sequence DRPGSDDYYMRDL (SEQ ID NO: 66).

[0272] In some embodiments, an antigen binding molecule or antibody that
 specifically binds to a CLL-1 binding molecule, 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 SNYFVC
 (SEQ ID NO: 64); and/or (b) a VH CDR2 comprising, consisting of, or consisting essentially
 of the amino acid sequence CINPGSGRTYSASWAK (SEQ ID NO: 65); and/or (c) a VH
 CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence
 DRPGSDDYYMRDL (SEQ ID NO: 66).

[0273] In some embodiments, the antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence comprising an amino acid sequence of SEQ ID NO: 20.

METGLRWLLLVAVLKGVCQSLEESGGDLVKPGASLTCTASGFSFSSNYF
VCWVRQAPGKGLEWVGCINPGSGRTYSASWAKGRFTISKSSSTTVTLQMTSL
TAADTATYFCARDRPGSDDYYMRDLWGPGTLVTVSS (SEQ ID NO: 20)

[0274] 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: 20.

[0275] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QASESIGSSLA (SEQ ID NO: 43).

[0276] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, 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: 44).

[0277] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence QCSYYLNTYVGNP (SEQ ID NO: 45).

[0278] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, 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 QASESIGSSLA (SEQ ID NO: 43); and/or (b) a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence AASTLAS (SEQ ID NO: 44); and/or (c) a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence QCSYYLNTYVGNP (SEQ ID NO: 45).

[0279] In some embodiments, the antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells

presenting this sequence, comprises a light chain variable region sequence comprising an amino acid sequence of SEQ ID NO: 27.

MDTRAPTQLLGLLLLWLPGVICDPVMTQTPASVSEPVGGTVTINCQASESIGSS
LAWYQQKPGQPPKLLIYAASLASGVSSRFKGS GSGTQFTLTISDLECADAAT
YYCQCSYYLNTYVGNPFGGGTEVVVK (SEQ ID NO: 27)

[0280] 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.

[0281] In some embodiments, an antigen binding molecule comprises (a) a VH comprising the amino acid sequence of SEQ ID NO: 20; 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: 64; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 65; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 66; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 43; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 44; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 45.

[0282] 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: 20; and (b) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 27.

[0283] The nucleotide sequence encoding the heavy chain variable region of clone 160-1 comprises:

ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGTC
CAGTGTCAGTCGTTGGAGGAGTCCGGGGGAGACCTGGTCAAGCCTGGGGC
ATCCCTGACACTCACCTGCACAGCCTCTGGATTCTCCTTCAGTAGCAACTA
CTTCGTGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCG
GATGTATTAATCCTGGTAGTGGTCGCACTTACTCCGCGAGCTGGGCGAAA
GGCCGATTCACCATCTCCAAGTCCTCGTCGACCACGGTGACTCTGCAAATG
ACCAGTCTGACAGCCGCGGACACGGCCACCTATTTCTGTGCGAGAGATCG
GCCTGGTAGTGATGATTATTATATGCGTGACTTGTGGGGCCCAGGCACCCT
GGTCACCGTCTCCTCA (SEQ ID NO: 6)

[0284] The nucleotide sequence encoding the light chain variable region of clone 160-1 comprises:

[0285] ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTC
TGGCTCCCAGGTGTCATATGTGACCCTGTGATGACCCAGACTCCAGCCTCCGTG
TCTGAACCTGTGGGAGGACAGTCACCATCAATTGCCAGGCCAGTGAGAGCATT
GGTAGTAGCTTAGCCTGGTATCAGCAGAAACCAGGGCAGCCTCCCAAGCTCCTG
ATCTATGCTGCATCCACTCTGGCATCTGGGGTCTCATCGCGGTTCAAAGGCAGT
GGATCTGGGACACAGTTCACTCTCACCATCAGCGACCTGGAGTGTGCCGATGCT
GCCACTTACTACTGTCAATGTAGTTATTATCTTAATACTTATGTTGGTAATCCTT
TCGGCGGAGGGACCGAGGTGGTGGTCAAA (SEQ ID NO: 13)

[0286] In some embodiments, the antibody or antigen binding molecule comprises: (a) a heavy chain variable region 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: 20; and (b) a light chain variable region 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: 27.

Clone 180-2

[0287] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence DNYVMC (SEQ ID NO: 67).

[0288] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence CIYGGHIDTTYASWVS (SEQ ID NO: 68).

[0289] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence RTIYDDNDDYSYALHL (SEQ ID NO: 69).

[0290] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, 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 DNYYMC (SEQ ID NO: 67); and/or (b) a VH CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence CIYGGHIDTTYASWVS (SEQ ID NO: 68); and/or (c) a VH CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence RTIYDDNDDYSYALHL (SEQ ID NO: 69).

[0291] In some embodiments, the antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting this sequence, comprises a heavy chain variable region sequence comprising an amino acid sequence of SEQ ID NO: 21.

METGLRWLLLVAVLKGVCQCSLEESGGGLVQPGGSLKLSCKASGFIFSDNYY
MCWVRQAPGKGLELIACIYGGHIDTTYASWVSGRFTSSKTSSTTVTLQLTSL
TAADTATYFCARRTIYDDNDDYSYALHLWPGTLVTVSS (SEQ ID NO: 21)

[0292] 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.

[0293] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR1 comprising, consisting of, or consisting essentially of the amino acid sequence QASQSIENLLA (SEQ ID NO: 46).

[0294] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence GASNLES (SEQ ID NO: 47).

[0295] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting such molecules, comprises a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence QQGDSSSNLDNT (SEQ ID NO: 48).

[0296] In some embodiments, an antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, 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

QASQSISNLLA (SEQ ID NO: 46); and/or (b) a VL CDR2 comprising, consisting of, or consisting essentially of the amino acid sequence GASNLES (SEQ ID NO: 47); and/or (c) a VL CDR3 comprising, consisting of, or consisting essentially of the amino acid sequence QQGDSSSNLDNT (SEQ ID NO: 48).

[0297] In some embodiments, the antigen binding molecule or antibody that specifically binds to a CLL-1 binding molecule, molecules comprising this sequence and cells presenting this sequence, comprises a light chain variable region sequence comprising an amino acid sequence of SEQ ID NO: 28.

MDTRAPTQLLGLLLLWLPGARCALVMTQTPSSVSEPVGGTVTINCQASQSISN
LLAWYQQKPGQPPKLLIYGASNLESGVPSRFRKGSGSGTEYTLTISGVECADAA
TYYCQQGDSSSNLDNTFGGGTEVVVK (SEQ ID NO: 28)

[0298] 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: 28.

[0299] 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: 28. In some embodiments, an antigen binding molecule comprises: (a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 67; (b) a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 68; (c) a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 69; (d) a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 46; (e) a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 47; and (f) a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 48.

[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: 21; and (b) a light chain variable region comprising the amino acid sequence of SEQ ID NO: 28.

[0301] The nucleotide sequence encoding the heavy chain variable region of clone 180-2 comprises:

ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGCTGTGCTCAAAGGTGTC
CAGTGTCAGTCGTTGGAGGAGTCCGGGGGAGGCCTGGTCCAGCCTGGGGG
ATCCCTGAAACTCTCCTGCAAAGCCTCCGGATTCATCTTCAGTGACAACTA
CTACATGTGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTTGATCG

CATGCATTTATGGTGGTCATATTGACACCACTTACTACGCGAGCTGGGTGA
 GTGGCCGATTCACCAGCTCCAAAACCTCGTCGACCACGGTGACTCTGCAA
 CTGACCAGTCTGACAGCCGCGGACACGGCCACCTATTTCTGTGCGCGACG
 GACCATTTACGATGACAATGATGATTACTCATATGCCTTGCACTTGTGGGG
 CCCAGGCACCCTGGTCACCGTCTCCTCA (SEQ ID NO: 7)

[0302] The nucleotide sequence encoding the light chain variable region of clone 180-2 comprises:

ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGCTCCTGCTGCTCTGGCTC
 CCAGGTGCCAGATGTGCCCTTGTGATGACCCAGACTCCATCCTCCGTGTCT
 GAACCTGTGGGAGGCACAGTCACCATCAATTGCCAGGCCAGTCAGAGCAT
 TAGCAACCTCTTAGCCTGGTATCAGCAGAAACCAGGGCAGCCTCCCAAGC
 TCCTGATCTATGGTGCATCCAATCTGGAATCTGGGGTCCCATCGCGCTTCA
 AAGGCAGTGGATCTGGGACAGAGTACACTCTCACCATCAGCGGCGTGGAG
 TGTGCCGATGCTGCCACTTACTACTGTCAACAGGGTGATAGTAGTAGTAAT
 CTTGATAATACTTTCGGCGGAGGGACCGAGGTGGTGGTCAA (SEQ ID NO:
 14)

[0303] In some embodiments, the antibody or antigen binding molecule comprises:
 (a) a heavy chain variable region 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: 21; and (b) a light chain variable region 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.

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 a CLL-1 binding molecule, 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: 15-21.

[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: 22-28.

[0307] In some embodiments, the polynucleotide comprises a heavy chain variable region coding sequence selected from the group consisting of SEQ ID NO: 1-7. In embodiments, the polynucleotide comprises a light chain coding sequence selected from the group consisting of SEQ ID NO: 8-14.

[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 disclosed polynucleotide sequences thus form an aspect of the instant disclosure.

IV. Vectors, Cells, and Pharmaceutical Compositions

[0309] In some 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 a CLL-1 binding molecule and fragments thereof, molecules comprising this sequence and cells presenting this sequence, as described herein.

[0310] Any vector known in the art may 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 a CLL-1 binding molecule, molecules comprising this sequence and cells presenting this sequence, as disclosed herein.

[0312] Any cell may 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 may 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, *Enterobacterales* 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 may 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 a CLL-1 binding molecule and fragments thereof, 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 a CLL-1 binding molecule, 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 a CLL-1 binding molecule and fragments thereof, 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 a CLL-1 binding molecule, 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 may 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 may be employed. Such T cells may come from any source known in the art. For example, T cells may be differentiated *in vitro* from a hematopoietic stem cell population, or T cells may be obtained from a subject. T cells may 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 may be derived from one or more

T cell lines available in the art. T cells may 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 a CLL-1 binding molecule, 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 some embodiments of the disclosed methods, an antigen binding molecule comprises a heavy chain CDR3 comprising one of SEQ ID NOs: 51, 54, 57, 60, 63, 66, and 69, or a light chain CDR3 comprising one of SEQ ID Nos: 31, 34, 36, 39, 42, 45, and 48, or both the heavy and light chain CDR3s. In some embodiments, the antigen binding molecule comprises a heavy chain CDR1 comprising an amino acid sequence comprising one of SEQ ID NOs: 49, 52, 55, 58, 61, 64, and 67, or a heavy chain CDR2 comprising the amino acid sequence of one of SEQ ID NOs: 50, 53, 56, 59, 62, 65, and 68, or a light chain CDR1 comprising the amino acid sequence of one of SEQ ID NOs: 29, 32, 35, 37, 40, 43, and 46 or a light chain CDR2 comprising the amino acid sequence of one of SEQ ID NOs: 30, 33, 38, 44, and 47. 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 Table C or D.

[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: 1-7 or 15-21. 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 Table C or D. Moreover, in embodiments of the disclosed methods, an antigen binding molecule may 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: 15-21.

[0320] In various embodiments of the disclosed methods, an antigen binding molecule comprises a light chain (LC), and the LC may comprise a heavy chain variable region (VL) sequence comprising one of SEQ ID NOs: 8-14 or 22-28. 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 Table C or D. Moreover, in embodiments of the disclosed methods, an antigen binding molecule may 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: 18-28).

[0321] In view of the above description of antigen binding molecules that may 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 a CLL-1 binding molecule, is provided.

[0323] In specific embodiments, the dose comprises 0.5×10^6 cells per kilogram of the subject, 1.0×10^6 cells per kilogram of the subject, 2.0×10^6 cells per kilogram of the subject, 3.0×10^6 cells per kilogram of the subject, 4.0×10^6 cells per kilogram of the subject, or 5.0×10^6 cells per kilogram of the subject, although the method may be employed using any dose. 1.0×10^6 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 may 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 a CLL-1 binding molecule, is provided. In the disclosed method, the number of cells may 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 may also be employed.

[0326] The cells of the method may 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 may be obtained as described herein and by methods known in the art. Any type of cell may be employed in the method, and the cell may 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 may be autologous, allogeneic, or heterologous. In additional embodiments, the cells are T cells presenting a CAR. The T cells may be CD4⁺ T cells or CD8⁺ T cells. When a T cell is employed in the disclosed methods, the T cell may be an *in vivo* T cell or an *in vitro* T cell. Moreover, the cells may 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 may also be employed in obtaining T cells.

[0327] The therapeutic molecule expressed by the cell may comprise any molecule known or suspected to provide a therapeutic benefit to a subject to which is it administered. Thus, a therapeutic molecule may be a peptide or polypeptide of any structure or design. Preferably the therapeutic molecule component is expressed or disposed, at least in part, extracellularly, *i.e.*, to a degree that it may 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 may 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, CD11a/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, BAFR, 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, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, 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 a CLL-1 binding molecule is provided. The aliquot may 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 a CLL-1 binding molecule further comprising a detectable label is provided. The antigen binding molecule is preferably an antigen binding molecule disclosed herein, *e.g.*, sequence listing or the instant disclosure. Any detectable label may be employed in the method, as described herein, and suitable labels may 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 ³H, ¹¹C, ¹⁴C, ¹⁵N, ¹⁸F, ³⁵S, ⁶⁴CU, ⁹⁰Y, ⁹⁹Tc, ¹¹¹In, ¹²⁴I, ¹²⁵I, ¹³¹I), 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 may be employed in the disclosed method.

[0331] The label may 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 a CLL-1 binding molecule (or fragment thereof) may be employed. Multiple examples of suitable antigen binding molecules are provided herein, *e.g.*, those having one or more of the CDRs shown in Table C or D.

[0332] The antigen binding molecule may be disposed on any surface, or no surface at all. For example, the antigen binding molecule may be present in a buffer and the buffer-antigen binding molecule may be contacted with the sample. Alternatively, the antigen binding molecule may 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 well

plate, a bag such as a cell culture bag, etc. The surface may 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 a CLL-1 binding molecule. 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 of in the aliquot is then determined. This calculation may be performed by comparing the number of cells bearing the detectable label to those that do not, and may be represented as percentage. The number of cells in binding complexes may 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 may be employed when a fluorescent label is selected; when an isotope label is selected mass spectrometry, NMR or other technique may be employed; magnetic-based cell sorting may be employed when a magnetic label is chosen; microscopy may 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 may be easily determined.

[0335] Continuing, the concentration of cells in the initial sample expressing a molecule comprising a CLL-1 binding molecule 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 may 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 may 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 may be used as a measure of the level of efficiency of the transfection. The disclosed method may 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 a CLL-1 binding molecule is provided.

[0342] In on embodiment, a sample comprising cells known or suspected to be expressing a molecule comprising the amino acid sequence of a CLL-1 binding molecule is provided.

[0343] The cell may be of any type, and may be human or non-human (*e.g.*, mouse, rat, rabbit, hamster, etc). In preferred embodiment, the cell is an immune cell. An immune cell of the method may 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 may be obtained as described herein and by methods known in the art. Any type of immune cell may be employed in this embodiment of the disclosed method, and the cell may 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 may be autologous, allogeneic, or heterologous. In additional embodiments, the cells are T cells presenting a CAR. The T cells may be CD4⁺ T cells or CD8⁺ T cells. When a T cell is employed in the disclosed methods, the T cell may be an *in vivo* T cell or an *in vitro* T cell. Moreover, the cells may 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 a CLL-1 binding molecule is a CAR. When the molecule is a CAR it may 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, CD11a/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, BAFR, 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, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, 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, Ly108), 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 a CLL-1 binding molecule 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 sequence listing or the instant section of the disclosure. Any antigen binding molecule that specifically binds a CLL-1 binding molecule may 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 Table C or D.

[0346] Any detectable label may be employed in the method, as described herein, and suitable labels may 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, Cascade 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 ³H, ¹¹C, ¹⁴C, ¹⁵N, ¹⁸F, ³⁵S, ⁶⁴CU, ⁹⁰Y, ⁹⁹Tc, ¹¹¹In, ¹²⁴I, ¹²⁵I, ¹³¹I), 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 may 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 may 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 a CLL-1 binding molecule (or fragment thereof) may be employed, such as those disclosed herein, *e.g.*, those having one or more of the CDRs shown in Table C or D.

[0348] The antigen binding molecule may be disposed on any surface, or no surface at all. For example, the antigen binding molecule may be present in a buffer and the buffer-antigen binding molecule may be contacted with the sample. Alternatively, the antigen binding molecule may 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 well plate, a bag such as a cell culture bag, etc. The surface may 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 may be employed when a fluorescent label is selected; when an isotope label is selected mass spectrometry, NMR or other technique may be employed; magnetic-based cell sorting may be employed when a magnetic label is chosen; microscopy may also be employed. The output of these detection methods may be in the form of a number of cells or the output may be of a form that allows the calculation of the number of cells based on the output.

Vc. Method of Isolating a Cell

[0351] It is of tremendous value to have the ability to separate different populations of cells, and particularly cells comprising biologically-relevant molecules, from one another.

Using the antigen binding molecules provided herein, such separation may 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 cell comprising a CLL-1 binding molecule is provided.

[0352] In some embodiments, the method comprises providing a sample known or suspected to comprise a molecule comprising a CLL-1 binding molecule.

[0353] In specific embodiments, the molecule comprising a CLL-1 binding molecule is a CAR. When the molecule is a CAR it may 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, CD11a/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, CD28, ICAM-1, GITR, BAFR, 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, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, 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, Ly108), 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 a CLL-1 binding molecule and optionally comprises a detectable label is provided. When it is decided to employ a detectable label, any detectable label may be employed in the method, as described herein, and suitable labels may 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, Cascade 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 ³H, ¹¹C, ¹⁴C, ¹⁵N, ¹⁸F, ³⁵S, ⁶⁴CU, ⁹⁰Y, ⁹⁹Tc, ¹¹¹In, ¹²⁴I, ¹²⁵I, ¹³¹I). 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. may also be employed. Strategies for the labeling of proteins are well known in the art and may 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 may 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-CLL-1 scFv (or fragment thereof) may be employed, such as those disclosed herein, *e.g.*, those having one or more of the CDRs shown in Table C or D.

[0356] The antigen binding molecule may be disposed on any surface, or no surface at all. For example, the antigen binding molecule may be present in a buffer and the buffer-antigen binding molecule may be contacted with the sample. Alternatively, the antigen binding molecule may 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 well plate, a bag such as a cell culture bag, etc. The surface may 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 may be disposed on surfaces as described herein, formed binding complexes may 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 a CLL-1 binding molecule (or one or more molecules comprising a CLL-1 binding molecule bound to an antigen binding molecule) may have formed. Unbound molecules comprising a CLL-1 binding molecule 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 may 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 may be used.

[0360] The solution used to induce the formation of binding complexes may be used, for example, as a wash solution to remove unbound components. Any suitable buffer or solution that does not disrupt formed binding complexes may 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 a CLL-1 binding molecule, and (b) an antigen binding molecule. The separation may be achieved using standard methodologies known to those of skill in the art. For example, a solution of suitable pH and composition may 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 may be employed to achieve the separation. Other solutions that may 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 a CLL-1 binding molecule is of primary interest it may be collected; alternatively, if the antigen binding molecule is of primary interest it may 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 a CLL-1 binding molecule, as provided herein. In other cases, simply knowing whether a molecule comprising a CLL-1 binding molecule 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. Thus, the qualitative determination of the presence or absence of a molecule comprising a CLL-1 binding molecule of the instant disclosure may be useful in multiple applications. In view thereof, a method of determining the presence or absence of a molecule comprising a CLL-1 binding molecule in a sample is provided.

[0364] In some embodiments, the method comprises providing a sample known or suspected to comprise a molecule comprising a CLL-1 binding molecule.

[0365] In some embodiments, the molecule comprising a CLL-1 binding molecule is a CAR. When the molecule is a CAR it may 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, CD11a/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, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, 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, Ly108), 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 a CLL-1 binding molecule is provided. Suitable labels may 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, Cascade 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 ³H, ¹¹C, ¹⁴C, ¹⁵N, ¹⁸F, ³⁵S, ⁶⁴CU, ⁹⁰Y, ⁹⁹Tc, ¹¹¹In, ¹²⁴I, ¹²⁵I, ¹³¹I), 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 may 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 may 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 a CLL-1 binding molecule or fragment thereof) may be employed, such as those disclosed herein, *e.g.*, those having one or more of the CDRs shown in Table C or D.

[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 a CLL-1 binding molecule (which may be presented on a cell) present in the sample and the antigen binding molecule. The antigen binding molecule may be disposed on any surface or no surface at all. For example, the antigen binding molecule may be present in a buffer and the buffer-antigen binding molecule may be contacted with the sample. Alternatively, the antigen binding molecule may 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 well plate, a bag such as a cell culture bag, etc. The surface may 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 may be disposed on surfaces as described herein, formed binding complexes may 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 a CLL-1 binding molecule (or one or more molecules comprising a CLL-1 binding molecule bound to an antigen binding molecule) may have formed. Unbound molecules comprising a CLL-1 binding molecule 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 may 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 may be used.

[0372] The solution used to induce the formation of binding complexes may be used, for example, as a wash solution to remove unbound components. Any suitable buffer or solution that does not disrupt formed binding complexes may 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 a CLL-1 binding molecule and an antigen binding molecule—is detected. The specific method employed to detect the presence or absence of a binding complex will be dependent on the nature of the label selected. For example, FACS may be employed when a fluorescent label is selected; when an isotope label is selected mass spectrometry, NMR or other technique may be employed; magnetic-based cell sorting may be employed when a magnetic label is chosen; microscopy may 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 a CLL-1 binding molecule.

[0374] As is the case with all of the disclosed methods, the molecule comprising a CLL-1 binding molecule may be disposed in any environment. In preferred embodiments, the molecule comprising a CLL-1 binding molecule is expressed on the surface of a cell. In this embodiment, the cell may be of any type, and may be human or non-human (*e.g.*, mouse, rat, rabbit, hamster, etc). In preferred embodiment, the cell is an immune cell. An immune cell of the method may 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 may be obtained as described herein and by methods known in the art. Any type of immune cell may be employed in this embodiment of the disclosed method, and the cell may 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 may be autologous, allogeneic,

or heterologous. In additional embodiments, the cells are T cells presenting a CAR. The T cells may be CD4⁺ T cells or CD8⁺ T cells. When a T cell is employed in the disclosed methods, the T cell may be an *in vivo* T cell or an *in vitro* T cell.

[0375] In additional embodiment, the cell may 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 may be true for molecules secreted from a cell; such molecules are often present in low quantities (but may still be detected using the methods provided herein, if the molecule comprises a CLL-1 binding molecule. One solution to the problem of low expression levels is to increase the concentration of the molecule of interest, which may be free in solution, or expressed on the surface of a cell. The concentration of intracellularly-expressed molecules of interest may 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 a CLL-1 binding molecule is provided.

[0377] In some embodiments, the method comprises providing a sample comprising cells known or suspected to present a molecule comprising a CLL-1 binding molecule.

[0378] In specific embodiments, the molecule comprising the sequence a CLL-1 binding molecule is a CAR. When the molecule is a CAR it may 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, CD11a/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, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, 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 a CLL-1 binding molecule, and optionally comprises a detectable label, is provided. When it is decided to employ a detectable label, any detectable label may be employed in the method, as described herein, and suitable labels may 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, Cascade 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 ³H, ¹¹C, ¹⁴C, ¹⁵N, ¹⁸F, ³⁵S, ⁶⁴CU, ⁹⁰Y, ⁹⁹Tc, ¹¹¹In, ¹²⁴I, ¹²⁵I, ¹³¹I), 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 (Clontech 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 may 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 may 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 a CLL-1 binding molecule (or fragment thereof) may be employed, such as those disclosed herein, e.g., those having one or more of the CDRs shown in Table C or D.

[0381] The antigen binding molecule may be disposed on any surface, or no surface at all. For example, the antigen binding molecule may be present in a buffer and the buffer-antigen binding molecule may be contacted with the sample. Alternatively, the antigen binding molecule may 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 well plate, a bag such as a cell culture bag, etc. The surface may itself be disposed in another structure, such as a column.

[0382] A cell presenting a molecule comprising a CLL-1 binding molecule may be of any type, and may be human or non-human (e.g., mouse, rat, rabbit, hamster, etc). In preferred embodiment, the cell is an immune cell. An immune cell of the method may 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 may be obtained as described herein and by methods known in the art. Any type of immune cell may be employed in this embodiment of the disclosed method, and the cell may 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 may be autologous, allogeneic, or heterologous. In additional embodiments, the cells are T cells presenting a CAR. The T cells may be CD4⁺ T cells or CD8⁺ T cells. When a T cell is employed in the disclosed methods, the T cell may be an *in vivo* T cell or an *in vitro* T cell. Moreover, the cells may 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 a CLL-1 binding molecule 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 may be disposed on surfaces as described herein, formed binding complexes may 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 a CLL-1 binding molecule (or one or more molecules comprising a CLL-1 binding molecule bound to an antigen binding molecule) may have formed. Unbound molecules comprising a CLL-1 binding molecule 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 may 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 may be used.

[0386] The solution used to induce the formation of binding complexes may be used, for example, as a wash solution to remove unbound components. Any suitable buffer or solution that does not disrupt formed binding complexes may 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 a CLL-1 binding molecule will be present. If a detectable label was employed, the concentration of the cells may be easily determined, consistent with the nature of the label. Cells not expressing the molecule comprising a CLL-1 binding molecule will be absent, and

thus the population (or concentration) of cells presenting a molecule comprising a CLL-1 binding molecule will be increased compared to the levels prior to performing the method.

[0388] If the concentration of the molecule comprising a CLL-1 binding molecule is not at a desired level, the above steps may be repeated a desired number of times. In the context of this step of the method, a desired number of times may 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 may 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 a CLL-1 binding molecule is provided. An antigen binding molecule that specifically recognizes an anti-CLL-1 scFv, *e.g.*, those having one or more of the CDRs shown in Table C or D, may 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 a CLL-1 binding molecule.

[0391] In specific embodiments, the molecule comprising a CLL-1 binding molecule is a CAR. When the molecule is a CAR it may 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, CD11a/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, BAFR, 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, CD11d, ITGAE, CD103, ITGAL, CD11a, LFA-1, ITGAM, CD11b, ITGAX, CD11c, ITGB1, CD29, ITGB2, CD18, LFA-1, ITGB7, NKG2D, TNFR2, TRANCE/RANKL, DNAM1 (CD226), SLAMF4 (CD244, 2B4), CD84, CD96 (Tactile), CEACAM1, CRTAM, Ly9 (CD229), CD160 (BY55), PSGL1, CD100 (SEMA4D), CD69, SLAMF6 (NTB-A, Ly108), SLAM (SLAMF1, CD150, IPO-3), BLAME (SLAMF8), SELPLG (CD162), LTBR, LAT, GADS, SLP-76, PAG/Cbp, CD19a, a ligand that specifically binds with CD83, and combinations thereof.

[0392] An immune cell expressing a molecule comprising a CLL-1 binding molecule sequence may be of any type, and may be human or non-human (*e.g.*, mouse, rat, rabbit, hamster, etc). An immune cell of the method may 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 may be obtained as described herein and by methods known in the art. Any type of immune cell may be employed in this embodiment of the disclosed method, and the cell may 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 may be autologous, allogeneic, or heterologous. In additional embodiments, the cells are T cells presenting a CAR. The T cells may be CD4⁺ T cells or CD8⁺ T cells. When a T cell is employed in the disclosed methods, the T cell may be an *in vivo* T cell or an *in vitro* T cell. Moreover, the cells may 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 may 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 a CLL-1 binding molecule, and (b) an activating molecule expressed on the surface of an immune cell, under conditions that permit the formation of a ternary binding complex comprising the molecule comprising a CLL-1

binding molecule, the activating molecule and the antigen binding molecule. In some embodiments, the immune cell expressing the activating molecule expresses a molecule comprising a CLL-1 binding molecule. In some embodiments, the immune cell expressing the activating molecule does not express a molecule comprising a CLL-1 binding molecule. The antigen binding molecule may be disposed on any surface, or no surface at all. For example, the antigen binding molecule (which may also comprise the population of immune cells to be depleted and/or may be present in a buffer) and the buffer-antigen binding molecule may be contacted with the sample. Alternatively, the antigen binding molecule may 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 well plate, a bag such as a cell culture bag, etc. The surface may 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 a CLL-1 binding molecule sequence, the antigen binding molecule and an activating molecule expressed on the surface of an immune cell not expressing the molecule comprising a CLL-1 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 may be disposed on surfaces as described herein, formed binding complexes may 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 a CLL-1 binding molecule 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 a CLL-1 binding molecule sequence serves to “tag” those cells presenting the molecule comprising a CLL-1 binding molecule (*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 a CLL-1

binding molecule, 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 a CLL-1 binding molecule. Thus, with multiple binding events occurring throughout the subject the population of immune cells bearing the molecule comprising a CLL-1 binding molecule 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, Table E below correlates each sequence with its appropriate description and SEQ ID NO.

Table E. Sequence ID Numbers

SEQ ID NO	SEQUENCE	DESCRIPTION
SEQ ID NO: 1	ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGC TGTGCTCAAAGGTGTCCAGTGTCAGGAGCAGCTG GTGGAGTCCGGGGGAGGCCTGGTCAAGCCTGGGG CATCCCTGACACTCACCTGCAAAGCCTCTGGATTC TCCTTCAGTGTCGGCTACGACATGTGCTGGGTCCG CCAGGCTCCAGGGAAGGGGCTGGAGTGGATCGCA TGCATTGATACTGATAGTAGTAGTAGGACATGGA ACGCGAGCTGGGCGAAAGGCCGATTCACCATCTC CAAACCCTCGTCGACCACGGTGACTCTGCAAATG ACCAGTCTGACAGCCGCGGACACGGCCACCTATT TCTGTGCGAGGAATGACGATACTAGTGGCTGGGG TTCTAAGTTGTGGGGCCCAGGCACCCTGGTCACCG TCTCCTCA	Variable Heavy Chain (VH) Nucleic acid Sequence >KIP-10_15-2_Vh
SEQ ID NO: 2	ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGC TGTGCTCAAAGGTGTCCAGTGTCAGCAGCAGTTG GAGGAGTCCGGGGGAGGCCTGGTCAAGCCTGGAG GAACCCTGACACTCACCTGCAAAGCCTCTGGATTC TCCTTCAGTAGCGACTACGACATGTGCTGGGTCCG CCAGGCTCCAGGGAAGGGGCTGGAGTGGATCGCA TGCATTTACGCTGGTAGTAGTGACAATACTTACTA CGCGACCTGGGCGAAAGGCCGATTCACCATCTCC AAAACCTCGTCGACCACGGTGACTCTGCAAATGA CCAGTCTGACAGCCGCGGACACGGCCACCTATTTC TGTGCGAGAGATACTGCTGATATTAATTTTACTT TAAGTTGTGGGGCCCAGGCACCCTAGTCACCGTCT CCTCA	Variable Heavy Chain (VH) Nucleic acid Sequence >KIP-10_63-2_Vh
SEQ ID NO: 3	ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGC TGTGCTCAAAGGTGTCCAGTGTCAGTCGGTGGAG GAGTCCGGGGGTCGCCTGGTCACGCCTGGGACAC CCCTGACACTCACCTGCACAGTCTCTGGATTCTCC CTCGGTAGCTACTACATGAGCTGGGTCCGCCAGG CTCCAGGGAAGGGGCTGGAATGGATCGGAATCAT TTATCAGAGTGGTAACACGGACTACGCGAGCTGG GCGAAAGGCCGATTCACCATCTCCAAAACCTCGT CGACCACGGTGGATCTGAAAATGACCAGTCTGAC AACCGAGGACACGGCCACCTATTTCTGTGCCAGA GAGGGGTATGCTGGTTATGTTGGTTATAGTTATAA CATCTGGGGCCCAGGCACCCTGGTCACCGTCTCCT CA	Variable Heavy Chain (VH) Nucleic acid Sequence >KIP-10_103-2_Vh

SEQ ID NO: 4	ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGC TGTGCTCAAAGGTGTCCAGTGTGTCAGGAGCAGCTG GAGGAGTCCGGGGGAGACCTGGTCAAGCCTGAGG GATCCCTGACACTCACCTGCACAGCCTCTGGATTCTCCTTCAGTGGCGACTACTACATGTGCTGGGTCCG CCAGGCTCCAGGGAAGGGGCTGGAGTGGATCGCA TGCATTTATGTTGGTAGTTATATTTACAGTTTCTAC GCGAGCTGGGCGAAAGGCCGATTCACCATCTCCA GAACCTCGTCGACCACGGTGACTCTGCAAATGAC CAGTCTGACAGCCGCGGACACGGCCACCTATTTCT GTGCGAGAGATCCATTTGCTACTGATAGTGATGTT GTCAGCTTGTGGGGCCCAGGCACCCTGGTCACCGT CTCCTCA	Variable Heavy Chain (VH) Nucleic acid Sequence >KIP-10_147-1_Vh
SEQ ID NO: 5	ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGC TGTGCTCAAAGGTGTCCAGTGTGTCAGGAGCAGCTG GAGGAGTCCGGGGGAGACCTGGTCAAGCCTGAGG GATCCCTGACACTCACCTGCACAGCCTCTGGATTCTCCTTCAGTGGCAGCTTTGACGTGTGCTGGGTCCG CCAGGCTCCAGGGAAGGGGCTGGAGTGGATCGCG TGCATTGTTGTTGATAGTAGTGATAGGACATGGTA CGCGAGCTGGGCGAAAGGCCGATTCACCATCTCC AAACCCTCGTCGACTACGGTGACTCTACAAATGA CCAGTCTGACAGCCGCGGACACGGCCACCTATTTCT TGTGCGAGGAATGACGATACTAGTGGCTGGGGTT TTAATTTGTGGGGCCCAGGCACCCTGGTCACCGTC TCCTCA	Variable Heavy Chain (VH) Nucleic acid Sequence >KIP-10_148-4_Vh
SEQ ID NO: 6	ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGC TGTGCTCAAAGGTGTCCAGTGTGTCAGTCGTTGGAGG AGTCCGGGGGAGACCTGGTCAAGCCTGGGGCATC CCTGACACTCACCTGCACAGCCTCTGGATTCTCCT TCAGTAGCAACTACTTCGTGTGCTGGGTCCGCCAG GCTCCAGGGAAGGGGCTGGAGTGGGTCGGATGTA TTAATCCTGGTAGTGGTCGCACTTACTCCGCGAGC TGGGCGAAAGGCCGATTCACCATCTCCAAGTCCTC GTCGACCACGGTGACTCTGCAAATGACCAGTCTG ACAGCCGCGGACACGGCCACCTATTTCTGTGCGA GAGATCGGCCTGGTAGTGATGATTATTATATGCGT GACTTGTGGGGCCCAGGCACCCTGGTCACCGTCTC CTCA	Variable Heavy Chain (VH) Nucleic acid Sequence >KIP-10_160-1_Vh
SEQ ID NO: 7	ATGGAGACTGGGCTGCGCTGGCTTCTCCTGGTCGC TGTGCTCAAAGGTGTCCAGTGTGTCAGTCGTTGGAGG AGTCCGGGGGAGGCCTGGTCCAGCCTGGGGGATC CCTGAAACTCTCCTGCAAAGCCTCCGGATTCATCT TCAGTGACAATACTACTACATGTGCTGGGTCCGCCAG GCTCCAGGGAAGGGGCTGGAGTTGATCGCATGCA TTTATGGTGGTCATATTGACACCACTTACTACGCG	Variable Heavy Chain (VH) Nucleic acid Sequence >KIP-10_180-2_Vh

	AGCTGGGGTGAGTGGCCGATTACACCAGCTCCAAAA CCTCGTCGACCACGGTGACTCTGCAACTGACCAGT CTGACAGCCGCGGACACGGCCACCTATTTCTGTGC GCGACGGACCATTTACGATGACAATGATGATTAC TCATATGCCTTGCACTTGTGGGGCCCAGGCACCCT GGTCACCGTCTCCTCA	
SEQ ID NO: 8	ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGC TCCTGCTGCTCTGGCTCCCAGGTGCCAGATGTGAT GTTGTGATGACCCAGACTCCAGCCTCCGTGTCTGA ACCTGTGGGAGGCACAGTCACCATCAAGTGCCAG GCCAGTCAGACCATTGGTAGTGCTTTAGCCTGGTA TCAGCAGAAACCAGGGCAGCCTCCCAAGCTCCTG ATCTATACTGCATCCAATCTGGCATCTGGGGTCTC ATCGCGGTTCAAAGGTAGTAGATCTGGGACAGAG TTCCTCTCACCATCAGCGACCTGGAGTGTGCCGA TGCTGCCACTTACTACTGTCAACATACTTTTTATG GTACTAGTTATGTTGATGCATTCGGCGGAGGGACC GAGGTGGTGGTCAA	Variable Kappa Light Chain (Vk) Nucleic acid Sequences >KIP-10_15-2_Vk
SEQ ID NO: 9	ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGC TCCTACTGCTCTGGCTCCCAGGTGCCAGATGTGCT GACATTGTGATGACCCAGACTCCAGCCTCCGTGTC TGCAGCTGTGGGAGGCACAGTCACCATCAAGTGC CAGGCCAGTGAGAGCGTTAGTCGTTGGTTAGCCT GGTATCAGCAGAAACCAGGGCAGCCTCCCAACCT CCTGATCTATTCTGCATCAACTCTGGCATCTGGGG TCCCATCGCGGTTCAAGGCAGTGGATCTGGGAC AGAGTACACTCTCACCATCAGCGACCTGGAGTGT GCCGATGCTGCCACTTACTACTGTCAAGGCGGTTA TTATAGTGGTGGTGAGACTTACCATAATAGTTTCG GCGGAGGGACCGAGGTGGTGGTCAA	Variable Kappa Light Chain (Vk) Nucleic acid Sequences >KIP-10_63-2_Vk
SEQ ID NO: 10	ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGC TCCTGCTGCTCTGGCTCCCAGGTGCCAGATGTGCC TATGATATGACCCAGACTCCAGCCTCCGTGTCTGC AGCTGTGGGAGGCACAGTCAGCATCAATTGCCAG GCCAGTGAGGACATTGAAAGCTATTTAGCCTGGT ATCAGCAGAGACCAGGGCAGCCTCCCAAGCTCCT GATCTATTCTGCATCCACTCTGGCATCTGGGGTCT CATCGCGGTTCAAAGGCAGTGGATCTGGGACGCA GTTCACTCTCACCATCAGCGACCTGGAGTGTGCCG ATGCTGCCACTTACTACTGTCAACAGGGCGCTAGT AGTAATGATGTTGAGGAGCCTTTCGGCGGAGGGA CCGAGGTGGTGGTCAA	Variable Kappa Light Chain (Vk) Nucleic acid Sequences >KIP-10_103-2_Vk
SEQ ID NO: 11	ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGC TCCTGCTGCTCTGGCTCCCAGGTGCCAGATGTGCC GTCGTGCTGACCCAGACTCCAGCCTCCGTGTCTGC AGCTGTGGGAGGCACAGTCACCATCAATTGCCAG	Variable Kappa Light Chain (Vk) Nucleic acid Sequences

	GCCAGTCAGAGCATTAGTACTGTATTAGCCTGGTA TCAGCAGAAACCAGGGCAGCGTCCCAAGCTCCTG ATCTACTGGGCATCCACTCTGGCATCTGGGGTCCC ATCGCGGTTCAAAGGCAGTGGATCTGGGACACAG TTCCTCTCACCATCAGTGGCGTGGAGTGTGACGA TGCTGCCACTTACTACTGTGCAGGCTATAAAAGTT ATAGTAATGATGATGGTGCTTTCGGCGGAGGGAC CGAGGTGGTGGTCAAA	>KIP-10_147-1_Vk
SEQ ID NO: 12	ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGC TCCTGCTGCTCTGGCTCCCAGGTGCCAGATGTGAT GTTACGATGACCCAGACTCCAGCCTCCGTGTCTGA ACCTGTGGGAGGCACAGTCACCATCAAGTGCCAG GCCAGTCAGAGCATTGGTAGTGCTTTAGCCTGGTA TCAGCAGAAACCAGGGCAGCCTCCCAAGCTCCTG ATCTGGACTGCATCCAATCTGGCATCTGGGGTCTC ATCGCGGTTCAAAGGCAGTAGATCTGGGACAGAT TTCCTCTCACCATCAGCGACCTGGAGTGTGCCGA TGCTGCCACTTACTACTGTCAAGTGTACTTATTATG GTAGTAGTTATATTAATGCATTTCGGCGGAGGGAC CGAGGTGGTGGTCAAA	Variable Kappa Light Chain (Vk) Nucleic acid Sequences >KIP-10_148-4_Vk
SEQ ID NO: 13	ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGC TCCTGCTGCTCTGGCTCCCAGGTGTCATATGTGAC CCTGTGATGACCCAGACTCCAGCCTCCGTGTCTGA ACCTGTGGGAGGCACAGTCACCATCAATTGCCAG GCCAGTGAGAGCATTGGTAGTAGCTTAGCCTGGT ATCAGCAGAAACCAGGGCAGCCTCCCAAGCTCCT GATCTATGCTGCATCCACTCTGGCATCTGGGGTCT CATCGCGGTTCAAAGGCAGTGGATCTGGGACACA GTTCACTCTCACCATCAGCGACCTGGAGTGTGCCG ATGCTGCCACTTACTACTGTCAATGTAGTTATTAT CTTAATACTTATGTTGGTAATCCTTTCGGCGGAGG GACCGAGGTGGTGGTCAAA	Variable Kappa Light Chain (Vk) Nucleic acid Sequences >KIP-10_160-1_Vk
SEQ ID NO: 14	ATGGACACGAGGGCCCCCACTCAGCTGCTGGGGC TCCTGCTGCTCTGGCTCCCAGGTGCCAGATGTGCC CTTGTGATGACCCAGACTCCATCCTCCGTGTCTGA ACCTGTGGGAGGCACAGTCACCATCAATTGCCAG GCCAGTCAGAGCATTAGCAACCTCTTAGCCTGGTA TCAGCAGAAACCAGGGCAGCCTCCCAAGCTCCTG ATCTATGGTGCATCCAATCTGGAATCTGGGGTCCC ATCGCGCTTCAAAGGCAGTGGATCTGGGACAGAG TACACTCTCACCATCAGCGGCGTGGAGTGTGCCG ATGCTGCCACTTACTACTGTCAACAGGGTGATAGT AGTAGTAATCTTGATAATACTTTCGGCGGAGGGA CCGAGGTGGTGGTCAAA	Variable Kappa Light Chain (Vk) Nucleic acid Sequences >KIP-10_180-2_Vk

SEQ ID NO: 15	METGLRWLLLVAVLKGVQCQEQLVESGGGLVKPG ASLTLTCKASGFSFSVGYDMCWVRQAPGKGLEWIA CIDTDSSSRTWNASWAKGRFTISKPSSTTVTLQMTSL TAADTATYFCARNDDTSGWGSKLWGPGTLVTVSS	Variable Heavy Chain Amino acid Sequences >KIP-10_15-2_Vh
SEQ ID NO: 16	METGLRWLLLVAVLKGVQCQQQLEESGGGLVKPG GTLTLTCKASGFSFSSDYDMCWVRQAPGKGLEWIA CIYAGSSDNTYYATWAKGRFTISKTSSTTVTLQMTS LTAADTATYFCARDTADINFYFKLWGPGTLVTVSS	Variable Heavy Chain Amino acid Sequences >KIP-10_63-2_Vh
SEQ ID NO: 17	METGLRWLLLVAVLKGVQCQSVEESGGRLVTPGTP LTLTCTVSGFSLGSYYMSWVRQAPGKGLEWIGIYQ SGNTDYASWAKGRFTISKTSSTTVDLKMTSLTTEDT ATYFCAREGYAGYVGYSYNIWGPGLTVTVSS	Variable Heavy Chain Amino acid Sequences >KIP-10_103-2_Vh
SEQ ID NO: 18	METGLRWLLLVAVLKGVQCQEQLVESGGDLVKPEG SLTLTCTASGFSFSGDYIMCWVRQAPGKGLEWIA YVGSYIYSFYASWAKGRFTISRTSSTTVTLQMTSLTA ADTATYFCARDPFATDSDVVSLLWGPGTLVTVSS	Variable Heavy Chain Amino acid Sequences >KIP-10_147-1_Vh
SEQ ID NO: 19	METGLRWLLLVAVLKGVQCQEQLVESGGDLVKPEG SLTLTCTASGFSFSGSFDVCWVRQAPGKGLEWIA VVDSSDRTWYASWAKGRFTISKPSSTTVTLQMTSLT AADTATYFCARNDDTSGWGFNLWGPGTLVTVSS	Variable Heavy Chain Amino acid Sequences >KIP-10_148-4_Vh
SEQ ID NO: 20	METGLRWLLLVAVLKGVQCQSLEESGGDLVKPGAS LTLTCTASGFSFSSNYFVCWVRQAPGKGLEWVGCIN PGSGRTYSASWAKGRFTISKSSSTTVTLQMTSLTAA DTATYFCARDRPGSDDYYMRDLWGPGTLVTVSS	Variable Heavy Chain Amino acid Sequences >KIP-10_160-1_Vh
SEQ ID NO: 21	METGLRWLLLVAVLKGVQCQSLEESGGGLVQPGGS LKLSCASGFIFSDNYIMCWVRQAPGKGLELIACIY GGHIDTTYASWVSGRFTSSKTSSTTVTLQLTSLTAA DTATYFCARRTIYDDNDYSYALHLWGPGTLVTVS S	Variable Heavy Chain Amino acid Sequences >KIP-10_180-2_Vh
SEQ ID NO: 22	MDTRAPTQLLGLLLLWLPGARCDVVMTPASVSE PVGGTVTIKCQASQTIGSALAWYQQKPGQPPKLLIY TASNLASGVSSRFKGSRSRGTEFTLTISDLECADAATY YCQHTFYGTSYVDAFGGGTEVVVK	Variable Kappa Light Chain (Vk) Amino acid Sequences >KIP-10_15-2_Vk
SEQ ID NO: 23	MDTRAPTQLLGLLLLWLPGARCAIVMTQTPASVS AAVGGTVTIKCQASESVSRWLAWYQQKPGQPPNLL IYSASTLASGVPSRFRGSGSGTEYTLTISDLECADA ATYYCQGGYYSGGETYHNSFGGGTEVVVK	Variable Kappa Light Chain (Vk) Amino acid Sequences >KIP-10_63-2_Vk
SEQ ID NO: 24	MDTRAPTQLLGLLLLWLPGARCAYDMTPASVSA AVGGTVSINCQASEDIESYLAWYQQRPGQPPKLLIYS ASTLASGVSSRFKGSFGSGTQFTLTISDLECADAATYY CQQGASSNDVEEPFGGGTEVVVK	Variable Kappa Light Chain (Vk) Amino acid Sequences

		>KIP-10_103-2_Vk
SEQ ID NO: 25	MDTRAPTQLLGLLLLWLPGARCAVVLTPASVSA AVGGT VTINCQASQSISTVLAWYQQKPGQRPKLLIY WASTLASGVPSRFRKGSGSGTQFTLTISGVECDDAAT YYCAGYKSYSNDDGAFGGGTEVVVK	Variable Kappa Light Chain (Vk) Amino acid Sequences >KIP-10_147-1_Vk
SEQ ID NO: 26	MDTRAPTQLLGLLLLWLPGARCDVTMTQTPASVSE PVGGT VTIKCQASQSIGSALAWYQQKPGQPPKLLIW TASN LASGVSSRFRKGSRS GTDFTLTISDLECADAATY YCQCTYYGSSYINAFGGGTEVVVK	Variable Kappa Light Chain (Vk) Amino acid Sequences >KIP-10_148-4_Vk
SEQ ID NO: 27	MDTRAPTQLLGLLLLWLPGVICDPVMTQTPASVSEP VGGT VTINCQASESIGSSLAWYQQKPGQPPKLLIYA ASTLASGVSSRFRKGSGSGTQFTLTISDLECADAATYY CQCSYYLNTYVGNPFGGGTEVVVK	Variable Kappa Light Chain (Vk) Amino acid Sequences >KIP-10_160-1_Vk
SEQ ID NO: 28	MDTRAPTQLLGLLLLWLPGARCALVMTQTPSSVSEP VGGT VTINCQASQSISNLLAWYQQKPGQPPKLLIYG ASNLESGVPSRFRKGSGSGTEYTLTISGVECDADAATY YCQQGDSSSNLDNTFGGGTEVVVK	Variable Kappa Light Chain (Vk) Amino acid Sequences >KIP-10_180-2_Vk
SEQ ID NO: 29	QASQTIGSALA	KIP-10_15-2_Vk CDR1 (Kabat)
SEQ ID NO: 32	QASESVSRWLA	KIP-10_63-2_Vk CDR1 (Kabat)
SEQ ID NO: 35	QASEDIESYLA	KIP-10_103-2_Vk CDR1 (Kabat)
SEQ ID NO: 37	QASQSISTVLA	KIP-10_147-1_Vk CDR1 (Kabat)
SEQ ID NO: 40	QASQSIGSALA	KIP-10_148-4_Vk CDR1 (Kabat)
SEQ ID NO: 43	QASESIGSSLA	KIP-10_160-1_Vk CDR1 (Kabat)
SEQ ID NO: 46	QASQSISNLLA	KIP-10_180-2_Vk CDR1 (Kabat)
SEQ ID NO: 49	VG YDMC	KIP-10_15-2_Vh CDR1 (Kabat)
SEQ ID NO: 52	SDYDMC	KIP-10_63-2_Vh CDR1 (Kabat)
SEQ ID NO: 55	SY YMS	KIP-10_103-2_Vh CDR1 (Kabat)
SEQ ID NO: 58	GDYYMC	KIP-10_147-1_Vh CDR1 (Kabat)
SEQ ID NO: 61	GSFDVC	KIP-10_148-4_Vh CDR1 (Kabat)
SEQ ID NO: 64	SNYFVC	KIP-10_160-1_Vh CDR1 (Kabat)
SEQ ID NO: 67	DNYYMC	KIP-10_180-2_Vh CDR1 (Kabat)

SEQ ID NO: 30	TASNLAS	KIP-10_15-2_Vk CDR2 (Kabat)
SEQ ID NO: 33	SASTLAS	KIP-10_63-2_Vk CDR2 (Kabat)
SEQ ID NO: 33	SASTLAS	KIP-10_103-2_Vk CDR2 (Kabat)
SEQ ID NO: 38	WASTLAS	KIP-10_147-1_Vk CDR2 (Kabat)
SEQ ID NO: 30	TASNLAS	KIP-10_148-4_Vk CDR2 (Kabat)
SEQ ID NO: 44	AASTLAS	KIP-10_160-1_Vk CDR2 (Kabat)
SEQ ID NO: 47	GASNLES	KIP-10_180-2_Vk CDR2 (Kabat)
SEQ ID NO: 50	CIDTDSSSRTWNASWAK	KIP-10_15-2_Vh CDR2 (Kabat)
SEQ ID NO: 53	CIYAGSSDNTYYATWAK	KIP-10_63-2_Vh CDR2 (Kabat)
SEQ ID NO: 56	IYQSGNTDYASWAK	KIP-10_103-2_Vh CDR2 (Kabat)
SEQ ID NO: 59	CIYVGSYIYSFYASWAK	KIP-10_147-1_Vh CDR2 (Kabat)
SEQ ID NO: 62	CIVVDSSDRTWYASWAK	KIP-10_148-4_Vh CDR2 (Kabat)
SEQ ID NO: 65	CINPGSGRTYSASWAK	KIP-10_160-1_Vh CDR2 (Kabat)
SEQ ID NO: 68	CIYGGHIDTTYASWVS	KIP-10_180-2_Vh CDR2 (Kabat)
SEQ ID NO: 31	QHTFYGTSYVDA	KIP-10_15-2_Vk CDR3 (Kabat)
SEQ ID NO: 34	QGGYYSGGETYHNS	KIP-10_63-2_Vk CDR3 (Kabat)
SEQ ID NO: 36	QQGASSNDVEEP	KIP-10_103-2_Vk CDR3 (Kabat)
SEQ ID NO: 39	AGYKSYSNDDGA	KIP-10_147-1_Vk CDR3 (Kabat)
SEQ ID NO: 42	QCTYYGSSYINA	KIP-10_148-4_Vk CDR3 (Kabat)
SEQ ID NO: 45	QCSYYLNTYVGNP	KIP-10_160-1_Vk CDR3 (Kabat)
SEQ ID NO: 48	QQGDSSSNLDNT	KIP-10_180-2_Vk CDR3 (Kabat)
SEQ ID NO: 51	NDDTSGWGSKL	KIP-10_15-2_Vh CDR3 (Kabat)
SEQ ID NO: 54	DTADINFYFKL	KIP-10_63-2_Vh CDR3 (Kabat)
SEQ ID NO: 57	EGYAGYVGYSYNI	KIP-10_103-2_Vh CDR3 (Kabat)
SEQ ID NO: 60	DPFATDSDVVSL	KIP-10_147-1_Vh

		CDR3 (Kabat)
SEQ ID NO: 63	NDDTSGWGFNL	KIP-10_148-4_Vh CDR3 (Kabat)
SEQ ID NO: 66	DRPGSDDYYMRDL	KIP-10_160-1_Vh CDR3 (Kabat)
SEQ ID NO: 69	RTIYDDNDDYSYALHL	KIP-10_180-2_Vh CDR3 (Kabat)
SEQ ID NO: 29	QASQTIGSALA	KIP-10_15-2_Vk CDR1 (Clothia)
SEQ ID NO: 32	QASESVSRWLA	KIP-10_63-2_Vk CDR1 (Clothia)
SEQ ID NO: 35	QASEDIESYLA	KIP-10_103-2_Vk CDR1 (Clothia)
SEQ ID NO: 37	QASQSISTVLA	KIP-10_147-1_Vk CDR1 (Clothia)
SEQ ID NO: 40	QASQSIGSALA	KIP-10_148-4_Vk CDR1 (Clothia)
SEQ ID NO: 43	QASESIGSSLA	KIP-10_160-1_Vk CDR1 (Clothia)
SEQ ID NO: 46	QASQSISNLLA	KIP-10_180-2_Vk CDR1 (Clothia)
SEQ ID NO: 76	GFSFSVGY	KIP-10_15-2_Vh CDR1 (Clothia)
SEQ ID NO: 78	GFSFSSDY	KIP-10_63-2_Vh CDR1 (Clothia)
SEQ ID NO: 80	GFSLGSY	KIP-10_103-2_Vh CDR1 (Clothia)
SEQ ID NO: 82	GFSFSGDY	KIP-10_147-1_Vh CDR1 (Clothia)
SEQ ID NO: 74	GFSFSGSF	KIP-10_148-4_Vh CDR1 (Clothia)
SEQ ID NO: 72	GFSFSSNY	KIP-10_160-1_Vh CDR1 (Clothia)
SEQ ID NO: 41	GFIFSDNY	KIP-10_180-2_Vh CDR1 (Clothia)
SEQ ID NO: 30	TASNLAS	KIP-10_15-2_Vk CDR2 (Clothia)
SEQ ID NO: 33	SASTLAS	KIP-10_63-2_Vk CDR2 (Clothia)
SEQ ID NO: 33	SASTLAS	KIP-10_103-2_Vk CDR2 (Clothia)
SEQ ID NO: 38	WASTLAS	KIP-10_147-1_Vk CDR2 (Clothia)
SEQ ID NO: 30	TASNLAS	KIP-10_148-4_Vk CDR2 (Clothia)
SEQ ID NO: 44	AASTLAS	KIP-10_160-1_Vk CDR2 (Clothia)
SEQ ID NO: 47	GASNLES	KIP-10_180-2_Vk CDR2 (Clothia)

SEQ ID NO: 77	DTDSSS	KIP-10_15-2_Vh CDR2 (Clothia)
SEQ ID NO: 79	YAGSSD	KIP-10_63-2_Vh CDR2 (Clothia)
SEQ ID NO: 81	YQSG	KIP-10_103-2_Vh CDR2 (Clothia)
SEQ ID NO: 75	YVGSI	KIP-10_147-1_Vh CDR2 (Clothia)
SEQ ID NO: 73	VVDSSD	KIP-10_148-4_Vh CDR2 (Clothia)
SEQ ID NO: 71	NPGSG	KIP-10_160-1_Vh CDR2 (Clothia)
SEQ ID NO: 70	YGGHID	KIP-10_180-2_Vh CDR2 (Clothia)
SEQ ID NO: 31	QHTFYGTSYVDA	KIP-10_15-2_Vk CDR3 (Clothia)
SEQ ID NO: 34	QGGYYSGGETYHNS	KIP-10_63-2_Vk CDR3 (Clothia)
SEQ ID NO: 36	QQGASSNDVEEP	KIP-10_103-2_Vk CDR3 (Clothia)
SEQ ID NO: 39	AGYKSYSNDDGA	KIP-10_147-1_Vk CDR3 (Clothia)
SEQ ID NO: 42	QCTYYGSSYINA	KIP-10_148-4_Vk CDR3 (Clothia)
SEQ ID NO: 45	QCSYYLNTYVGNP	KIP-10_160-1_Vk CDR3 (Clothia)
SEQ ID NO: 48	QQGDSSSNLDNT	KIP-10_180-2_Vk CDR3 (Clothia)
SEQ ID NO: 51	NDDTSGWGSKL	KIP-10_15-2_Vh CDR3 (Clothia)
SEQ ID NO: 54	DTADINFYFKL	KIP-10_63-2_Vh CDR3 (Clothia)
SEQ ID NO: 57	EGYAGYVGYSYNI	KIP-10_103-2_Vh CDR3 (Clothia)
SEQ ID NO: 60	DPFATDSDVVS	KIP-10_147-1_Vh CDR3 (Clothia)
SEQ ID NO: 63	NDDTSGWGFNL	KIP-10_148-4_Vh CDR3 (Clothia)
SEQ ID NO: 66	DRPGSDDYYMRDL	KIP-10_160-1_Vh CDR3 (Clothia)
SEQ ID NO: 69	RTIYDDNDDYSYALHL	KIP-10_180-2_Vh CDR3 (Clothia)

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 an anti-CLL-1 scFv, conjugated to Fc as immunogen. Titer was determined via screening polyclonal sera by ELISA. 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 of proliferating CAR T cells. The sequences of the final 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 OpTmizer media + OpTmizer supplements + IL-2 (300IU/ml, Proleukin®, Prometheus® Therapeutics and Diagnostics). Two days after

stimulation, CAR T cells presenting the anti-CLL-1 scFv were generated through viral transduction of these activated primary human T cells. Transduction was performed using lentivirus to express the CAR. Confirmation of CAR construct expression and viral transduction efficiency was determined using a two-step staining protocol with biotinylated Protein L and PE-conjugated streptavidin. Monoclonal antibody supernatants were incubated with CAR⁺ cells and detected with a FITC-conjugated goat anti-rabbit F(ab')₂ antibody. Results from flow cytometry experiments showing antibody binding to the anti-CLL-1 CAR, but not two control CARs are shown in **Error! Reference source not found.** Anti-CLL CAR antibodies bind anti-CLL-1 CAR selectively. Histograms in Figure 1 show antibody binding to CAR-expressing T cells demonstrating that KIP-10 clonal supernatants bind anti-CLL-1 CAR-expressing T cells, but not two control CAR-expressing T cells (CAR 2 and CAR3).

EXAMPLE 2

Use of an Antibody to an Anti-CLL-1 scFv for Purifying Macromolecules and Cells

[0401] The antigen binding molecules disclosed herein are anti-idiotypic antigen binding molecules, and recognize an epitope on a CLL-1 binding molecule. An antigen binding molecule (*e.g.*, an antibody) disclosed herein may thus be used to purify a molecule, such as a CLL-1 binding molecule, macromolecule, polymer, cell, material, etc., displaying an epitope that is recognized by the antigen binding molecules disclosed herein.

[0402] In some embodiments, an antigen binding molecule disclosed herein (*e.g.*, Clones 15-2, 63-2, 103-2, 147-1, 148-4, 160-1/or and 180-2 and fragments thereof) may be attached to beads, attached to or associated with a resin, which may be disposed in a column or other structure. A sample comprising a molecule comprising all or a fragment of anti-CLL-1 scFv may 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 a CLL-1 binding molecule. The beads or resin may 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 a CLL-1 binding molecule. The washing may remove unwanted and unbound components of the sample. Following the washing step, the

molecule comprising all or a fragment of a CLL-1 binding molecule may 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 a CLL-1 binding molecule is collected, and purity may be subsequently checked by running a sample on an SDS polyacrylamide gel.

[0403] In another embodiment, an antigen binding molecule may 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 may be used to return materials to desired buffer conditions.

[0404] In some embodiments, cells displaying a molecule comprising all or a fragment of a CLL-1 binding molecule may 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).

[0405] Cells bound by the beads (which will be presenting molecules comprising a CLL-1 binding molecule) are then separated from cells not displaying a molecule comprising a CLL-1 binding molecule or fragment thereof. In some embodiments, the beads may be washed with media, such as RPMI-1640 supplemented with 10% FBS, in the presence of a magnet.

[0406] Selected cells, *i.e.*, those presenting molecules that comprise a CLL-1 binding molecule may then be separated from the beads: First, selected cells are grown out in media. After growing out cells for 48 hours, the magnetic beads may be separated from cells in solution and discarded, leaving a pure population of cells expressing desired molecule.

[0407] In an alternative embodiment, the beads are not magnetic, and in this embodiment the above steps may also be followed and adapted to maintain cell integrity, but also to allow separation of bead-bound cells from non-bead bound cells.

[0408] In another alternative embodiment, an antigen binding molecule disclosed herein (*e.g.*, 9-1, 9-9, 18-4, 63-1, 80-7, 137-2, and/or 154-7 and fragments thereof) may 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 may then be incubated with cells known or suspected to be expressing a CLL-1 binding molecule 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 may be disposed in a solid structure such as a well plate, column or other structure. The antigen binding molecule-cell complexes may 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 may then be spun down, washed in RPMI or other suitable media, and then resuspended in media.

EXAMPLE 3

Activating CAR-positive T cells Using Antibodies to an Anti-CLL-1 CAR

[0409] 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 comprises a CLL-1 binding molecule, such as those disclosed herein: Clone 15-2, 63-2, 103-2, 147-1, 148-4, 160-1 and 180-2, 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 a CLL-1 binding molecule. Activation may 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.

[0410] In some embodiments, the method may be performed as follows: first, a 12-well tissue culture treated plate is coated with 1.5 $\mu\text{g/mL}$ of a CLL-1 binding molecule 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 .

[0411] After 2 days, the cells are examined to determine any increase in the percent CAR-positive cells. This determination may 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 4

Generation of Humanized Sequences from Rabbit Antibodies

[0412] The Molecular Operating Environment (MOE) software developed by Chemical Computing Group (CCG) may be used to generate alignments between the rabbit antibody Clones 15-2, 63-2, 103-2, 147-1, 148-4, 160-1 and 180-2 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.

[0413] 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 may be exported and clustered using kClust (Hauser, Mayer, & Soding, (2013) *BMC Bioinformatics*, 248). Tables for VL and VH sequences for each of the antibodies, may be constructed, with sequences from each of the two databases clustered at 90% and 95%.

CLAIMS

What is claimed is:

1. An isolated antigen binding molecule that specifically binds a molecule comprising a CLL-1 binding molecule, wherein the antigen binding molecule is optionally humanized, and optionally wherein the antigen binding molecule is selected from the group consisting of an antibody, an scFv, a Fab, a Fab', a Fv, a F(ab')₂, a dAb, a human antibody, a humanized antibody, a chimeric antibody, a monoclonal antibody, a polyclonal antibody, a recombinant antibody, an IgE antibody, an IgD antibody, an IgM antibody, an IgG1 antibody, an IgG1 antibody having at least one mutation in the hinge region, an IgG2 antibody an IgG2 antibody having at least one mutation in the hinge region, an IgG3 antibody, an 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.
2. The antigen binding molecule of claim 1, wherein the antigen binding molecule comprises a heavy chain (HC) and/or a light chain (LC).
3. The antigen binding molecule of claim 4, wherein the HC comprises a heavy chain variable region (VH) sequence selected from the group consisting of SEQ ID NOs: 1-7 and 15-21 and/or the LC comprises a light chain variable region (VL) sequence selected from the group consisting of SEQ ID NOs: 22-28.
4. The antigen binding molecule of claim any one of the preceding claims, wherein the antigen binding molecule comprises a heavy chain CDR1 selected from the group consisting of SEQ ID NOs: 49, 52, 55, 58, 61, 64, and 67, a heavy chain CDR2 selected from the group consisting of SEQ ID NOs: 50, 53, 56, 59, 62, 65, and 68, and a heavy chain CDR3 selected from the group consisting of SEQ ID NOs: 51, 54, 57, 60, 63, 66, and 69; and/or wherein the antigen binding molecule comprises a light chain CDR1 selected from the group consisting of SEQ ID NOs: 29, 32, 35, 37, 40, 43, and 46, a light chain CDR2 selected from the group consisting of SEQ ID NOs: 30, 33, 38, 44, and 47, and a light chain CDR3 selected from the group consisting of SEQ ID NOs: 31, 34, 36, 39, 42, 45, and 48.

5. The antigen binding molecule of any one of the preceding claims, 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 Table C and D; and/or 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 Table C or D.
6. 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; and/or 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 4.
7. The antigen binding molecule of any one of the preceding claims, wherein the antigen binding molecule comprises:
 - (a) a VH comprising the amino acid sequence of SEQ ID NO: 15 and a VL comprising the amino acid sequence of SEQ ID NO: 22;
 - (b) a VH comprising the amino acid sequence of SEQ ID NO: 16 and a VL comprising the amino acid sequence of SEQ ID NO: 23;
 - (c) a VH comprising the amino acid sequence of SEQ ID NO: 17 and a VL comprising the amino acid sequence of SEQ ID NO: 24;
 - (d) a VH comprising the amino acid sequence of SEQ ID NO: 18 and a VL comprising the amino acid sequence of SEQ ID NO: 25;
 - (e) a VH comprising the amino acid sequence of SEQ ID NO: 19 and a VL comprising the amino acid sequence of SEQ ID NO: 26;
 - (f) a VH comprising the amino acid sequence of SEQ ID NO: 20 and a VL comprising the amino acid sequence of SEQ ID NO: 27; or
 - (g) a VH comprising the amino acid sequence of SEQ ID NO: 21 and a VL comprising the amino acid sequence of SEQ ID NO: 28.

8. 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: 49, a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 50, a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 51, a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 29, a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 30, and a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 31;
 - (b) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 52, a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 53, a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 54, a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 32, a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 33, and a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 34;
 - (c) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 55, a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 56, a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 57, a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 35, a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 33, and a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 36;
 - (d) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 58, a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 59, a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 60, a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 37, a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 38, and a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 39;
 - (e) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 61, a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 62, a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 63, a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 40, a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 30, and a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 42;

- (f) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 64, a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 65, a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 66, a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 43, a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 44, and a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 45; or
 - (g) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 46, a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 47, a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 48, a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 67, a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 68, and a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 69.
9. The antigen binding molecule of any of claims 1-8, wherein the antigen binding molecule further comprises a detectable label, 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, and optionally 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-phycoerythrin (BPE), mCherry, HcRed1, Katusha, P3, Peridinin Chlorophyll (PerCP), mKate (TagFP635), TurboFP635, mPlum, and mRaspberry.

10. A polynucleotide encoding the heavy chain or the light chain of an antigen binding molecule of any of claims 1-8.
11. A vector comprising the polynucleotide of claim 10.
12. A cell comprising the vector of claim 11, and optionally wherein the cell is selected from the group consisting of a CHO cell, a Sp2/0 cell, a rabbit cell and an *E. coli* cell.
13. A method of making an antigen binding molecule of claims 1-8, comprising incubating the cell of claim 12 under suitable conditions.
14. 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 a CLL-1 binding molecule, 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 a CLL-1 binding molecule;
 - (b) providing an aliquot of the sample comprising a population of cells presenting a therapeutic molecule comprising a CLL-1 binding molecule;
 - (c) providing an antigen binding molecule that specifically binds the a CLL-1 binding molecule, 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 a CLL-1 binding molecule 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; and optionally wherein (a) the molecule comprising a CLL-1 binding molecule is a CAR; and (b) the cell is an immune cell selected from the group consisting of CD8⁺ T cells,

CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells, and optionally wherein the dose comprises 1.0×10^6 cells per kg.

15. A method of determining a number of cells presenting a molecule comprising a CLL-1 binding molecule in a sample, the method comprising:
 - (a) providing a sample comprising cells known or suspected to be presenting a molecule comprising a CLL-1 binding molecule;
 - (b) contacting the sample of (a) with an antigen binding molecule that specifically binds the molecule comprising a CLL-1 binding molecule, 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; andoptionally wherein (a) the molecule comprising a CLL-1 binding molecule is a CAR; and (b) the cell is an immune cell selected from the group consisting of CD8+ T cells, CD4+ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells.
16. A method of isolating a cell comprising a CLL-1 binding molecule, the method comprising:
 - (a) providing a sample known or suspected to comprise a molecule comprising a CLL-1 binding molecule;
 - (b) providing an antigen binding molecule that specifically binds a molecule comprising a CLL-1 binding molecule, 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 a CLL-1 binding molecule 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 a CLL-1 binding molecule, and (b) an antigen binding molecule; andoptionally wherein the CLL-1 binding molecule is a CAR.

17. A method of determining the presence or absence of a molecule comprising a CLL-1 binding molecule in a sample, the method comprising:
- (a) providing a sample known or suspected to comprise a molecule comprising a CLL-1 binding molecule;
 - (b) providing an antigen binding molecule comprising a detectable label that specifically binds a molecule comprising a CLL-1 binding molecule;
 - (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; and
- optionally wherein the molecule comprising a CLL-1 binding molecule is a CAR.
18. A method of increasing the concentration of cells presenting a molecule comprising a CLL-1 binding molecule, the method comprising:
- (a) providing a sample comprising a cell known or suspected to present a molecule comprising a CLL-1 binding molecule;
 - (b) providing an antigen binding molecule that specifically binds a molecule comprising a CLL-1 binding molecule, 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 a CLL-1 binding molecule 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; and
- optionally wherein (a) the molecule comprising a CLL-1 binding molecule is a CAR; and (b) the cell is an immune cell selected from the group consisting of CD8⁺ T cells, CD4⁺ T cells, tumor infiltrating lymphocytes (TILs), NK cells, TCR-expressing cells, dendritic cells, and NK-T cells.
19. A method of depleting a population of immune cells presenting a molecule comprising a CLL-1 binding molecule, 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 a CLL-1 binding molecule; and

- (b) contacting the immune cells with an antigen binding molecule that specifically binds to (a) the molecule comprising a CLL-1 binding molecule, and (b) an activating molecule expressed on the surface of the an immune cell not presenting the molecule comprising a CLL-1 binding molecule, under conditions that permit the formation of a ternary binding complex comprising the molecule comprising a CLL-1 binding molecule, the activating molecule and the antigen binding molecule; and
- optionally wherein (a) the molecule comprising a CLL-1 binding molecule 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.
20. The method of any one of claims 14-19, wherein the immune cell is a T cell, and optionally:
- wherein the T cell is disposed *in vitro*;
- wherein the T cell is disposed *in vivo*;
- wherein the T cell is in one of blood, extracted tissue, tissue grown *ex vivo*, and cell culture media;
- wherein the T cell is an autologous T cell;
- wherein the T cell is an allogenic T cell; and/or
- wherein the antigen binding molecule comprises an antigen binding molecule of claims 1-8, and humanized forms thereof.

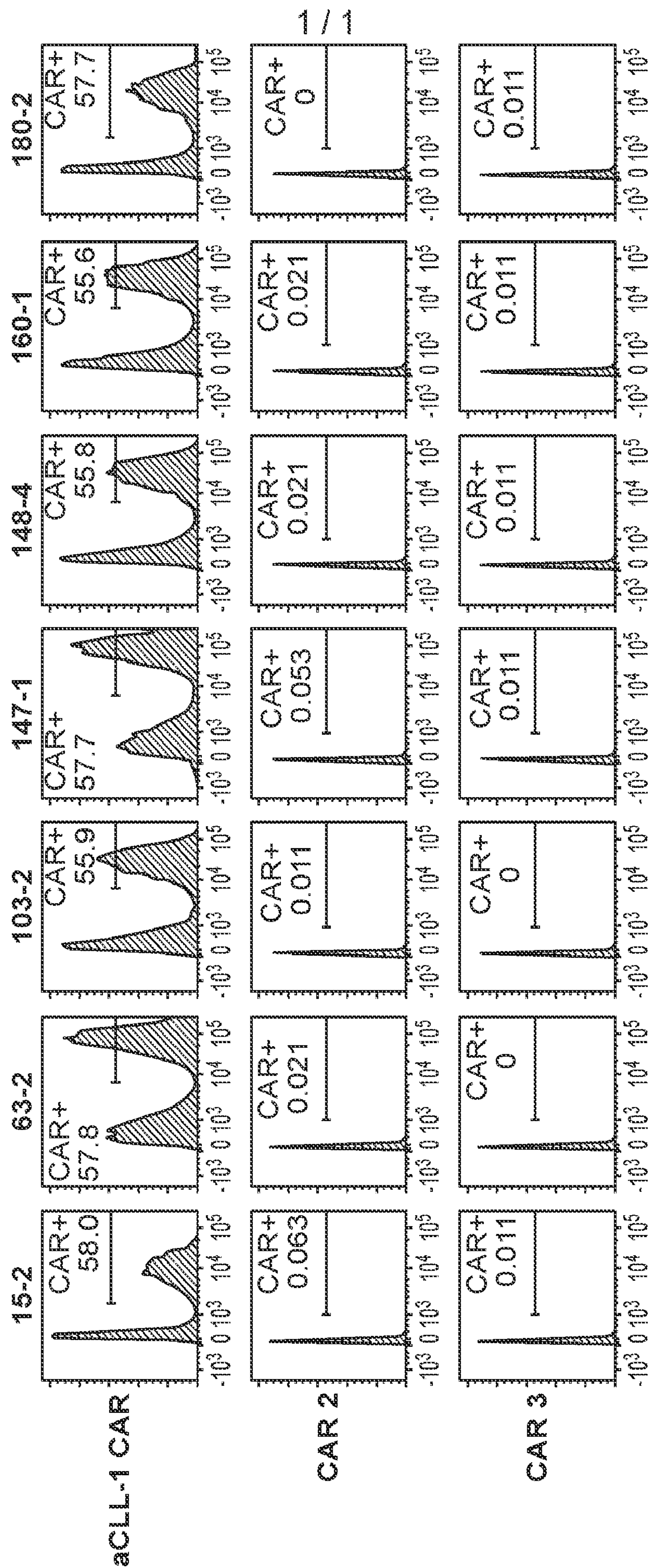


FIG. 1

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2020/057072

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07K16/28
ADD.

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)
C07K

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

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

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2009/051974 A1 (NUVELO INC [US]; ABO ARIE [US]; KORVER WOUTER [US]) 23 April 2009 (2009-04-23) page 4, line 1 - page 7, line 17; figure 1 page 27, lines 13-22 page 76, lines 19-29 page 94, line 27 - page 102, line 24 -----	1-13, 15-18,20
X	US 9 163 090 B2 (CELLERANT THERAPEUTICS INC [US]) 20 October 2015 (2015-10-20) column 1, line 40 - column 8, line 42 column 22, line 39 - column 27, line 37 column 31, line 25 - column 38, line 49 ----- -/--	1-13, 15-18,20

☒ 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

12 February 2021

Date of mailing of the international search report

25/02/2021

Name and mailing address of the ISA/

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Page, Michael

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2020/057072

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	W0 2017/091615 A1 (CELLERANT THERAPEUTICS INC [US]) 1 June 2017 (2017-06-01) paragraphs [0006] - [0029], [0073] - [0077], [0121] - [0123], [0153], [0158] - [0162] -----	1-13, 15-20
X	W0 2016/040868 A1 (GENENTECH INC [US]) 17 March 2016 (2016-03-17) paragraphs [0007] - [0029], [0249] - [0252] -----	1-13, 15-18,20
X	US 2016/368994 A1 (KELLEY ROBERT F [US] ET AL) 22 December 2016 (2016-12-22) paragraphs [0008] - [0032], [0053], [0410] - [0442] -----	1-13, 15-18,20
A	X. ZHAO ET AL: "Targeting C-type lectin-like molecule-1 for antibody-mediated immunotherapy in acute myeloid leukemia", HAEMATOLOGICA, vol. 95, no. 1, 31 July 2009 (2009-07-31), pages 71-78, XP055094666, ISSN: 0390-6078, DOI: 10.3324/haematol.2009.009811 -----	1-20

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2020/057072

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:

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2020/057072

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2009051974 A1	23-04-2009	EP 2211903 A1 US 2010285037 A1 WO 2009051974 A1	04-08-2010 11-11-2010 23-04-2009
US 9163090 B2	20-10-2015	AU 2013259850 A1 BR 112014027659 A2 CA 2872513 A1 CN 104736562 A EP 2847222 A1 ES 2699244 T3 IL 235397 A JP 6262724 B2 JP 2015519336 A KR 20150023355 A US 2013295118 A1 US 2015376290 A1 US 2018273633 A1 WO 2013169625 A1	20-11-2014 08-08-2017 14-11-2013 24-06-2015 18-03-2015 08-02-2019 31-12-2018 17-01-2018 09-07-2015 05-03-2015 07-11-2013 31-12-2015 27-09-2018 14-11-2013
WO 2017091615 A1	01-06-2017	AU 2016361426 A1 BR 112018010385 A2 CA 3004743 A1 CN 108290955 A EP 3380524 A1 HK 1258375 A1 KR 20180085002 A US 2018355044 A1 WO 2017091615 A1	31-05-2018 04-12-2018 01-06-2017 17-07-2018 03-10-2018 08-11-2019 25-07-2018 13-12-2018 01-06-2017
WO 2016040868 A1	17-03-2016	AR 101846 A1 AU 2015314744 A1 BR 112017004802 A2 CA 2958479 A1 CL 2017000590 A1 CN 107001465 A CR 201700095 A EP 3191520 A1 EP 3693391 A1 JP 2017534256 A JP 2020203901 A KR 20170066421 A PE 20170670 A1 SG 10201804931Q A SG 11201701627P A TW 201625690 A US 2016075787 A1 US 2018009894 A1 US 2018044420 A1 US 2018044421 A1 US 2019248903 A1 WO 2016040868 A1	18-01-2017 02-03-2017 12-12-2017 17-03-2016 06-10-2017 01-08-2017 19-07-2017 19-07-2017 12-08-2020 24-11-2017 24-12-2020 14-06-2017 06-06-2017 30-07-2018 30-03-2017 16-07-2016 17-03-2016 11-01-2018 15-02-2018 15-02-2018 15-08-2019 17-03-2016
US 2016368994 A1	22-12-2016	CN 107847568 A EP 3310378 A1 HK 1252858 A1 JP 2018522541 A TW 201718647 A US 2016368994 A1	27-03-2018 25-04-2018 06-06-2019 16-08-2018 01-06-2017 22-12-2016

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2020/057072

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		US 2020148774 A1	14-05-2020
		WO 2016205200 A1	22-12-2016
