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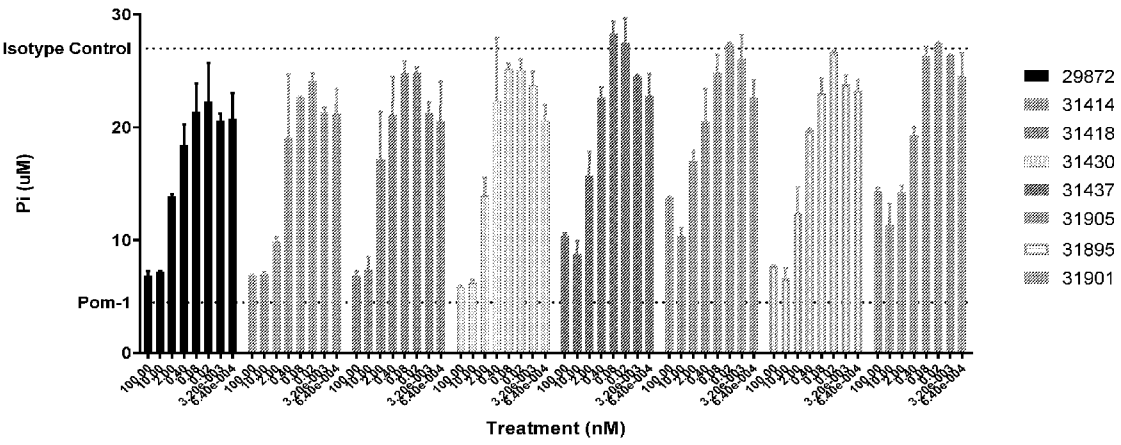
(54) Title: ANTI-CD39 ANTIBODIES, COMPOSITIONS COMPRISING ANTI-CD39 ANTIBODIES AND METHODS OF USING ANTI-CD39 ANTIBODIES

FIG. 11



(57) Abstract: Provided herein are antibodies that selectively bind to CD39 and its isoforms and homologs, and compositions comprising the antibodies. Also provided are methods of using the antibodies, such as therapeutic and diagnostic methods.

[Continued on next page]

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ANTI-CD39 ANTIBODIES, COMPOSITIONS COMPRISING ANTI-CD39 ANTIBODIES AND METHODS OF USING ANTI-CD39 ANTIBODIES

RELATED APPLICATION

[0001] This application claims priority to U.S. provisional application number 62/539,527, filed July 31, 2017, which is incorporated by reference herein in its entirety.

FIELD

[0002] Provided herein are antibodies with binding specificity for CD39 and compositions comprising the antibodies, including pharmaceutical compositions, diagnostic compositions and kits. Also provided are methods of using anti-CD39 antibodies for therapeutic and diagnostic purposes.

BACKGROUND

[0003] CD39 is an integral membrane protein that phosphohydrolyzes ATP to yield ADP and AMP. Human CD39 is a 510-amino acid protein with seven potential N-linked glycosylation sites, 11 cysteine residues, and two transmembrane regions. Structurally, it is characterized by two transmembrane domains, a small cytoplasmic domain comprising the NH_2- and COOH-terminal segments, and a large extracellular hydrophobic domain consisting of five highly conserved domains, known as apyrase conserved regions (ACR) 1−5, which are pivotal for the catabolic activity of the enzyme. CD39 becomes catalytically active upon its localization on the cell surface, and its glycosylation is important for protein folding, membrane targeting, and enzyme activity.

[0004] CD39 is constitutively expressed in spleen, thymus, lung, and placenta and in these tissues it is associated primarily with endothelial cells and immune cell populations, such as B cells, natural killer (NK) cells, dendritic cells, Langerhans cells, monocytes, macrophages, mesangial cells, neutrophils, and regulatory T cells (Tregs). Given that CD39, along with other enzymes, degrades ATP, ADP, and AMP to adenosine, CD39 can be viewed as an immunological switch that shifts ATP-driven pro-inflammatory immune cell activity toward an anti-inflammatory state mediated by adenosine.

[0005] Within a neoplastic *milieu*, cancer and immune cells can closely interact to generate an immunosuppressive environment by releasing immunomodulatory factors, which support neoplastic growth. The expression of CD39 is increased in many solid tumors (for

example, colorectal cancer, head and neck cancer, pancreatic cancer (Kunzli et al., *Am J Physiol,* 2006, 292: 223-230), bladder cancer, brain cancer, breast cancer, gastric cancer, hepatocellular carcinoma, lung cancer, non-small cell lung cancer (Li et al., *Oncoimmunology*, 2017, 6: 6), chronic lymphocytic leukemia (Pulte et al., *Clin Lymphoma Myeloma Leuk,* 2011, 11(4): 367-372) and lymphoma, melanoma (Dzhandzhugazyan et al., *FEBS Letters*, 1998, 430: 227-230), ovarian cancer, and prostate cancer, among others) suggesting this enzyme is involved in the development and progression of malignancies. Modulators of CD39 may provide potential therapies for these types of cancers.

[0006] Interactions between tumor cells and their microenvironment are important for tumorigenesis. CD39 can participate in tumor immunoescape by inhibiting the activation, clonal expansion, and homing of tumor-specific T cells, impairing tumor cell killing by effector T lymphocytes. In addition to these immunoregulatory roles, CD39 can contribute directly to the modulation of cancer cell growth, differentiation, invasion, migration, metastasis, and angiogenesis. CD39 is important for both the initiation of angiogenesis and the progression of neovascularization. CD39 on vasculature mediates the angiogenic process in mouse models of melanoma, lung, and liver malignancy.

[0007] Modulators of CD39 activity may also provide potential therapeutics for the treatment of CD39 conditions including, but not limited to, autoimmune diseases and infections. In particular, modulators of CD39 activity may provide potential therapeutics for diseases such as, for example, without limitation, Celiac disease (Cook et al., *American Academy of Allergy, Asthma & Immunology*, 2017, Article in Press), colitis (Longhi et al., *JCI Insight.* 2017, 2(9)), thrombotic disease (Marcus et al., *Journal of Pharmacology and Experimental Therapeutics,* 2003, 305, 1: 9-16), HIV infection (zur Wiesch et al., *Journal of Virology*, 2011, Feb: 1287-1297), HBV infection, HCV infection, and inflammatory bowel disease (Friedman et al. *PNAS*, 2009, 106, 39: 16788-16793) and Crohn′s disease (Bai et al., *J Immunol,* 2014, 3366-3377).

SUMMARY

[0008] Provided herein are antibodies that selectively bind CD39. In some embodiments, the antibodies bind human CD39. In some embodiments, the antibodies also bind homologs of human CD39.

[0009] In some embodiments, the antibodies comprise at least one CDR sequence defined by a consensus sequence provided in this disclosure. In some embodiments, the

antibodies comprise an illustrative CDR, V_H, or V_L sequence provided in this disclosure, heavy chain or light chain provided in the disclosure, or a variant thereof. In some aspects, the variant is a variant with one or more conservative amino acid substitutions.

[0010] Also provided are compositions and kits comprising the antibodies. In some embodiments, the compositions are pharmaceutical compositions. Any suitable pharmaceutical composition may be used. In some embodiments, the pharmaceutical composition is a composition for parenteral administration.

[0011] This disclosure also provides methods of using the anti-CD39 antibodies provided herein. In some embodiments, the method is a method of treatment. In some embodiments, the method is a diagnostic method. In some embodiments, the method is an analytical method. In some embodiments, the method is a method of purifying and/or quantifying CD39.

[0012] In some embodiments, the antibodies are used to treat a disease or condition. In some aspects, the disease or condition is selected from a cancer, autoimmune disease, and infection.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] **FIG. 1** provides a table showing monovalent affinity of anti-huCD39 antibodies to recombinant human CD39 extracellular domain. The table provides binding kinetics of anti-CD39 antibodies interacting with soluble recombinant human CD39 (ENTDP1) extracellular domain (ECD) by biolayer interferometry (ForteBio Octet). Anti-CD39 antibodies were captured on an anti-human Fc sensor and exposed to recombinant human CD39 ECD at concentration ranging from 10-300 nanomolar. The kinetic data was globally fit with a simple 1:1 Langmuir binding model to yield on-rate (kon) and off-rate (koff) values. The equilibrium dissociation constants (K_D) were calculated from the kon and koff values.

[0014] **FIGS. 2 A-E** show inhibition of enzymatic catabolism of ATP and ADP to Pi by human CD39 extracellular domain (ECD). Recombinant human CD39 at a final concentration of either 10 nanomolar (A-D) or 5 nanomolar (E) was incubated with anti-CD39 IgGs at a final concentration of either 1 micromolar (A-D) or 0.25 micromolar (E) in 25 mM Tris, 5 mM $CaCl_2$, pH 7.5 at room temperature for 2 hours. ATP (500 micromolar) was added to the reaction and incubated at 37°C for 60 minutes. Residual ATP levels in the reaction were measured using the CellTiter-Glo assay. Data values are the average of two replicates.

[0015] **FIG. 2 F** shows antibodies that bind to CHO cells expressing human or cyno

CD39.

[0016] **FIG. 3** shows evaluation of antibody binding to MEL-28 (A) and 721 (B) cells. Anti-CD39 antibodies (each antibody clone number indicated in the figure) were titrated from 15 to 0.001 μg/ml. EC_{50}s were calculated using GraphPad Prism Software. The figure represents three independent experiments.

[0017] **FIG. 4** provides evaluation of antibody driven inhibition of ATP hydrolysis of CD39 on MEL-28 cells in a short term ATP assay. FIG. 4A shows the results when anti-CD39 antibodies were compared to the non-specific small molecule inhibitors POM-1 and ARL. Inhibition is determined by decreased phosphate release (Pi). Data is representative of at least 10 independent experiments. Anti-CD39 antibodies (each antibody clone number is indicated in the figure) were titrated from 15 to 0.001 μg/ml. IC50 values were calculated using GraphPad Prism Software, as can be seen in FIG. 4B. Three independent experiments were performed.

[0018] **FIG. 5** provides an illustration of quantification when MEL-28 cells are treated with CD39 enzymatic inhibitors. FIG. 5A shows evaluation of ATP levels after incubating MEL-28 cells with a dose titration of anti-CD39 antibodies that inhibit enzymatic activity. FIG. 5B provides IC50 values calculated using GrapPad Prism. At least three independent experiments were performed.

[0019] **FIG. 6** shows that antibodies were evaluated for inhibiting CD39 enzymatic activity overnight to MEL-28 cells. FIG. 6A shows anti-CD39 antibodies (each number represents a unique clone indicated in the figure) were titrated from 100nM to 0.000610 nM. FIG. 6B provide IC50 values calculated using GraphPad Prism Software. Three independent experiments are represented.

[0020] **FIG. 7** shows results of testing of antibodies for binding to CD39 on human and cyno primary B cells. In FIG. 7A, anti-CD39 antibodies were titrated on purified B cells from healthy donor and detected with anti-human IgG-PE secondary antibody. EC50 was calculated using GrapPad Prism software. In FIG. 7B, anti-CD39 antibodies were titrated on cyno PBMCs and detected using a-human IgG PE secondary antibody. B cells were gated using FlowJo software and EC_{50}s were calculated using GraphPad Prism.

[0021] **FIG. 8** sets forth antibodies that were evaluated for inhibition of CD39 activity on primary human B cells. Anti-CD39 antibodies (each unique antibody clone number indicated is in the figure) were titrated from 100 to 0.00013 nM.

[0022] **FIG. 9** provides evaluation of inhibition of CD39 activity on primary human (a) and cyno (b) monocytes. Anti-CD39 antibodies (each number represents a unique antibody clone number as indicated in the figure) were titrated from 100 to 0.00013 nM and incubated with monocytes in presence of ATP. Phosphate release by CD39 processing of ATP was quantified using Malachite Green assay.

[0023] **FIG. 10** shows binding of anti-CD39 antibodies on purified human $CD4^+CD25^+CD127^{dim}$ Treg cells by FACS. Anti-CD39 antibodies were titrated on purified Treg from healthy donor and detected with anti-human IgG secondary antibody. EC_{50}s were calculated using GraphPad Prism software.

[0024] **FIG. 11** shows results for antibody ability to inhibit primary Treg CD39 activity. $CD24^+CD25^+CD127^{dim}$ T regulatory cells were incubated with serially diluted anti-CD39 antibodies and tested for ATPase activity after addition of exogenous ATP. Free phosphate (Pi) was used as a readout of CD39 activity.

[0025] **FIG. 12** shows treatment with anti-CD39 antibodies increase the percent of IFN gamma producing $CD8^+$ T cells that respond to CMV peptides in an antigen recall response assay.

[0026] **FIG. 13** shows evaluation of antibodies for inhibition of CD39 activity on MEL-28 (FIG. 13A.) and human monocytes (FIG. 13B.) as compared to the anti-CD39 antibodies generated based on Innate/Orega (BY-40v9) and Igenica (9-8B) and variants thereof. Anti-CD39 antibodies were titrated as indicated and incubated in presence of ATP. Phosphate release by CD39 processing of ATP was quantified using Malachite Green assay.

[0027] **FIGS. 14 A-G** provides examples of antibodies. FIG. 14A provides examples of antibodies that bind soluble recombinant CD39 ECD and cellular CD39 but do not inhibit ATPase activity and do not compete with cellular inhibitors for binding to ECD inhibitors. FIG. 14B provides examples of antibodies that have limited ability to inhibit the ATPase activity of both soluble recombinant and cellular CD39 and bin separately from other cellular CD39 inhibitors. FIG. 14C provides example of antibodies that inhibit the ATPase activity of soluble recombinant CD39 ECD but do not inhibit cellular CD39 and bin separately from other CD39 ECD inhibitors. FIG. 14D provides examples of antibodies that inhibit the ATPase activity of ECD and cellular CD39 and bin separately from other CD39 ECD and/or cellular inhibitors. FIG. 14E provides examples of inhibitory antibodies that make distinct contacts with CD39. FIG. 14E has two tables, Table 1 and Table 2. Table 1 provides examples of

inhibitory antibodies that make distinct contacts with CD39. Table 2 provides examples of inhibitory antibodies that bind critical yet distinct contacts residues with CD39. FIG. 14F and FIG. 14G provide FACS plotting highlighting the importance of certain human CD39 residues.

[0028] **FIG. 15** shows that anti-CD39 antibodies inihibit CD39 by 75-90%. Anti-CD39 antibodies (100 nanomolar), isotype control antibody (100 nanomolar), or ARL (200 micromolar) were incubated with MEL-28 cells endogenously expressing human CD39 for 2 hours. ATP was then added and the rate of ATP hydrolysis to Pi by CD39 was monitored using the EnzChek kinetic Pi detection assay. The initial enzyme velocity, $\nu 0$, was determined from the linear region of Pi vs. time curve over the first 15 minutes post-ATP addition. Each value is the mean of 3 replicates.

[0029] **FIGS. 16A-B** shows that the CD39 inhibitor 29872 is not a competitive inhibitor due to suppression of V_{max} suppression.

[0030] **FIG. 17** shows that anti-CD39 antibodies can induce internalization of CD39 on cyno monocytes.

[0031] **FIG. 18** provides a comparison of the Kabat and Chothia numbering systems for CDR-H1. *Adapted from* Martin A.C.R. (2010). Protein Sequence and Structure Analysis of Antibody Variable Domains. In R. Kontermann & S. Dübel (Eds.), *Antibody Engineering* vol. 2 (pp. 33-51). Springer-Verlag, Berlin Heidelberg.

[0032] **FIG. 19** shows an anti-CD39 antibody increases proliferation of stimulated $CD4^+$ and $CD8^+$ T cells.

[0033] **FIG. 20** shows anti-CD39 antibody increases stimulated PBMC secretion of INF-γ, TNF-α and IL-2.

[0034] **FIG. 21** shows anti-CD39 antibody increases stimulated PBMC secretion of INF-γ, TNF-α, IL-2 and IL-1β.

[0035] **FIG. 22** shows CD39 inhibition leads to accumulation of ATP and blocks generation of adenosine.

DETAILED DESCRIPTION

1. Definitions

[0036] Unless otherwise defined, all terms of art, notations and other scientific terminology used herein are intended to have the meanings commonly understood by those of skill in the art to which this invention pertains. In some cases, terms with commonly understood

meanings are defined herein for clarity and/or for ready reference, and the inclusion of such definitions herein should not necessarily be construed to represent a difference over what is generally understood in the art. The techniques and procedures described or referenced herein are generally well understood and commonly employed using conventional methodologies by those skilled in the art, such as, for example, the widely utilized molecular cloning methodologies described in Sambrook et al., *Molecular Cloning: A Laboratory Manual* 2nd ed. (1989) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY. As appropriate, procedures involving the use of commercially available kits and reagents are generally carried out in accordance with manufacturer defined protocols and/or parameters unless otherwise noted.

[0037] As used herein, the singular forms "a," "an," and "the" include the plural referents unless the context clearly indicates otherwise.

[0038] The term "about" indicates and encompasses an indicated value and a range above and below that value. In certain embodiments, the term "about" indicates the designated value ± 10%, ± 5%, or ± 1%. In certain embodiments, the term "about" indicates the designated value ± one standard deviation of that value.

[0039] The term "combinations thereof" includes every possible combination of elements to which the term refers.

[0040] The terms "CD39" and "CD39 antigen" and "Cluster of Differentiation 39" are used interchangeably herein. CD39 is also known as also known as ectonucleoside triphosphate diphosphohydrolase-1 (gene: *ENTPD1*; protein: NTPDase1, *See* www.ncbi.nlm.nih.gov/gene/953). CD39 has also been referred to as ATPDase and SPG64. Each of the terms set forth may be used interchangeably. Unless specified otherwise, the terms include any variants, isoforms and species homologs of human CD39 that are naturally expressed by cells, or that are expressed by cells transfected with a CD39 gene. In some embodiments, CD39 proteins include murine CD39. In some embodiments, CD39 proteins include cynomolgus CD39.

[0041] The term "immunoglobulin" refers to a class of structurally related proteins generally comprising two pairs of polypeptide chains: one pair of light (L) chains and one pair of heavy (H) chains. In an "intact immunoglobulin," all four of these chains are interconnected by disulfide bonds. The structure of immunoglobulins has been well characterized. *See, e.g.,* Paul, *Fundamental Immunology* 7th ed., Ch. 5 (2013) Lippincott Williams & Wilkins,

Philadelphia, PA. Briefly, each heavy chain typically comprises a heavy chain variable region (V_H) and a heavy chain constant region (C_H). The heavy chain constant region typically comprises three domains, C_{H1}, C_{H2}, and C_{H3}. Each light chain typically comprises a light chain variable region (V_L) and a light chain constant region. The light chain constant region typically comprises one domain, abbreviated C_L.

[0042] The term "antibody" describes a type of immunoglobulin molecule and is used herein in its broadest sense. An antibody specifically includes intact antibodies (e.g., intact immunoglobulins), and antibody fragments. Antibodies comprise at least one antigen-binding domain. One example of an antigen-binding domain is an antigen binding domain formed by a V_H-V_L dimer. A "CD39 antibody," "anti-CD39 antibody," "CD39 Ab," "CD39-specific antibody" or "anti-CD39 Ab" is an antibody, as described herein, which binds specifically to the antigen CD39. In some embodiments, the antibody binds the extracellular domain of CD39.

[0043] The V_H and V_L regions may be further subdivided into regions of hypervariability ("hypervariable regions (HVRs);" also called "complementarity determining regions" (CDRs)) interspersed with regions that are more conserved. The more conserved regions are called framework regions (FRs). Each V_H and V_L generally comprises three CDRs and four FRs, arranged in the following order (from N-terminus to C-terminus): FR1 - CDR1 - FR2 - CDR2 - FR3 - CDR3 - FR4. The CDRs are involved in antigen binding, and confer antigen specificity and binding affinity to the antibody. See Kabat et al., *Sequences of Proteins of Immunological Interest* 5th ed. (1991) Public Health Service, National Institutes of Health, Bethesda, MD, incorporated by reference in its entirety.

[0044] The light chain from any vertebrate species can be assigned to one of two types, called kappa and lambda, based on the sequence of the constant domain.

[0045] The heavy chain from any vertebrate species can be assigned to one of five different classes (or isotypes): IgA, IgD, IgE, IgG, and IgM. These classes are also designated α, δ, ε, γ, and μ, respectively. The IgG and IgA classes are further divided into subclasses on the basis of differences in sequence and function. Humans express the following subclasses: IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2.

[0046] The amino acid sequence boundaries of a CDR can be determined by one of skill in the art using any of a number of known numbering schemes, including those described by Kabat et al., *supra* ("Kabat" numbering scheme); Al-Lazikani et al., 1997, *J. Mol. Biol.*, 273:927-948 ("Chothia" numbering scheme); MacCallum et al., 1996, *J. Mol. Biol.* 262:732-

745 ("Contact" numbering scheme); Lefranc et al., *Dev. Comp. Immunol.*, 2003, 27:55-77 ("IMGT" numbering scheme); and Honegge and Plückthun, *J. Mol. Biol.*, 2001, 309:657-70 ("AHo" numbering scheme), each of which is incorporated by reference in its entirety.

[0047] Table 1 provides the positions of CDR-L1, CDR-L2, CDR-L3, CDR-H1, CDR-H2, and CDR-H3 as identified by the Kabat and Chothia schemes. For CDR-H1, residue numbering is provided using both the Kabat and Chothia numbering schemes. FIG. 1 provides a comparison of the Kabat and Chothia numbering schemes for CDR-H1. *See* Martin (2010), *supra.*

[0048] Unless otherwise specified, the numbering scheme used for identification of a particular CDR herein is the Kabat/Chothia numbering scheme. Where the residues encompassed by these two numbering schemes diverge, the numbering scheme is specified as either Kabat or Chothia.

Table 1. Residues in CDRs according to Kabat and Chothia numbering schemes.

CDR	Kabat	Chothia
L1	L24-L34	L24-L34
L2	L50-L56	L50-L56
L3	L89-L97	L89-L97
H1 (Kabat Numbering)	H31-H35B	H26-H32 or H34*
H1 (Chothia Numbering)	H31-H35	H26-H32
H2	H50-H65	H52-H56
H3	H95-H102	H95-H102

* The C-terminus of CDR-H1, when numbered using the Kabat numbering convention, varies between H32 and H34, depending on the length of the CDR, as illustrated in FIG. 1.

[0049] The "EU numbering scheme" is generally used when referring to a residue in an antibody heavy chain constant region (e.g., as reported in Kabat et al., *supra*). Unless stated otherwise, the EU numbering scheme is used to refer to residues in antibody heavy chain constant regions described herein.

[0050] An "antibody fragment" comprises a portion of an intact antibody, such as the antigen binding or variable region of an intact antibody. Antibody fragments include, for example, Fv fragments, Fab fragments, $F(ab')_2$ fragments, Fab′ fragments, scFv (sFv) fragments, and scFv-Fc fragments.

[0051] "Fv" fragments comprise a non-covalently-linked dimer of one heavy chain variable domain and one light chain variable domain.

[0052] "Fab" fragments comprise, in addition to the heavy and light chain variable domains, the constant domain of the light chain and the first constant domain (C_{H1}) of the heavy chain. Fab fragments may be generated, for example, by papain digestion of a full-length antibody.

[0053] "F(ab')$_2$" fragments contain two Fab' fragments joined, near the hinge region, by disulfide bonds. F(ab')$_2$ fragments may be generated, for example, by pepsin digestion of an intact antibody. The F(ab') fragments can be dissociated, for example, by treatment with ß-mercaptoethanol.

[0054] "Single-chain Fv" or "sFv" or "scFv" antibody fragments comprise a V_H domain and a V_L domain in a single polypeptide chain. The V_H and V_L are generally linked by a peptide linker. *See* Plückthun A. (1994). Antibodies from *Escherichia coli*. In Rosenberg M. & Moore G.P. (Eds.), *The Pharmacology of Monoclonal Antibodies* vol. 113 (pp. 269-315). Springer-Verlag, New York, incorporated by reference in its entirety. "scFv-Fc" fragments comprise an scFv attached to an Fc domain. For example, an Fc domain may be attached to the C-terminal of the scFv. The Fc domain may follow the V_H or V_L, depending on the orientation of the variable domains in the scFv (i.e., V_H-V_L or V_L-V_H). Any suitable Fc domain known in the art or described herein may be used.

[0055] The term "monoclonal antibody" refers to an antibody from a population of substantially homogeneous antibodies. A population of substantially homogeneous antibodies comprises antibodies that are substantially similar and that bind the same epitope(s), except for variants that may normally arise during production of the monoclonal antibody. Such variants are generally present in only minor amounts. A monoclonal antibody is typically obtained by a process that includes the selection of a single antibody from a plurality of antibodies. For example, the selection process can be the selection of a unique clone from a plurality of clones, such as a pool of hybridoma clones, phage clones, yeast clones, bacterial clones, or other recombinant DNA clones. The selected antibody can be further altered, for example, to improve affinity for the target ("affinity maturation"), to humanize the antibody, to improve its production in cell culture, and/or to reduce its immunogenicity in a subject.

[0056] The term "chimeric antibody" refers to an antibody in which a portion of the heavy and/or light chain is derived from a particular source or species, while the remainder of the heavy and/or light chain is derived from a different source or species.

[0057] "Humanized" forms of non-human antibodies are chimeric antibodies that

contain minimal sequence derived from the non-human antibody. A humanized antibody is generally a human immunoglobulin (recipient antibody) in which residues from one or more CDRs are replaced by residues from one or more CDRs of a non-human antibody (donor antibody). The donor antibody can be any suitable non-human antibody, such as a mouse, rat, rabbit, chicken, or non-human primate antibody having a desired specificity, affinity, or biological effect. In some instances, selected framework region residues of the recipient antibody are replaced by the corresponding framework region residues from the donor antibody. Humanized antibodies may also comprise residues that are not found in either the recipient antibody or the donor antibody. Such modifications may be made to further refine antibody function. For further details, *see* Jones et al., *Nature*, 1986, 321:522-525; Riechmann et al., *Nature*, 1988, 332:323-329; and Presta, *Curr. Op. Struct. Biol.*, 1992, 2:593-596, each of which is incorporated by reference in its entirety.

[0058] A "human antibody" is one which possesses an amino acid sequence corresponding to that of an antibody produced by a human or a human cell, or derived from a non-human source that utilizes a human antibody repertoire or human antibody-encoding sequences (e.g., obtained from human sources or designed *de novo*). Human antibodies specifically exclude humanized antibodies.

[0059] An "isolated antibody" is one that has been separated and/or recovered from a component of its natural environment. Components of the natural environment may include enzymes, hormones, and other proteinaceous or nonproteinaceous materials. In some embodiments, an isolated antibody is purified to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence, for example by use of a spinning cup sequenator. In some embodiments, an isolated antibody is purified to homogeneity by gel electrophoresis (e.g., SDS-PAGE) under reducing or nonreducing conditions, with detection by Coomassie blue or silver stain. An isolated antibody includes an antibody *in situ* within recombinant cells, since at least one component of the antibody's natural environment is not present. In some aspects, an isolated antibody is prepared by at least one purification step.

[0060] In some embodiments, an isolated antibody is purified to at least 80%, 85%, 90%, 95%, or 99% by weight. In some embodiments, an isolated antibody is provided as a solution comprising at least 85%, 90%, 95%, 98%, 99% to 100% by weight of an antibody, the remainder of the weight comprising the weight of other solutes dissolved in the solvent.

[0061] "Affinity" refers to the strength of the sum total of non-covalent interactions

between a single binding site of a molecule (e.g., an antibody) and its binding partner (e.g., an antigen). Unless indicated otherwise, as used herein, "binding affinity" refers to intrinsic binding affinity, which reflects a 1:1 interaction between members of a binding pair (e.g., antibody and antigen). The affinity of a molecule X for its partner Y can generally be represented by the dissociation constant (K_D). Affinity can be measured by common methods known in the art, including those described herein. Affinity can be determined, for example, using surface plasmon resonance (SPR) technology, such as a Biacore® instrument.

[0062] With regard to the binding of an antibody to a target molecule, the terms "specific binding," "specifically binds to," "specific for," "selectively binds," and "selective for" a particular antigen (e.g., a polypeptide target) or an epitope on a particular antigen mean binding that is measurably different from a non-specific or non-selective interaction. Specific binding can be measured, for example, by determining binding of a molecule compared to binding of a control molecule. Specific binding can also be determined by competition with a control molecule that is similar to the target, such as an excess of non-labeled target. In that case, specific binding is indicated if the binding of the labeled target to a probe is competitively inhibited by the excess non-labeled target.

[0063] The term "k_d" (sec^{-1}), as used herein, refers to the dissociation rate constant of a particular antibody-antigen interaction. This value is also referred to as the k_{off} value.

[0064] The term "k_a" ($M^{-1} \times sec^{-1}$), as used herein, refers to the association rate constant of a particular antibody-antigen interaction. This value is also referred to as the k_{on} value.

[0065] The term "K_D" (M), as used herein, refers to the dissociation equilibrium constant of a particular antibody-antigen interaction. $K_D = k_d/k_a$.

[0066] The term "K_A" (M^{-1}), as used herein, refers to the association equilibrium constant of a particular antibody-antigen interaction. $K_A = k_a/k_d$.

[0067] An "affinity matured" antibody is one with one or more alterations in one or more CDRs or FRs that result in an improvement in the affinity of the antibody for its antigen, compared to a parent antibody which does not possess the alteration(s). In one embodiment, an affinity matured antibody has nanomolar or picomolar affinity for the target antigen. Affinity matured antibodies may be produced using a variety of methods known in the art. For example, Marks et al. (*Bio/Technology*, 1992, 10:779-783, incorporated by reference in its entirety) describes affinity maturation by V_H and V_L domain shuffling. Random mutagenesis of CDR and/or framework residues is described by, for example, Barbas et al. (*Proc. Nat. Acad. Sci.*

U.S.A., 1994, 91:3809-3813); Schier et al., *Gene*, 1995, 169:147-155; Yelton et al., *J. Immunol.*, 1995, 155:1994-2004; Jackson et al., *J. Immunol.*, 1995, 154:3310-33199; and Hawkins et al, *J. Mol. Biol.*, 1992, 226:889-896, each of which is incorporated by reference in its entirety.

[0068] When used herein in the context of two or more antibodies, the term "competes with" or "cross-competes with" indicates that the two or more antibodies compete for binding to an antigen (e.g., CD39). In one exemplary assay, CD39 is coated on a plate and allowed to bind a first antibody, after which a second, labeled antibody is added. If the presence of the first antibody reduces binding of the second antibody, then the antibodies compete. The term "competes with" also includes combinations of antibodies where one antibody reduces binding of another antibody, but where no competition is observed when the antibodies are added in the reverse order. However, in some embodiments, the first and second antibodies inhibit binding of each other, regardless of the order in which they are added. In some embodiments, one antibody reduces binding of another antibody to its antigen by at least 50%, at least 60%, at least 70%, at least 80%, or at least 90%.

[0069] The term "epitope" means a portion of an antigen capable of specific binding to an antibody. Epitopes frequently consist of surface-accessible amino acid residues and/or sugar side chains and may have specific three dimensional structural characteristics, as well as specific charge characteristics. Conformational and non-conformational epitopes are distinguished in that the binding to the former but not the latter is lost in the presence of denaturing solvents. An epitope may comprise amino acid residues that are directly involved in the binding, and other amino acid residues, which are not directly involved in the binding. The epitope to which an antibody binds can be determined using known techniques for epitope determination such as, for example, testing for antibody binding to CD39 variants with different point-mutations.

[0070] Percent "identity" between a polypeptide sequence and a reference sequence is defined as the percentage of amino acid residues in the polypeptide sequence that are identical to the amino acid residues in the reference sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN, MEGALIGN (DNASTAR), CLUSTALW, or CLUSTAL OMEGA software. Those skilled in the art can determine appropriate parameters for aligning

sequences, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared.

[0071] A "conservative substitution" or a "conservative amino acid substitution," refers to the substitution of one or more amino acids with one or more chemically or functionally similar amino acids. Conservative substitution tables providing similar amino acids are well known in the art. Polypeptide sequences having such substitutions are known as "conservatively modified variants." Such conservatively modified variants are in addition to and do not exclude polymorphic variants, interspecies homologs, and alleles. By way of example, the following groups of amino acids are considered conservative substitutions for one another.

Acidic Residues	D and E
Basic Residues	K, R, and H
Hydrophilic Uncharged Residues	S, T, N, and Q
Aliphatic Uncharged Residues	G, A, V, L, and I
Non-polar Uncharged Residues	C, M, and P
Aromatic Residues	F, Y, and W

Alcohol Group-Containing Residues	S and T
Aliphatic Residues	I, L, V, and M
Cycloalkenyl-associated Residues	F, H, W, and Y
Hydrophobic Residues	A, C, F, G, H, I, L, M, R, T, V, W, and Y
Negatively Charged Residues	D and E
Polar Residues	C, D, E, H, K, N, Q, R, S, and T
Positively Charged Residues	H, K, and R
Small Residues	A, C, D, G, N, P, S, T, and V
Very Small Residues	A, G, and S
Residues Involved in Turn Formation	A, C, D, E, G, H, K, N, Q, R, S, P, and T
Flexible Residues	Q, T, K, S, G, P, D, E, and R

Group 1	A, S, and T
Group 2	D and E
Group 3	N and Q
Group 4	R and K
Group 5	I, L, and M
Group 6	F, Y, and W

Group A	A and G
Group B	D and E
Group C	N and Q
Group D	R, K, and H

Group E	I, L, M, V
Group F	F, Y, and W
Group G	S and T
Group H	C and M

Additional conservative substitutions may be found, for example, in Creighton, *Proteins: Structures and Molecular Properties* 2nd ed. (1993) W. H. Freeman & Co., New York, NY. An antibody generated by making one or more conservative substitutions of amino acid residues in a parent antibody is referred to as a "conservatively modified variant."

[0072] The term "amino acid" refers to the twenty common naturally occurring amino acids. Naturally occurring amino acids include alanine (Ala; A), arginine (Arg; R), asparagine (Asn; N), aspartic acid (Asp; D), cysteine (Cys; C); glutamic acid (Glu; E), glutamine (Gln; Q), Glycine (Gly; G); histidine (His; H), isoleucine (Ile; I), leucine (Leu; L), lysine (Lys; K), methionine (Met; M), phenylalanine (Phe; F), proline (Pro; P), serine (Ser; S), threonine (Thr; T), tryptophan (Trp; W), tyrosine (Tyr; Y), and valine (Val; V).

[0073] "Treating" or "treatment" of any disease or disorder refers, in certain embodiments, to ameliorating a disease or disorder that exists in a subject. In another embodiment, "treating" or "treatment" includes ameliorating at least one physical parameter, which may be indiscernible by the subject. In yet another embodiment, "treating" or "treatment" includes modulating the disease or disorder, either physically (e.g., stabilization of a discernible symptom) or physiologically (e.g., stabilization of a physical parameter) or both. In yet another embodiment, "treating" or "treatment" includes delaying or preventing the onset of the disease or disorder.

[0074] As used herein, the term "therapeutically effective amount" or "effective amount" refers to an amount of an antibody or composition that when administered to a subject is effective to treat a disease or disorder.

[0075] As used herein, the term "subject" means a mammalian subject. Exemplary subjects include, but are not limited to humans, monkeys, dogs, cats, mice, rats, cows, horses, camels, avians, goats, and sheep. In certain embodiments, the subject is a human. In some embodiments, the subject has cancer, an autoimmune disease or condition, and/or an infection that can be treated with an antibody provided herein. In some embodiments, the subject is a human that is suspected to have cancer, an autoimmune disease or condition, and/or an infection.

2. Antibodies

[0076] Provided herein are antibodies that selectively bind human CD39, as well as the nucleic acids that encode the antibodies. In some aspects, the antibody selectively binds to the extracellular domain of human CD39.

[0077] In some embodiments, the antibody binds to homologs of human CD39. In some aspects, the antibody binds to a homolog of human CD39 from a species selected from monkeys, mice, dogs, cats, rats, cows, horses, goats, and sheep. In some aspects, the homolog is a cynomolgus monkey homolog. In some aspects, the homolog is a murine homolog.

[0078] In some embodiments, the antibody has one or more CDRs having particular lengths, in terms of the number of amino acid residues. In some embodiments, the Chothia CDR-H1 of the antibody is 6, 7, 8, or 9 residues in length. In some embodiments, the Kabat CDR-H1 of the antibody is 4, 5, 6, or 7 residues in length. In some embodiments, the Chothia CDR-H2 of the antibody is 5, 6, or 7 residues in length. In some embodiments, the Kabat CDR-H2 of the antibody is 15, 16, 17, or 18 residues in length. In some embodiments, the Kabat/Chothia CDR-H3 of the antibody is 5, 6, 7, 8, 9, 10, 11, or 12 residues in length.

[0079] In some aspects, the Kabat/Chothia CDR-L1 of the antibody is 9, 10, 11, 12, 13, 14, 15, or 16 residues in length. In some aspects, the Kabat/Chothia CDR-L2 of the antibody is 6, 7, or 8 residues in length. In some aspects, the Kabat/Chothia CDR-L3 of the antibody is 8, 9, 10, 11, or 12 residues in length.

[0080] In some embodiments, the antibody comprises a light chain. In some aspects, the light chain is a kappa light chain. In some aspects, the light chain is a lambda light chain.

[0081] In some embodiments, the antibody comprises a heavy chain. In some aspects, the heavy chain is an IgA. In some aspects, the heavy chain is an IgD. In some aspects, the heavy chain is an IgE. In some aspects, the heavy chain is an IgG. In some aspects, the heavy chain is an IgM. In some aspects, the heavy chain is an IgG1. In some aspects, the heavy chain is an IgG2. In some aspects, the heavy chain is an IgG3. In some aspects, the heavy chain is an IgG4. In some aspects, the heavy chain is an IgA1. In some aspects, the heavy chain is an IgA2.

[0082] In some embodiments, the antibody is an antibody fragment. In some aspects, the antibody fragment is an Fv fragment. In some aspects, the antibody fragment is a Fab fragment. In some aspects, the antibody fragment is a $F(ab')_2$ fragment. In some aspects, the antibody fragment is a Fab′ fragment. In some aspects, the antibody fragment is an scFv (sFv) fragment. In some aspects, the antibody fragment is an scFv-Fc fragment.

[0083] In some embodiments, the antibody is a monoclonal antibody. In some embodiments, the antibody is a polyclonal antibody.

[0084] In some embodiments, the antibody is a chimeric antibody. In some embodiments, the antibody is a humanized antibody. In some embodiments, the antibody is a human antibody.

[0085] In some embodiments, the antibody is an affinity matured antibody. In some aspects, the antibody is an affinity matured antibody derived from an illustrative sequence provided in this disclosure.

[0086] In some aspects, the antibody inhibits conversion by CD39 of ATP to ADP and/or ADP to AMP. In some aspects, the antibody decreases the levels of phosphate, ADP, AMP, and/or adenosine and/or increases the levels of ATP.

[0087] In some embodiments, the antibody increases proliferation of stimulated $CD4^+$ and $CD8^+$ T cells. In some embodiments, the antibody increases stimulated PBMC secretion of INF-γ, TNF-α, IL-2, and/or IL-1β.

[0088] In some embodiments, the antibody increases a T effector cell function. In some embodiments, the antibody decreases the number of regulatory T cells in tissues or in circulation. In some embodiments, the antibody suppresses a regulatory or T cell activity. In some embodiments, the antibody increase B cell function. In some embodiments, the antibody increases antigen presenting cell function. In some embodiments, the antibody decreases or prevents activation of phospho antigen specific T cells selected from MAIT cells and gamma delta T cells.

[0089] In some aspects, the decrease is about or less than a 10% decrease, about or less than a 20% decrease, about or less than a 30% decrease, about or less than a 40% decrease, about or less than a 50% decrease, about or less than a 60% decrease, about or less than a 70% decrease, about or less than an 80% decrease, about or less than a 90% decrease, or about a complete decrease. In some aspects, the increase is about or greater than a 10% increase, about or greater than a 20% increase, about or greater than a 30% increase, about or greater than a 40% increase, about or greater than a 50% increase, about or greater than a 60% increase, about or greater than a 70% increase, about or greater than an 80% increase, about or greater than a 90% increase, or a complete increase.

[0090] Given that CD39 degrades ATP and ADP to adenosine, CD39 can be viewed as

an immunological switch that shifts ATP-driven pro-inflammatory immune cell activity toward an anti-inflammatory state mediated by adenosine. CD39 has a role in regulating the function of several immune cell types, including lymphocytes, neutrophils, monocytes/macrophages, dendritic cells, and endothelial cells and shifting the switch can have a significant impact on disease. For example, the generation of adenosine via CD39 is recognized as a major mechanism of regulatory T cell (Treg) immunosuppressive function.

[0091] The antibodies provided herein may be useful for the treatment of a variety of diseases and conditions, including cancers, autoimmune diseases, and infections. In some embodiments, the antibody inhibits CD39 function on tumor cells. In some embodiments, the antibody inhibits angiogenesis.

[0092] The frequency of $CD39^+$ Tregs and the expression on the cell surface is increased in some human cancers, and the importance of $CD39^+$ Tregs in promoting tumor growth and metastasis has been demonstrated using several in vivo models. Immunohistochemical staining of normal and tumor tissues has revealed that CD39 expression is significantly higher in several types of human cancer than in normal tissues. In cancer specimens, CD39 is expressed by infiltrating lymphocytes, the tumor stroma, and/or tumor cells. CD39 in cancer cells displays ATPase activity and generates adenosine. $CD39^+$ cancer cells inhibited the proliferation of CD4 and CD8 T cells and the generation of cytotoxic effector CD8 T cells (CTL) in a CD39- and adenosine-dependent manner.

2.1. CDR-H3 Sequences

[0093] In some embodiments, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 82-109. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 82. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 83. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 84. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 85. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 86. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 87. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 88. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting

of, or consisting essentially of SEQ ID NO: 89. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 90. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 91. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 92. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 93. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 94. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 95. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 96. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 97. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 98. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 99. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 100. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 101. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 102. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 103. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 104. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 105. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 106. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 107. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 108. In some aspects, the antibody comprises a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 109.

[0094] In some aspects, the CDR-H3 sequence comprises, consists of, or consists essentially of a variant of an illustrative CDR-H3 sequence provided in this disclosure. In some aspects, the CDR-H3 sequence comprises, consists of, or consists essentially of a sequence

having at least 70%, 75%, 80%, 85%, 90%, or 95% identity with any of the illustrative CDR-H3 sequences provided in this disclosure. In some aspects, the CDR-H3 sequence comprises, consists of, or consists essentially of any of the illustrative CDR-H3 sequences provided in this disclosure, with 1, 2, or 3 amino acid substitutions. In some aspects, the amino acid substitutions are conservative amino acid substitutions.

2.2. V_H Sequences Comprising Illustrative CDRs

[0095] In some embodiments, the antibody comprises a V_H sequence comprising one or more CDR-H sequences comprising, consisting of, or consisting essentially of one or more illustrative CDR-H sequences provided in this disclosure, and variants thereof.

2.2.1. V_H Sequences Comprising Illustrative Kabat CDRs

[0096] In some embodiments, the antibody comprises a V_H sequence comprising one or more Kabat CDR-H sequences comprising, consisting of, or consisting essentially of one or more illustrative Kabat CDR-H sequences provided in this disclosure, and variants thereof.

2.2.1.1.Kabat CDR-H3

[0097] In some embodiments, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 82-109. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 82. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 83. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 84. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 85. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 86. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 88. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 89. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 90. In some aspects, the

antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 91. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 92. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 93. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 94. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 95. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 96. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 97. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 98. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 99. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 100. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 101. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 102. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 103. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 104. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 105. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 106. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 107. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 108. In some aspects, the

antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 109.

2.2.1.2.Kabat CDR-H2

[0098] In some embodiments, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 63-81. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 63. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 64. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 65. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 66. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 67. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 68. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 69. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 70. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 71. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 72. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 73. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 74. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 75. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 76. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 77. In some aspects, the

antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 78. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 79. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 80. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 81.

2.2.1.3.Kabat CDR-H1

[0099] In some embodiments, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 25-45. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 25. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 26. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 27. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 28. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 29. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 30. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 31. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 32. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 33. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 34. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 35. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting

essentially of SEQ ID NO: 36. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 37. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 38. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 39. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 40. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 41. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 42. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 43. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 44. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 45.

2.2.1.4.Kabat CDR-H3 + Kabat CDR-H2

[00100] In some embodiments, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 82-109, and a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 63-81. In some aspects, the Kabat CDR-H3 sequence and the Kabat CDR-H2 sequence are both from a single illustrative V_H sequence provided in this disclosure. For example, in some aspects, the Kabat CDR-H3 and Kabat CDR-H2 are both from a single illustrative V_H sequence selected from SEQ ID NOs: 179-218.

2.2.1.5.Kabat CDR-H3 + Kabat CDR-H1

[00101] In some embodiments, the antibody comprises a V_H sequence comprising a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 82-109, and a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 25-45. In some aspects, the Kabat CDR-H3 sequence and the Kabat CDR-H1 sequence are both from a single illustrative V_H sequence provided in this disclosure. For example, in some aspects, the Kabat CDR-H3 and

Kabat CDR-H1 are both from a single illustrative V_H sequence selected from SEQ ID NOs: 179-218.

2.2.1.6.Kabat CDR-H1 + Kabat CDR-H2

[00102] In some embodiments, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 25-45 and a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 63-81. In some aspects, the Kabat CDR-H1 sequence and the Kabat CDR-H2 sequence are both from a single illustrative V_H sequence provided in this disclosure. For example, in some aspects, the Kabat CDR-H1 and Kabat CDR-H2 are both from a single illustrative V_H sequence selected from SEQ ID NOs: 179-218.

2.2.1.7.Kabat CDR-H1 + Kabat CDR-H2 + Kabat CDR-H3

[00103] In some embodiments, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 25-45, a Kabat CDR-H2 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 63-81, and a Kabat CDR-H3 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 82-109. In some aspects, the Kabat CDR-H1 sequence, Kabat CDR-H2 sequence, and Kabat CDR-H3 sequence are all from a single illustrative V_H sequence provided in this disclosure. For example, in some aspects, the Kabat CDR-H1, Kabat CDR-H2, and Kabat CDR-H3 are all from a single illustrative V_H sequence selected from SEQ ID NOs: 179-218.

[00104] In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 25, a Kabat CDR-H2 sequence comprising SEQ ID NO: 63, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 82. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 26, a Kabat CDR-H2 sequence comprising SEQ ID NO: 64, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 83. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 27, a Kabat CDR-H2 sequence comprising SEQ ID NO: 65, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 84. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 26, a Kabat CDR-H2 sequence comprising SEQ ID NO: 64, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 85. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 26, a Kabat

CDR-H2 sequence comprising SEQ ID NO: 64, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 86. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 25, a Kabat CDR-H2 sequence comprising SEQ ID NO: 66, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 82. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 26, a Kabat CDR-H2 sequence comprising SEQ ID NO: 65, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 82. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 27, a Kabat CDR-H2 sequence comprising SEQ ID NO: 65, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 82. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 28, a Kabat CDR-H2 sequence comprising SEQ ID NO: 67, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 82. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 29, a Kabat CDR-H2 sequence comprising SEQ ID NO: 68, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 82. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 26, a Kabat CDR-H2 sequence comprising SEQ ID NO: 64, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 82. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 30, a Kabat CDR-H2 sequence comprising SEQ ID NO: 69, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 31, a Kabat CDR-H2 sequence comprising SEQ ID NO: 70, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 88. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 32, a Kabat CDR-H2 sequence comprising SEQ ID NO: 71, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 89. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 33, a Kabat CDR-H2 sequence comprising SEQ ID NO: 70, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 90. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 34, a Kabat CDR-H2 sequence comprising SEQ ID NO: 72, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 91. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 30, a Kabat CDR-H2 sequence comprising SEQ ID NO: 71, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 92. In some aspects, the antibody comprises a V_H sequence

comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 35, a Kabat CDR-H2 sequence comprising SEQ ID NO: 70, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 93. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 33, a Kabat CDR-H2 sequence comprising SEQ ID NO: 70, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 92. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 36, a Kabat CDR-H2 sequence comprising SEQ ID NO: 72, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 30, a Kabat CDR-H2 sequence comprising SEQ ID NO: 73, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 37, a Kabat CDR-H2 sequence comprising SEQ ID NO: 74, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 38, a Kabat CDR-H2 sequence comprising SEQ ID NO: 75, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 94. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 39, a Kabat CDR-H2 sequence comprising SEQ ID NO: 76, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 95. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 40, a Kabat CDR-H2 sequence comprising SEQ ID NO: 76, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 96. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 39, a Kabat CDR-H2 sequence comprising SEQ ID NO: 76, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 94. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 38, a Kabat CDR-H2 sequence comprising SEQ ID NO: 69, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 97. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 41, a Kabat CDR-H2 sequence comprising SEQ ID NO: 69, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 98. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 41, a Kabat CDR-H2 sequence comprising SEQ ID NO: 69, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 99. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 41, a Kabat CDR-H2 sequence comprising SEQ ID NO: 69, and a Kabat CDR-H3 sequence comprising

SEQ ID NO: 100. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 38, a Kabat CDR-H2 sequence comprising SEQ ID NO: 75, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 101. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 42, a Kabat CDR-H2 sequence comprising SEQ ID NO: 78, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 102. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 38, a Kabat CDR-H2 sequence comprising SEQ ID NO: 75, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 103. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 43, a Kabat CDR-H2 sequence comprising SEQ ID NO: 79, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 104. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 38, a Kabat CDR-H2 sequence comprising SEQ ID NO: 69, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 103. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 38, a Kabat CDR-H2 sequence comprising SEQ ID NO: 69, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 106. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 38, a Kabat CDR-H2 sequence comprising SEQ ID NO: 69, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 107. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 44, a Kabat CDR-H2 sequence comprising SEQ ID NO: 80, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 108. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 45, a Kabat CDR-H2 sequence comprising SEQ ID NO: 81, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 109.

[00105] In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 26, a Kabat CDR-H2 sequence comprising SEQ ID NO: 65, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 83. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 26, a Kabat CDR-H2 sequence comprising SEQ ID NO: 65, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 84. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 26, a Kabat CDR-H2 sequence comprising SEQ ID NO: 65, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 85. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence

comprising SEQ ID NO: 26, a Kabat CDR-H2 sequence comprising SEQ ID NO: 65, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 86. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 26, a Kabat CDR-H2 sequence comprising SEQ ID NO: 64, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 84. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 26, a Kabat CDR-H2 sequence comprising SEQ ID NO: 64, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 86. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 27, a Kabat CDR-H2 sequence comprising SEQ ID NO: 65, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 83. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 27, a Kabat CDR-H2 sequence comprising SEQ ID NO: 65, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 86. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 30, a Kabat CDR-H2 sequence comprising SEQ ID NO: 71, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 93. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 30, a Kabat CDR-H2 sequence comprising SEQ ID NO: 73, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 30, a Kabat CDR-H2 sequence comprising SEQ ID NO: 72, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 30, a Kabat CDR-H2 sequence comprising SEQ ID NO: 70, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 31, a Kabat CDR-H2 sequence comprising SEQ ID NO: 70, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 31, a Kabat CDR-H2 sequence comprising SEQ ID NO: 71, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 32, a Kabat CDR-H2 sequence comprising SEQ ID NO: 71, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 33, a Kabat CDR-H2 sequence comprising SEQ ID NO: 71, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the

antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 33, a Kabat CDR-H2 sequence comprising SEQ ID NO: 72, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 33, a Kabat CDR-H2 sequence comprising SEQ ID NO: 70, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 33, a Kabat CDR-H2 sequence comprising SEQ ID NO: 71, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 93. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 33, a Kabat CDR-H2 sequence comprising SEQ ID NO: 70, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 93. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 34, a Kabat CDR-H2 sequence comprising SEQ ID NO: 72, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 30, a Kabat CDR-H2 sequence comprising SEQ ID NO: 71, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 35, a Kabat CDR-H2 sequence comprising SEQ ID NO: 70, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 35, a Kabat CDR-H2 sequence comprising SEQ ID NO: 70, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 90. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 30, a Kabat CDR-H2 sequence comprising SEQ ID NO: 70, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 39, a Kabat CDR-H2 sequence comprising SEQ ID NO: 76, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 94.

2.2.1.8.Variants of V_H Sequences Comprising Illustrative Kabat CDRs

[00106] In some embodiments, the V_H sequences provided herein comprise a variant of an illustrative Kabat CDR-H3, CDR-H2, and/or CDR-H1 sequence provided in this disclosure.

[00107] In some aspects, the Kabat CDR-H3 sequence comprises, consists of, or consists essentially of a variant of an illustrative Kabat CDR-H3 sequence provided in this disclosure. In some aspects, the Kabat CDR-H3 sequence comprises, consists of, or consists essentially of a sequence having at least 70%, 75%, 80%, 85%, 90%, or 95% identity with any of the

illustrative Kabat CDR-H3 sequences provided in this disclosure. In some aspects, the Kabat CDR-H3 sequence comprises, consists of, or consists essentially of any of the illustrative Kabat CDR-H3 sequences provided in this disclosure, with 1, 2, or 3 amino acid substitutions. In some aspects, the amino acid substitutions are conservative amino acid substitutions.

[00108] In some aspects, the Kabat CDR-H2 sequence comprises, consists of, or consists essentially of a variant of an illustrative Kabat CDR-H2 sequence provided in this disclosure. In some aspects, the Kabat CDR-H2 sequence comprises, consists of, or consists essentially of a sequence having at least 70%, 75%, 80%, 85%, 90%, or 95% identity with any of the illustrative Kabat CDR-H2 sequences provided in this disclosure. In some aspects, the Kabat CDR-H2 sequence comprises, consists of, or consists essentially of any of the illustrative Kabat CDR-H2 sequences provided in this disclosure, with 1, 2, or 3 amino acid substitutions. In some aspects, the amino acid substitutions are conservative amino acid substitutions.

[00109] In some aspects, the Kabat CDR-H1 sequence comprises, consists of, or consists essentially of a variant of an illustrative Kabat CDR-H1 sequence provided in this disclosure. In some aspects, the Kabat CDR-H1 sequence comprises, consists of, or consists essentially of a sequence having at least 70%, 75%, 80%, 85%, 90%, or 95% identity with any of the illustrative Kabat CDR-H1 sequences provided in this disclosure. In some aspects, the Kabat CDR-H1 sequence comprises, consists of, or consists essentially of any of the illustrative Kabat CDR-H1 sequences provided in this disclosure, with 1, 2, or 3 amino acid substitutions. In some aspects, the amino acid substitutions are conservative amino acid substitutions.

2.2.2. V_H Sequences Comprising Illustrative Chothia CDRs

[00110] In some embodiments, the antibody comprises a V_H sequence comprising one or more Chothia CDR-H sequences comprising, consisting of, or consisting essentially of one or more illustrative Chothia CDR-H sequences provided in this disclosure, and variants thereof.

2.2.2.1.Chothia CDR-H3

[00111] In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 82-109. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 82. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 83. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence

comprising, consisting of, or consisting essentially of SEQ ID NO: 84. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 85. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 86. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 87. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 88. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 89. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 90. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 91. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 92. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 93. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 94. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 95. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 96. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 97. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 98. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 99. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 100. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 101. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3

sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 102. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 103. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 104. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 105. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 106. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 107. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 108. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 109.

2.2.2.2.Chothia CDR-H2

[00112] In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 46-62. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 46. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 47. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 48. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 49. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 50. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 51. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 52. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 53. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence

comprising, consisting of, or consisting essentially of SEQ ID NO: 54. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 55. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 56. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 57. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 58. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 59. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 60. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 61. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 62.

2.2.2.3.Chothia CDR-H1

[00113] In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 1-24. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 1. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 2. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 3. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 4. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 5. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 6. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 7. In some aspects, the antibody comprises a V_H sequence comprising a Chothia

CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 8. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 9. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 10. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 11. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 12. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 13. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 14. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 15. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 16. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 17. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 18. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 19. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 20. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 21. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 22. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 23. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 24.

2.2.2.4.Chothia CDR-H3 + Chothia CDR-H2

[00114] In some embodiments, the antibody comprises a V_H sequence comprising a

Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 82-109, and a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 46-62. In some aspects, the Chothia CDR-H3 sequence and the Chothia CDR-H2 sequence are both from a single illustrative V_H sequence provided in this disclosure. For example, in some aspects, the Chothia CDR-H3 and Chothia CDR-H2 are both from a single illustrative V_H sequence selected from SEQ ID NOs: 179-218.

2.2.2.5.Chothia CDR-H3 + Chothia CDR-H1

[00115] In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 82-109, and a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 1-24. In some aspects, the Chothia CDR-H3 sequence and the Chothia CDR-H1 sequence are both from a single illustrative V_H sequence provided in this disclosure. For example, in some aspects, the Chothia CDR-H3 and Chothia CDR-H1 are both from a single illustrative V_H sequence selected from SEQ ID NOs: 179-218.

2.2.2.6.Chothia CDR-H1 + Chothia CDR-H2

[00116] In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 1-24 and a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 46-62. In some aspects, the Chothia CDR-H1 sequence and the Chothia CDR-H2 sequence are both from a single illustrative V_H sequence provided in this disclosure. For example, in some aspects, the Chothia CDR-H1 and Chothia CDR-H2 are both from a single illustrative V_H sequence selected from SEQ ID NOs: 179-218.

2.2.2.7.Chothia CDR-H1 + Chothia CDR-H2 + Chothia CDR-H3

[00117] In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 1-24, a Chothia CDR-H2 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 46-62, and a Chothia CDR-H3 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 82-109. In some aspects, the Chothia CDR-H1 sequence, Chothia CDR-H2 sequence, and Chothia CDR-H3 sequence are all from a single illustrative V_H sequence

provided in this disclosure. For example, in some aspects, the Chothia CDR-H1, Chothia CDR-H2, and Chothia CDR-H3 are all from a single illustrative V_H sequence selected from SEQ ID NOs: 179-218.

[00118] In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 1, a Chothia CDR-H2 sequence comprising SEQ ID NO: 46, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 82. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 2, a Chothia CDR-H2 sequence comprising SEQ ID NO: 47, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 83. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 1, a Chothia CDR-H2 sequence comprising SEQ ID NO: 46, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 84. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 2, a Chothia CDR-H2 sequence comprising SEQ ID NO: 47, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 85. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 3, a Chothia CDR-H2 sequence comprising SEQ ID NO: 47, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 86. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 4, a Chothia CDR-H2 sequence comprising SEQ ID NO: 46, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 82. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 2, a Chothia CDR-H2 sequence comprising SEQ ID NO: 46, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 82. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 5, a Chothia CDR-H2 sequence comprising SEQ ID NO: 49, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 82. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 6, a Chothia CDR-H2 sequence comprising SEQ ID NO: 50, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 82. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 2, a Chothia CDR-H2 sequence comprising SEQ ID NO: 47, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 82. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 7, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3

sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 8, a Chothia CDR-H2 sequence comprising SEQ ID NO: 52, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 88. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 9, a Chothia CDR-H2 sequence comprising SEQ ID NO: 53, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 89. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 10, a Chothia CDR-H2 sequence comprising SEQ ID NO: 52, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 90. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 11, a Chothia CDR-H2 sequence comprising SEQ ID NO: 54, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 91. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 12, a Chothia CDR-H2 sequence comprising SEQ ID NO: 53, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 92. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 13, a Chothia CDR-H2 sequence comprising SEQ ID NO: 52, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 93. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 10, a Chothia CDR-H2 sequence comprising SEQ ID NO: 52, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 92. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 14, a Chothia CDR-H2 sequence comprising SEQ ID NO: 54, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 15, a Chothia CDR-H2 sequence comprising SEQ ID NO: 55, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 16, a Chothia CDR-H2 sequence comprising SEQ ID NO: 56, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 94. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 18, a Chothia CDR-H2 sequence comprising SEQ ID NO: 57, and a Chothia CDR-H3

sequence comprising SEQ ID NO: 95. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 19, a Chothia CDR-H2 sequence comprising SEQ ID NO: 57, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 96. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 21, a Chothia CDR-H2 sequence comprising SEQ ID NO: 57, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 94. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 97. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 22, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 98. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 22, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 99. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 22, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 100. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 101. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 59, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 102. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 103. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 23, a Chothia CDR-H2 sequence comprising SEQ ID NO: 60, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 104. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 105. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3

sequence comprising SEQ ID NO: 106. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 107. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 61, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 108. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 62, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 109.

[00119] In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 2, a Chothia CDR-H2 sequence comprising SEQ ID NO: 46, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 83. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 2, a Chothia CDR-H2 sequence comprising SEQ ID NO: 46, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 84. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 2, a Chothia CDR-H2 sequence comprising SEQ ID NO: 46, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 85. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 2, a Chothia CDR-H2 sequence comprising SEQ ID NO: 46, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 86. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 2, a Chothia CDR-H2 sequence comprising SEQ ID NO: 47, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 84. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 2, a Chothia CDR-H2 sequence comprising SEQ ID NO: 47, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 86. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 1, a Chothia CDR-H2 sequence comprising SEQ ID NO: 46, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 83. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 1, a Chothia CDR-H2 sequence comprising SEQ ID NO: 46, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 86. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 10, a Chothia CDR-H2 sequence

comprising SEQ ID NO: 53, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 93. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 10, a Chothia CDR-H2 sequence comprising SEQ ID NO: 55, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 10, a Chothia CDR-H2 sequence comprising SEQ ID NO: 54, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 10, a Chothia CDR-H2 sequence comprising SEQ ID NO: 52, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 8, a Chothia CDR-H2 sequence comprising SEQ ID NO: 52, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 8, a Chothia CDR-H2 sequence comprising SEQ ID NO: 53, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 9, a Chothia CDR-H2 sequence comprising SEQ ID NO: 53, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 10, a Chothia CDR-H2 sequence comprising SEQ ID NO: 53, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 10, a Chothia CDR-H2 sequence comprising SEQ ID NO: 54, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 10, a Chothia CDR-H2 sequence comprising SEQ ID NO: 52, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 10, a Chothia CDR-H2 sequence comprising SEQ ID NO: 53, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 93. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 10, a Chothia CDR-H2 sequence comprising SEQ ID NO: 52, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 93. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 11, a Chothia CDR-H2 sequence

comprising SEQ ID NO: 54, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 12, a Chothia CDR-H2 sequence comprising SEQ ID NO: 53, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 13, a Chothia CDR-H2 sequence comprising SEQ ID NO: 52, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 13, a Chothia CDR-H2 sequence comprising SEQ ID NO: 52, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 90. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 15, a Chothia CDR-H2 sequence comprising SEQ ID NO: 52, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87. In some embodiments, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 18, a Chothia CDR-H2 sequence comprising SEQ ID NO: 57, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 94.

2.2.2.8.Variants of V_H Sequences Comprising Illustrative Chothia CDRs

[00120] In some embodiments, the V_H sequences provided herein comprise a variant of an illustrative Chothia CDR-H3, CDR-H2, and/or CDR-H1 sequence provided in this disclosure.

[00121] In some aspects, the Chothia CDR-H3 sequence comprises, consists of, or consists essentially of a variant of an illustrative Chothia CDR-H3 sequence provided in this disclosure. In some aspects, the Chothia CDR-H3 sequence comprises, consists of, or consists essentially of a sequence having at least 70%, 75%, 80%, 85%, 90%, or 95% identity with any of the illustrative Chothia CDR-H3 sequences provided in this disclosure. In some aspects, the Chothia CDR-H3 sequence comprises, consists of, or consists essentially of any of the illustrative Chothia CDR-H3 sequences provided in this disclosure, with 1, 2, or 3 amino acid substitutions. In some aspects, the amino acid substitutions are conservative amino acid substitutions.

[00122] In some aspects, the Chothia CDR-H2 sequence comprises, consists of, or consists essentially of a variant of an illustrative Chothia CDR-H2 sequence provided in this disclosure. In some aspects, the Chothia CDR-H2 sequence comprises, consists of, or consists essentially of a sequence having at least 70%, 75%, 80%, 85%, 90%, or 95% identity with any of the illustrative Chothia CDR-H2 sequences provided in this disclosure. In some aspects, the

Chothia CDR-H2 sequence comprises, consists of, or consists essentially of any of the illustrative Chothia CDR-H2 sequences provided in this disclosure, with 1, 2, or 3 amino acid substitutions. In some aspects, the amino acid substitutions are conservative amino acid substitutions.

[00123] In some aspects, the Chothia CDR-H1 sequence comprises, consists of, or consists essentially of a variant of an illustrative Chothia CDR-H1 sequence provided in this disclosure. In some aspects, the Chothia CDR-H1 sequence comprises, consists of, or consists essentially of a sequence having at least 70%, 75%, 80%, 85%, 90%, or 95% identity with any of the illustrative Chothia CDR-H1 sequences provided in this disclosure. In some aspects, the Chothia CDR-H1 sequence comprises, consists of, or consists essentially of any of the illustrative Chothia CDR-H1 sequences provided in this disclosure, with 1, 2, or 3 amino acid substitutions. In some aspects, the amino acid substitutions are conservative amino acid substitutions.

2.3. V_H Sequences

[00124] In some embodiments, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 179-218. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 179. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 180. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 181. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 182. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 183. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 184. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 185. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 186. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 187. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 188. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 189. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 190. In some aspects, the

antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 191. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 192. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 193. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 194. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 195. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 196. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 197. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 198. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 199. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 200. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 201. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 202. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 203. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 204. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 205. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 206. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 207. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 208. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 209. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 210. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 211. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 212. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 213. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting

essentially of SEQ ID NO: 214. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 215. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 216. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 217. In some aspects, the antibody comprises a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 218.

2.3.1. Variants of V_H Sequences

[00125] In some embodiments, the V_H sequences provided herein comprise, consist of, or consist essentially of a variant of an illustrative V_H sequence provided in this disclosure.

[00126] In some aspects, the V_H sequence comprises, consists of, or consists essentially of a variant of an illustrative V_H sequence provided in this disclosure. In some aspects, the V_H sequence comprises, consists of, or consists essentially of a sequence having at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 99.5% identity with any of the illustrative V_H sequences provided in this disclosure.

[00127] In some embodiments, the V_H sequence comprises, consists of, or consists essentially of any of the illustrative V_H sequences provided in this disclosure, 20 or fewer, 19 or fewer, 18 or fewer, 17 or fewer, 16 or fewer, 15 or fewer, 14 or fewer, 13 or fewer, 12 or fewer, 11 or fewer, 10 or fewer, 9 or fewer, 8 or fewer, 7 or fewer, 6 or fewer, 5 or fewer, 4 or fewer, 3 or fewer, 2 or fewer, or 1 or fewer amino acid substitutions. In some aspects, the amino acid substitutions are conservative amino acid substitutions.

2.4. CDR-L3 Sequences

[00128] In some embodiments, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 141-166. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 141. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 142. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 143. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 144. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 145. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 146. In some aspects, the antibody

comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 147. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 148. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 149. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 150. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 151. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 152. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 153. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 154. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 155. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 156. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 157. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 158. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 159. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 160. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 161. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 162. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 163. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 164. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 165. In some aspects, the antibody comprises a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 166.

[00129] In some aspects, the CDR-L3 sequence comprises, consists of, or consists essentially of a variant of an illustrative CDR-L3 sequence provided in this disclosure. In some aspects, the CDR-L3 sequence comprises, consists of, or consists essentially of a sequence having at least 70%, 75%, 80%, 85%, 90%, or 95% identity with any of the illustrative CDR-

L3 sequences provided in this disclosure. In some aspects, the CDR-L3 sequence comprises, consists of, or consists essentially of any of the illustrative CDR-L3 sequences provided in this disclosure, with 1, 2, or 3 amino acid substitutions. In some aspects, the amino acid substitutions are conservative amino acid substitutions.

2.5. V_L Sequences Comprising Illustrative CDRs

[00130] In some embodiments, the antibody comprises a V_L sequence comprising one or more CDR-L sequences comprising, consisting of, or consisting essentially of one or more illustrative CDR-L sequences provided in this disclosure, and variants thereof.

2.5.1. CDR-L3

[00131] In some embodiments, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 141-166. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 141. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 142. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 143. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 144. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 145. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 146. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 147. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 148. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 149. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 150. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 151. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 152. In some aspects, the antibody comprises a V_L

sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 153. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 154. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 155. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 156. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 157. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 158. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 159. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 160. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 161. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 162. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 163. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 164. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 165. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 166.

2.5.2. CDR-L2

[00132] In some embodiments, the antibody comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 125-140. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 125. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 126. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 127. In some aspects, the antibody

comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 128. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 129. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 130. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 131. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 132. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 133. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 134. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 135. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 136. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 137. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 138. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 139. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L2 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 140.

2.5.3. CDR-L1

[00133] In some embodiments, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 110-124. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 110. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 111. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 112. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or

consisting essentially of SEQ ID NO: 113. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 114. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 115. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 116. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 117. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 118. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 119. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 120. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 121. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 122. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 123. In some aspects, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 124.

2.5.4. CDR-L3 + CDR-L2

[00134] In some embodiments, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 141-166 and a CDR-L2 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 125-140. In some aspects, the CDR-L3 sequence and the CDR-L2 sequence are both from a single illustrative V_L sequence provided in this disclosure. For example, in some aspects, the CDR-L3 and CDR-L2 are both from a single illustrative V_L sequence selected from SEQ ID NOs: 219-248.

2.5.5. CDR-L3 + CDR-L1

[00135] In some embodiments, the antibody comprises a V_L sequence comprising a CDR-L3 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 141-166 and a CDR-L1 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 110-124. In some aspects, the CDR-L3

sequence and the CDR-L1 sequence are both from a single illustrative V_L sequence provided in this disclosure. For example, in some aspects, the CDR-L3 and CDR-L1 are both from a single illustrative V_L sequence selected from SEQ ID NOs: 219-248.

2.5.6. CDR-L1 + CDR-L2

[00136] In some embodiments, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 110-124 and a CDR-L2 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 125-140. In some aspects, the CDR-L1 sequence and the CDR-L2 sequence are both from a single illustrative V_L sequence provided in this disclosure. For example, in some aspects, the CDR-L1 and CDR-L2 are both from a single illustrative V_L sequence selected from SEQ ID NOs: 219-248.

2.5.7. CDR-L1 + CDR-L2 + CDR-L3

[00137] In some embodiments, the antibody comprises a V_L sequence comprising a CDR-L1 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 110-124, a CDR-L2 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 125-140, and a CDR-L3 sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L1 sequence, CDR-L2 sequence, and CDR-L3 sequence are all from a single illustrative V_L sequence provided in this disclosure. For example, in some aspects, the CDR-L1, CDR-L2, and CDR-L3 are all from a single illustrative V_L sequence selected from SEQ ID NOs: 219-248.

[00138] In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence SEQ ID NO: 141. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 111, a CDR-L2 sequence comprising SEQ ID NO: 126, and a CDR-L3 sequence comprising SEQ ID NO: 142. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 127, and a CDR-L3 sequence comprising sequence selected from SEQ ID NO: 142. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence comprising SEQ ID NO: 143. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 112, a CDR-L2 sequence comprising SEQ ID NO: 128, and a CDR-L3 sequence

comprising SEQ ID NO: 144. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 111, a CDR-L2 sequence comprising SEQ ID NO: 126, and a CDR-L3 sequence comprising SEQ ID NO: 145. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 113, a CDR-L2 sequence comprising SEQ ID NO: 129, and a CDR-L3 sequence comprising SEQ ID NO: 146. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 114, a CDR-L2 sequence comprising SEQ ID NO: 130, and a CDR-L3 sequence comprising SEQ ID NO: 147. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence comprising SEQ ID NO: 148. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence comprising SEQ ID NO: 148. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 116, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence comprising SEQ ID NO: 149. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence comprising SEQ ID NO: 148. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 132, and a CDR-L3 sequence comprising SEQ ID NO: 149. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 117, a CDR-L2 sequence comprising SEQ ID NO: 133, and a CDR-L3 sequence comprising SEQ ID NO: 150. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 134, and a CDR-L3 sequence comprising SEQ ID NO: 148. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 118, a CDR-L2 sequence comprising SEQ ID NO: 135, and a CDR-L3 sequence comprising SEQ ID NO: 151. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 118, a CDR-L2 sequence comprising SEQ ID NO: 135, and a CDR-L3 sequence comprising SEQ ID NO: 152. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 118, a CDR-L2 sequence comprising SEQ ID NO: 136, and a CDR-L3 sequence comprising SEQ ID NO: 152. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1

sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence comprising SEQ ID NO: 153. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 119, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence comprising SEQ ID NO: 154. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 120, a CDR-L2 sequence comprising SEQ ID NO: 137, and a CDR-L3 sequence comprising SEQ ID NO: 155. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 138, and a CDR-L3 sequence comprising SEQ ID NO: 156. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 138, and a CDR-L3 sequence comprising SEQ ID NO: 157. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 122, a CDR-L2 sequence comprising SEQ ID NO: 138, and a CDR-L3 sequence comprising SEQ ID NO: 158. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 138, and a CDR-L3 sequence comprising SEQ ID NO: 159. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 118, a CDR-L2 sequence comprising SEQ ID NO: 135, and a CDR-L3 sequence comprising SEQ ID NO: 160. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 139, and a CDR-L3 sequence comprising SEQ ID NO: 161. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 123, a CDR-L2 sequence comprising SEQ ID NO: 140, and a CDR-L3 sequence comprising SEQ ID NO: 162. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 138, and a CDR-L3 sequence comprising SEQ ID NO: 163. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 139, and a CDR-L3 sequence comprising SEQ ID NO: 164. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 120, a CDR-L2 sequence comprising SEQ ID NO: 137, and a CDR-L3 sequence comprising SEQ ID NO: 165. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 124, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence

comprising SEQ ID NO: 166.

[00139] In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 128, and a CDR-L3 sequence SEQ ID NO: 144. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence comprising SEQ ID NO: 144. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 126, and a CDR-L3 sequence comprising sequence selected from SEQ ID NO: 144. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 116, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence comprising SEQ ID NO: 150. In some aspects, the antibody comprises a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 117, a CDR-L2 sequence comprising SEQ ID NO: 134, and a CDR-L3 sequence comprising SEQ ID NO: 150.

2.5.8. Variants of V_L Sequences Comprising Illustrative CDR-Ls

[00140] In some embodiments, the V_L sequences provided herein comprise a variant of an illustrative CDR-L3, CDR-L2, and/or CDR-L1 sequence provided in this disclosure.

[00141] In some aspects, the CDR-L3 sequence comprises, consists of, or consists essentially of a variant of an illustrative CDR-L3 sequence provided in this disclosure. In some aspects, the CDR-L3 sequence comprises, consists of, or consists essentially of a sequence having at least 70%, 75%, 80%, 85%, 90%, or 95% identity with any of the illustrative CDR-L3 sequences provided in this disclosure. In some aspects, the CDR-L3 sequence comprises, consists of, or consists essentially of any of the illustrative CDR-L3 sequences provided in this disclosure, with 1, 2, or 3 amino acid substitutions. In some aspects, the amino acid substitutions are conservative amino acid substitutions.

[00142] In some aspects, the CDR-L2 sequence comprises, consists of, or consists essentially of a variant of an illustrative CDR-L2 sequence provided in this disclosure. In some aspects, the CDR-L2 sequence comprises, consists of, or consists essentially of a sequence having at least 70%, 75%, 80%, 85%, 90%, or 95% identity with any of the illustrative CDR-L2 sequences provided in this disclosure. In some aspects, the CDR-L2 sequence comprises, consists of, or consists essentially of any of the illustrative CDR-L2 sequences provided in this disclosure, with 1, 2, or 3 amino acid substitutions. In some aspects, the amino acid

substitutions are conservative amino acid substitutions.

[00143] In some aspects, the CDR-L1 sequence comprises, consists of, or consists essentially of a variant of an illustrative CDR-L1 sequence provided in this disclosure. In some aspects, the CDR-L1 sequence comprises, consists of, or consists essentially of a sequence having at least 70%, 75%, 80%, 85%, 90%, or 95% identity with any of the illustrative CDR-L1 sequences provided in this disclosure. In some aspects, the CDR-L1 sequence comprises, consists of, or consists essentially of any of the illustrative CDR-L1 sequences provided in this disclosure, with 1, 2, or 3 amino acid substitutions. In some aspects, the amino acid substitutions are conservative amino acid substitutions.

2.6. V_L Sequences

[00144] In some embodiments, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of a sequence selected from SEQ ID NOs: 219-248. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 219. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 220. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 221. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 222. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 223. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 224. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 225. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 226. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 227. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 228. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 229. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 230. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 231. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 232. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 233. In some

aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 234. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 235. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 236. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 237. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 238. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 239. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 240. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 241. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 242. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 243. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 244. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 245. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 246. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 247. In some aspects, the antibody comprises a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 248.

2.6.1. Variants of V_L Sequences

[00145] In some embodiments, the V_L sequences provided herein comprise, consist of, or consist essentially of a variant of an illustrative V_L sequence provided in this disclosure.

[00146] In some aspects, the V_L sequence comprises, consists of, or consists essentially of a variant of an illustrative V_L sequence provided in this disclosure. In some aspects, the V_L sequence comprises, consists of, or consists essentially of a sequence having at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 99.05% identity with any of the illustrative V_L sequences provided in this disclosure.

[00147] In some embodiments, the V_L sequence comprises, consists of, or consists essentially of any of the illustrative V_L sequences provided in this disclosure, 20 or fewer, 19 or fewer, 18 or fewer, 17 or fewer, 16 or fewer, 15 or fewer, 14 or fewer, 13 or fewer, 12 or fewer, 11 or fewer, 10 or fewer, 9 or fewer, 8 or fewer, 7 or fewer, 6 or fewer, 5 or fewer, 4 or

fewer, 3 or fewer, 2 or fewer, or 1 or fewer amino acid substitutions. In some aspects, the amino acid substitutions are conservative amino acid substitutions.

2.7. Pairs

2.7.1. CDR-H3 – CDR-L3 Pairs

[00148] In some embodiments, the antibody comprises a CDR-H3 sequence and a CDR-L3 sequence. In some aspects, the CDR-H3 sequence is part of a V_H and the CDR-L3 sequence is part of a V_L.

[00149] In some aspects, the CDR-H3 sequence is a CDR-H3 sequence comprising, consisting of, or consisting essentially of SEQ ID NOs: 82-109, and the CDR-L3 sequence is a CDR-L3 sequence comprising, consisting of, or consisting essentially of SEQ ID NOs: 141-166.

[00150] In some aspects, the CDR-H3 sequence is SEQ ID NO: 82 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00151] In some aspects, the CDR-H3 sequence is SEQ ID NO: 83 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is

SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00152] In some aspects, the CDR-H3 sequence is SEQ ID NO: 84 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is

SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00153] In some aspects, the CDR-H3 sequence is SEQ ID NO: 85 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00154] In some aspects, the CDR-H3 sequence is SEQ ID NO: 86 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some

aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00155] In some aspects, the CDR-H3 sequence is SEQ ID NO: 87 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00156] In some aspects, the CDR-H3 sequence is SEQ ID NO: 88 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is

SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00157] In some aspects, the CDR-H3 sequence is SEQ ID NO: 89 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00158] In some aspects, the CDR-H3 sequence is SEQ ID NO: 90 and the CDR-L3

sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00159] In some aspects, the CDR-H3 sequence is SEQ ID NO: 91 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some

aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00160] In some aspects, the CDR-H3 sequence is SEQ ID NO: 92 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00161] In some aspects, the CDR-H3 sequence is SEQ ID NO: 93 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is

SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00162] In some aspects, the CDR-H3 sequence is SEQ ID NO: 94 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00163] In some aspects, the CDR-H3 sequence is SEQ ID NO: 95 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some

aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00164] In some aspects, the CDR-H3 sequence is SEQ ID NO: 96 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00165] In some aspects, the CDR-H3 sequence is SEQ ID NO: 97 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00166] In some aspects, the CDR-H3 sequence is SEQ ID NO: 98 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is

SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00167] In some aspects, the CDR-H3 sequence is SEQ ID NO: 99 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00168] In some aspects, the CDR-H3 sequence is SEQ ID NO: 100 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some

aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00169] In some aspects, the CDR-H3 sequence is SEQ ID NO: 101 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00170] In some aspects, the CDR-H3 sequence is SEQ ID NO: 102 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is

SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00171] In some aspects, the CDR-H3 sequence is SEQ ID NO: 103 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is

SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00172] In some aspects, the CDR-H3 sequence is SEQ ID NO: 104 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00173] In some aspects, the CDR-H3 sequence is SEQ ID NO: 105 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some

aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00174] In some aspects, the CDR-H3 sequence is SEQ ID NO: 106 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00175] In some aspects, the CDR-H3 sequence is SEQ ID NO: 107 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is

SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00176] In some aspects, the CDR-H3 sequence is SEQ ID NO: 108 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

[00177] In some aspects, the CDR-H3 sequence is SEQ ID NO: 109 and the CDR-L3 sequence is selected from SEQ ID NOs: 141-166. In some aspects, the CDR-L3 sequence is SEQ ID NO: 141. In some aspects, the CDR-L3 sequence is SEQ ID NO: 142. In some

aspects, the CDR-L3 sequence is SEQ ID NO: 143. In some aspects, the CDR-L3 sequence is SEQ ID NO: 144. In some aspects, the CDR-L3 sequence is SEQ ID NO: 145. In some aspects, the CDR-L3 sequence is SEQ ID NO: 146. In some aspects, the CDR-L3 sequence is SEQ ID NO: 147. In some aspects, the CDR-L3 sequence is SEQ ID NO: 148. In some aspects, the CDR-L3 sequence is SEQ ID NO: 149. In some aspects, the CDR-L3 sequence is SEQ ID NO: 150. In some aspects, the CDR-L3 sequence is SEQ ID NO: 151. In some aspects, the CDR-L3 sequence is SEQ ID NO: 152. In some aspects, the CDR-L3 sequence is SEQ ID NO: 153. In some aspects, the CDR-L3 sequence is SEQ ID NO: 154. In some aspects, the CDR-L3 sequence is SEQ ID NO: 155. In some aspects, the CDR-L3 sequence is SEQ ID NO: 156. In some aspects, the CDR-L3 sequence is SEQ ID NO: 157. In some aspects, the CDR-L3 sequence is SEQ ID NO: 158. In some aspects, the CDR-L3 sequence is SEQ ID NO: 159. In some aspects, the CDR-L3 sequence is SEQ ID NO: 160. In some aspects, the CDR-L3 sequence is SEQ ID NO: 161. In some aspects, the CDR-L3 sequence is SEQ ID NO: 162. In some aspects, the CDR-L3 sequence is SEQ ID NO: 163. In some aspects, the CDR-L3 sequence is SEQ ID NO: 164. In some aspects, the CDR-L3 sequence is SEQ ID NO: 165. In some aspects, the CDR-L3 sequence is SEQ ID NO: 166.

2.7.1.1.Variants of CDR-H3 – CDR-L3 Pairs

[00178] In some embodiments, the CDR-H3 – CDR-L3 pairs provided herein comprise a variant of an illustrative CDR-H3 and/or CDR-L1 sequence provided in this disclosure.

[00179] In some aspects, the CDR-H3 sequence comprises, consists of, or consists essentially of a variant of an illustrative CDR-H3 sequence provided in this disclosure. In some aspects, the CDR-H3 sequence comprises, consists of, or consists essentially of a sequence having at least 70%, 75%, 80%, 85%, 90%, or 95% identity with any of the illustrative CDR-H3 sequences provided in this disclosure. In some aspects, the CDR-H3 sequence comprises, consists of, or consists essentially of any of the illustrative CDR-H3 sequences provided in this disclosure, with 1, 2, or 3 amino acid substitutions. In some aspects, the amino acid substitutions are conservative amino acid substitutions.

[00180] In some aspects, the CDR-L3 sequence comprises, consists of, or consists essentially of a variant of an illustrative CDR-L3 sequence provided in this disclosure. In some aspects, the CDR-L3 sequence comprises, consists of, or consists essentially of a sequence having at least 70%, 75%, 80%, 85%, 90%, or 95% identity with any of the illustrative CDR-L3 sequences provided in this disclosure. In some aspects, the CDR-L3 sequence comprises, consists of, or consists essentially of any of the illustrative CDR-L3 sequences provided in this

disclosure, with 1, 2, or 3 amino acid substitutions. In some aspects, the amino acid substitutions are conservative amino acid substitutions.

2.7.2. V_H – V_L Pairs

[00181] In some embodiments, the antibody comprises a V_H sequence and a V_L sequence.

[00182] In some aspects, the V_H sequence is a V_H sequence comprising, consisting of, or consisting essentially of SEQ ID NOs: 179-218 and the V_L sequence is a V_L sequence comprising, consisting of, or consisting essentially of SEQ ID NOs: 219-248.

[00183] In some aspects, the V_H sequence is SEQ ID NO: 179 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00184] In some aspects, the V_H sequence is SEQ ID NO: 180 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the

V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00185] In some aspects, the V_H sequence is SEQ ID NO: 181 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some

aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00186] In some aspects, the V_H sequence is SEQ ID NO: 182 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00187] In some aspects, the V_H sequence is SEQ ID NO: 183 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L

sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00188] In some aspects, the V_H sequence is SEQ ID NO: 184 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00189] In some aspects, the V_H sequence is SEQ ID NO: 185 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is

SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00190] In some aspects, the V_H sequence is SEQ ID NO: 186 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L

sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00191] In some aspects, the V_H sequence is SEQ ID NO: 187 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00192] In some aspects, the V_H sequence is SEQ ID NO: 188 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID

NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00193] In some aspects, the V_H sequence is SEQ ID NO: 189 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00194] In some aspects, the V_H sequence is SEQ ID NO: 190 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219.

In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00195] In some aspects, the V_H sequence is SEQ ID NO: 191 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID

NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00196] In some aspects, the V_H sequence is SEQ ID NO: 192 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00197] In some aspects, the V_H sequence is SEQ ID NO: 193 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some

aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00198] In some aspects, the V_H sequence is SEQ ID NO: 194 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00199] In some aspects, the V_H sequence is SEQ ID NO: 195 and the V_L sequence is

selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00200] In some aspects, the V_H sequence is SEQ ID NO: 196 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some

aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00201] In some aspects, the V_H sequence is SEQ ID NO: 197 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00202] In some aspects, the V_H sequence is SEQ ID NO: 198 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L

sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00203] In some aspects, the V_H sequence is SEQ ID NO: 199 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00204] In some aspects, the V_H sequence is SEQ ID NO: 200 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00205] In some aspects, the V_H sequence is SEQ ID NO: 201 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L

sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00206] In some aspects, the V_H sequence is SEQ ID NO: 202 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00207] In some aspects, the V_H sequence is SEQ ID NO: 203 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ

ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00208] In some aspects, the V_H sequence is SEQ ID NO: 204 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L

sequence is SEQ ID NO: 248.

[00209] In some aspects, the V_H sequence is SEQ ID NO: 205 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00210] In some aspects, the V_H sequence is SEQ ID NO: 206 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID

NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00211] In some aspects, the V_H sequence is SEQ ID NO: 207 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00212] In some aspects, the V_H sequence is SEQ ID NO: 208 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In

some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00213] In some aspects, the V_H sequence is SEQ ID NO: 209 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID

NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00214] In some aspects, the V_H sequence is SEQ ID NO: 210 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00215] In some aspects, the V_H sequence is SEQ ID NO: 211 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some

aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00216] In some aspects, the V_H sequence is SEQ ID NO: 212 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00217] In some aspects, the V_H sequence is SEQ ID NO: 213 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the

V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00218] In some aspects, the V_H sequence is SEQ ID NO: 214 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some

aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00219] In some aspects, the V_H sequence is SEQ ID NO: 215 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00220] In some aspects, the V_H sequence is SEQ ID NO: 216 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L

sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00221] In some aspects, the V_H sequence is SEQ ID NO: 217 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

[00222] In some aspects, the V_H sequence is SEQ ID NO: 218 and the V_L sequence is selected from SEQ ID NOs: 219-248. In some aspects, the V_L sequence is SEQ ID NO: 219. In some aspects, the V_L sequence is SEQ ID NO: 220. In some aspects, the V_L sequence is

SEQ ID NO: 221. In some aspects, the V_L sequence is SEQ ID NO: 222. In some aspects, the V_L sequence is SEQ ID NO: 223. In some aspects, the V_L sequence is SEQ ID NO: 224. In some aspects, the V_L sequence is SEQ ID NO: 225. In some aspects, the V_L sequence is SEQ ID NO: 226. In some aspects, the V_L sequence is SEQ ID NO: 227. In some aspects, the V_L sequence is SEQ ID NO: 228. In some aspects, the V_L sequence is SEQ ID NO: 229. In some aspects, the V_L sequence is SEQ ID NO: 230. In some aspects, the V_L sequence is SEQ ID NO: 231. In some aspects, the V_L sequence is SEQ ID NO: 232. In some aspects, the V_L sequence is SEQ ID NO: 233. In some aspects, the V_L sequence is SEQ ID NO: 234. In some aspects, the V_L sequence is SEQ ID NO: 235. In some aspects, the V_L sequence is SEQ ID NO: 236. In some aspects, the V_L sequence is SEQ ID NO: 237. In some aspects, the V_L sequence is SEQ ID NO: 238. In some aspects, the V_L sequence is SEQ ID NO: 239. In some aspects, the V_L sequence is SEQ ID NO: 240. In some aspects, the V_L sequence is SEQ ID NO: 241. In some aspects, the V_L sequence is SEQ ID NO: 242. In some aspects, the V_L sequence is SEQ ID NO: 243. In some aspects, the V_L sequence is SEQ ID NO: 244. In some aspects, the V_L sequence is SEQ ID NO: 245. In some aspects, the V_L sequence is SEQ ID NO: 246. In some aspects, the V_L sequence is SEQ ID NO: 247. In some aspects, the V_L sequence is SEQ ID NO: 248.

2.7.3. CDR-H1 + CDR-H2 + CDR-H3 + CDR-L1 + CDR-L2 + CDR-L3

[00223] In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 25, a Kabat CDR-H2 sequence comprising SEQ ID NO: 63, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 82 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence SEQ ID NO: 141. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 26, a Kabat CDR-H2 sequence comprising SEQ ID NO: 64, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 83 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 111, a CDR-L2 sequence comprising SEQ ID NO: 126, and a CDR-L3 sequence SEQ ID NO: 142. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 27, a Kabat CDR-H2 sequence comprising SEQ ID NO: 65, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 84 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence SEQ ID NO: 141. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 26,

a Kabat CDR-H2 sequence comprising SEQ ID NO: 64, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 85 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence SEQ ID NO: 141. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 26, a Kabat CDR-H2 sequence comprising SEQ ID NO: 64, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 86 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 127, and a CDR-L3 sequence SEQ ID NO: 142. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 25, a Kabat CDR-H2 sequence comprising SEQ ID NO: 66, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 82 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence SEQ ID NO: 141. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 26, a Kabat CDR-H2 sequence comprising SEQ ID NO: 65, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 82 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence SEQ ID NO: 143. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 26, a Kabat CDR-H2 sequence comprising SEQ ID NO: 65, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 82 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 112, a CDR-L2 sequence comprising SEQ ID NO: 128, and a CDR-L3 sequence SEQ ID NO: 144. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 27, a Kabat CDR-H2 sequence comprising SEQ ID NO: 65, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 82 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 111, a CDR-L2 sequence comprising SEQ ID NO: 126, and a CDR-L3 sequence SEQ ID NO: 145. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 28, a Kabat CDR-H2 sequence comprising SEQ ID NO: 67, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 82 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 113, a CDR-L2 sequence comprising SEQ ID NO: 129, and a CDR-L3 sequence SEQ ID NO: 146. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 29, a Kabat CDR-H2 sequence comprising SEQ ID NO: 68, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 82 and a VL sequence

comprising a CDR-L1 sequence comprising SEQ ID NO: 114, a CDR-L2 sequence comprising SEQ ID NO: 130, and a CDR-L3 sequence SEQ ID NO: 147. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 26, a Kabat CDR-H2 sequence comprising SEQ ID NO: 64, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 82 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence SEQ ID NO: 141. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 30, a Kabat CDR-H2 sequence comprising SEQ ID NO: 69, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 148. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 31, a Kabat CDR-H2 sequence comprising SEQ ID NO: 70, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 88 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 116, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 149. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 32, a Kabat CDR-H2 sequence comprising SEQ ID NO: 71, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 89 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 148. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 33, a Kabat CDR-H2 sequence comprising SEQ ID NO: 70, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 90 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 132, and a CDR-L3 sequence SEQ ID NO: 149. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 34, a Kabat CDR-H2 sequence comprising SEQ ID NO: 72, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 91 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 148. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 30, a Kabat CDR-H2 sequence comprising SEQ ID NO: 71, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 92 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence

SEQ ID NO: 148. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 35, a Kabat CDR-H2 sequence comprising SEQ ID NO: 70, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 93 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 117, a CDR-L2 sequence comprising SEQ ID NO: 133, and a CDR-L3 sequence SEQ ID NO: 150. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 33, a Kabat CDR-H2 sequence comprising SEQ ID NO: 70, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 92 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 134, and a CDR-L3 sequence SEQ ID NO: 148. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 36, a Kabat CDR-H2 sequence comprising SEQ ID NO: 72, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 148. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 30, a Kabat CDR-H2 sequence comprising SEQ ID NO: 73, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 148. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 37, a Kabat CDR-H2 sequence comprising SEQ ID NO: 74, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 87 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 148. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 38, a Kabat CDR-H2 sequence comprising SEQ ID NO: 75, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 94 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 118, a CDR-L2 sequence comprising SEQ ID NO: 135, and a CDR-L3 sequence SEQ ID NO: 151. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 39, a Kabat CDR-H2 sequence comprising SEQ ID NO: 76, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 95 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 118, a CDR-L2 sequence comprising SEQ ID NO: 135, and a CDR-L3 sequence SEQ ID NO: 152. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 40,

a Kabat CDR-H2 sequence comprising SEQ ID NO: 76, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 96 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 118, a CDR-L2 sequence comprising SEQ ID NO: 136, and a CDR-L3 sequence SEQ ID NO: 152. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 39, a Kabat CDR-H2 sequence comprising SEQ ID NO: 76, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 94 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 118, a CDR-L2 sequence comprising SEQ ID NO: 135, and a CDR-L3 sequence SEQ ID NO: 152. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 38, a Kabat CDR-H2 sequence comprising SEQ ID NO: 69, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 97 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 153. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 41, a Kabat CDR-H2 sequence comprising SEQ ID NO: 69, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 98 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 119, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 154. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 41, a Kabat CDR-H2 sequence comprising SEQ ID NO: 69, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 99 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 120, a CDR-L2 sequence comprising SEQ ID NO: 137, and a CDR-L3 sequence SEQ ID NO: 155. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 41, a Kabat CDR-H2 sequence comprising SEQ ID NO: 69, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 100 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 138, and a CDR-L3 sequence SEQ ID NO: 156. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 38, a Kabat CDR-H2 sequence comprising SEQ ID NO: 75, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 101 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 138, and a CDR-L3 sequence SEQ ID NO: 157. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 42, a Kabat CDR-H2 sequence comprising SEQ ID NO: 78, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 102 and a VL sequence

comprising a CDR-L1 sequence comprising SEQ ID NO: 122, a CDR-L2 sequence comprising SEQ ID NO: 138, and a CDR-L3 sequence SEQ ID NO: 158. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 38, a Kabat CDR-H2 sequence comprising SEQ ID NO: 75, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 103 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 138, and a CDR-L3 sequence SEQ ID NO: 159. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 43, a Kabat CDR-H2 sequence comprising SEQ ID NO: 79, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 104 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 118, a CDR-L2 sequence comprising SEQ ID NO: 135, and a CDR-L3 sequence SEQ ID NO: 160. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 38, a Kabat CDR-H2 sequence comprising SEQ ID NO: 75, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 103 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 139, and a CDR-L3 sequence SEQ ID NO: 161. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 38, a Kabat CDR-H2 sequence comprising SEQ ID NO: 69, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 105 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 123, a CDR-L2 sequence comprising SEQ ID NO: 140, and a CDR-L3 sequence SEQ ID NO: 162. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 38, a Kabat CDR-H2 sequence comprising SEQ ID NO: 69, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 106 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 138, and a CDR-L3 sequence SEQ ID NO: 163. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 38, a Kabat CDR-H2 sequence comprising SEQ ID NO: 69, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 107 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 139, and a CDR-L3 sequence SEQ ID NO: 164. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 44, a Kabat CDR-H2 sequence comprising SEQ ID NO: 80, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 108 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 120, a CDR-L2 sequence comprising SEQ ID NO: 137, and a CDR-L3 sequence

SEQ ID NO: 165. In some aspects, the antibody comprises a V_H sequence comprising a Kabat CDR-H1 sequence comprising SEQ ID NO: 45, a Kabat CDR-H2 sequence comprising SEQ ID NO: 81, and a Kabat CDR-H3 sequence comprising SEQ ID NO: 109 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 124, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence SEQ ID NO: 166.

[00224] In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 1, a Chothia CDR-H2 sequence comprising SEQ ID NO: 46, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 82 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence SEQ ID NO: 141. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 2, a Chothia CDR-H2 sequence comprising SEQ ID NO: 47, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 83 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 111, a CDR-L2 sequence comprising SEQ ID NO: 126, and a CDR-L3 sequence SEQ ID NO: 142. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 1, a Chothia CDR-H2 sequence comprising SEQ ID NO: 46, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 84 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence SEQ ID NO: 141. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 2, a Chothia CDR-H2 sequence comprising SEQ ID NO: 47, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 85 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence SEQ ID NO: 141. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 3, a Chothia CDR-H2 sequence comprising SEQ ID NO: 47, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 86 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 127, and a CDR-L3 sequence SEQ ID NO: 142. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 4, a Chothia CDR-H2 sequence comprising SEQ ID NO: 46, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 82 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence SEQ ID NO: 141. In some aspects, the antibody

comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 2, a Chothia CDR-H2 sequence comprising SEQ ID NO: 46, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 82 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence SEQ ID NO: 143. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 2, a Chothia CDR-H2 sequence comprising SEQ ID NO: 46, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 82 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 112, a CDR-L2 sequence comprising SEQ ID NO: 128, and a CDR-L3 sequence SEQ ID NO: 144. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 1, a Chothia CDR-H2 sequence comprising SEQ ID NO: 46, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 82 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 111, a CDR-L2 sequence comprising SEQ ID NO: 126, and a CDR-L3 sequence SEQ ID NO: 145. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 5, a Chothia CDR-H2 sequence comprising SEQ ID NO: 49, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 82 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 113, a CDR-L2 sequence comprising SEQ ID NO: 129, and a CDR-L3 sequence SEQ ID NO: 146. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 6, a Chothia CDR-H2 sequence comprising SEQ ID NO: 50, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 82 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 114, a CDR-L2 sequence comprising SEQ ID NO: 130, and a CDR-L3 sequence SEQ ID NO: 147. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 2, a Chothia CDR-H2 sequence comprising SEQ ID NO: 47, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 82 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 110, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence SEQ ID NO: 141. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 7, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 148. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence

comprising SEQ ID NO: 8, a Chothia CDR-H2 sequence comprising SEQ ID NO: 52, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 88 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 116, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 149. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 9, a Chothia CDR-H2 sequence comprising SEQ ID NO: 53, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 89 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 148. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 10, a Chothia CDR-H2 sequence comprising SEQ ID NO: 52, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 90 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 132, and a CDR-L3 sequence SEQ ID NO: 149. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 11, a Chothia CDR-H2 sequence comprising SEQ ID NO: 54, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 91 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 148. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 12, a Chothia CDR-H2 sequence comprising SEQ ID NO: 53, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 92 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 148. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 13, a Chothia CDR-H2 sequence comprising SEQ ID NO: 52, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 93 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 117, a CDR-L2 sequence comprising SEQ ID NO: 133, and a CDR-L3 sequence SEQ ID NO: 150. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 10, a Chothia CDR-H2 sequence comprising SEQ ID NO: 52, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 92 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 134, and a CDR-L3 sequence SEQ ID NO: 148. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 14, a Chothia CDR-H2 sequence comprising SEQ ID NO:

54, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 148. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 15, a Chothia CDR-H2 sequence comprising SEQ ID NO: 55, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 148. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 16, a Chothia CDR-H2 sequence comprising SEQ ID NO: 56, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 87 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 148. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 94 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 118, a CDR-L2 sequence comprising SEQ ID NO: 135, and a CDR-L3 sequence SEQ ID NO: 151. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 18, a Chothia CDR-H2 sequence comprising SEQ ID NO: 57, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 95 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 118, a CDR-L2 sequence comprising SEQ ID NO: 135 and a CDR-L3 sequence SEQ ID NO: 152. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 19, a Chothia CDR-H2 sequence comprising SEQ ID NO: 57, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 96 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 118, a CDR-L2 sequence comprising SEQ ID NO: 136, and a CDR-L3 sequence SEQ ID NO: 152. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 21, a Chothia CDR-H2 sequence comprising SEQ ID NO: 57, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 94 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 118, a CDR-L2 sequence comprising SEQ ID NO: 135, and a CDR-L3 sequence SEQ ID NO: 152. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 97 and

a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 115, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 153. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 22, a Chothia CDR-H2 sequence comprising SEQ ID NO: 52, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 98 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 119, a CDR-L2 sequence comprising SEQ ID NO: 131, and a CDR-L3 sequence SEQ ID NO: 154. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 22, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 99 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 120, a CDR-L2 sequence comprising SEQ ID NO: 137, and a CDR-L3 sequence SEQ ID NO: 155. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 22, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 100 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 138, and a CDR-L3 sequence SEQ ID NO: 156. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 101 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 138, and a CDR-L3 sequence SEQ ID NO: 157. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 59, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 102 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 122, a CDR-L2 sequence comprising SEQ ID NO: 138, and a CDR-L3 sequence SEQ ID NO: 158. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 103 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 138, and a CDR-L3 sequence SEQ ID NO: 159. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 23, a Chothia CDR-H2 sequence comprising SEQ ID NO: 60, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 104 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO:

118, a CDR-L2 sequence comprising SEQ ID NO: 135, and a CDR-L3 sequence SEQ ID NO: 160. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 103 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 139, and a CDR-L3 sequence SEQ ID NO: 161. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 105 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 123, a CDR-L2 sequence comprising SEQ ID NO: 140, and a CDR-L3 sequence SEQ ID NO: 162. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 106 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 138, and a CDR-L3 sequence SEQ ID NO: 163. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 51, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 107 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 121, a CDR-L2 sequence comprising SEQ ID NO: 139, and a CDR-L3 sequence SEQ ID NO: 164. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 61, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 108 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 120, a CDR-L2 sequence comprising SEQ ID NO: 137, and a CDR-L3 sequence SEQ ID NO: 165. In some aspects, the antibody comprises a V_H sequence comprising a Chothia CDR-H1 sequence comprising SEQ ID NO: 17, a Chothia CDR-H2 sequence comprising SEQ ID NO: 62, and a Chothia CDR-H3 sequence comprising SEQ ID NO: 109 and a VL sequence comprising a CDR-L1 sequence comprising SEQ ID NO: 124, a CDR-L2 sequence comprising SEQ ID NO: 125, and a CDR-L3 sequence SEQ ID NO: 166.

2.7.3.1.Variants of V_H – V_L Pairs

[00225] In some embodiments, the V_H – V_L pairs provided herein comprise a variant of an illustrative V_H and/or V_L sequence provided in this disclosure.

[00226] In some aspects, the V_H sequence comprises, consists of, or consists essentially

of a variant of an illustrative V_H sequence provided in this disclosure. In some aspects, the V_H sequence comprises, consists of, or consists essentially of a sequence having at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 99.1% identity with any of the illustrative V_H sequences provided in this disclosure.

[00227] In some embodiments, the V_H sequence comprises, consists of, or consists essentially of any of the illustrative V_H sequences provided in this disclosure, 20 or fewer, 19 or fewer, 18 or fewer, 17 or fewer, 16 or fewer, 15 or fewer, 14 or fewer, 13 or fewer, 12 or fewer, 11 or fewer, 10 or fewer, 9 or fewer, 8 or fewer, 7 or fewer, 6 or fewer, 5 or fewer, 4 or fewer, 3 or fewer, 2 or fewer, or 1 or fewer amino acid substitutions. In some aspects, the amino acid substitutions are conservative amino acid substitutions.

[00228] In some aspects, the V_L sequence comprises, consists of, or consists essentially of a variant of an illustrative V_L sequence provided in this disclosure. In some aspects, the V_L sequence comprises, consists of, or consists essentially of a sequence having at least 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 99.05% identity with any of the illustrative V_L sequences provided in this disclosure.

[00229] In some embodiments, the V_L sequence comprises, consists of, or consists essentially of any of the illustrative V_L sequences provided in this disclosure, 20 or fewer, 19 or fewer, 18 or fewer, 17 or fewer, 16 or fewer, 15 or fewer, 14 or fewer, 13 or fewer, 12 or fewer, 11 or fewer, 10 or fewer, 9 or fewer, 8 or fewer, 7 or fewer, 6 or fewer, 5 or fewer, 4 or fewer, 3 or fewer, 2 or fewer, or 1 or fewer amino acid substitutions. In some aspects, the amino acid substitutions are conservative amino acid substitutions.

2.7.4 HC + LC

[00230] In some embodiments, the antibody comprises or consists of one or more heavy chains consisting of an HC sequence and one or more light chains consisting of an LC sequence. In some embodiments, the antibody comprises or consists of two identical heavy chains consisting of an HC sequence and two identical light chains consisting of an LC sequence.

[00231] In some embodiments, the HC sequence is an HC sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 255, SEQ ID NO: 257, SEQ ID NO: 259, SEQ ID NO: 261, SEQ ID NO: 263, SEQ ID NO: 265, SEQ ID NO: 267, SEQ ID NO: 269, SEQ ID NO: 271, SEQ ID NO: 273, SEQ ID NO: 275, SEQ ID NO: 277, SEQ ID NO: 279, SEQ ID NO: 281, SEQ ID NO: 283, SEQ ID NO: 285, SEQ ID NO: 287, SEQ ID NO:

289, SEQ ID NO: 291, SEQ ID NO: 293, SEQ ID NO: 295, or SEQ ID NO: 297 and the LC sequence is a LC sequence comprising, consisting of, or consisting essentially of SEQ ID NO: 256, SEQ ID NO: 258, SEQ ID NO: 260, SEQ ID NO: 262, SEQ ID NO: 264, SEQ ID NO: 266, SEQ ID NO: 268, SEQ ID NO: 270, SEQ ID NO: 272, SEQ ID NO: 274, SEQ ID NO: 276, SEQ ID NO: 278, SEQ ID NO: 280, SEQ ID NO: 282, SEQ ID NO: 284, SEQ ID NO: 286, SEQ ID NO: 288, SEQ ID NO: 290, SEQ ID NO: 292, SEQ ID NO: 294, SEQ ID NO: 296, or SEQ ID NO: 298. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 255, SEQ ID NO: 257, SEQ ID NO: 259, SEQ ID NO: 261, SEQ ID NO: 263, SEQ ID NO: 265, SEQ ID NO: 267, SEQ ID NO: 269, SEQ ID NO: 271, SEQ ID NO: 273, SEQ ID NO: 275, SEQ ID NO: 277, SEQ ID NO: 279, SEQ ID NO: 281, SEQ ID NO: 283, SEQ ID NO: 285, SEQ ID NO: 287, SEQ ID NO: 289, SEQ ID NO: 291, SEQ ID NO: 293, SEQ ID NO: 295, or SEQ ID NO: 297 and the LC sequence is an LC sequence consisting of SEQ ID NO: 256, SEQ ID NO: 258, SEQ ID NO: 260, SEQ ID NO: 262, SEQ ID NO: 264, SEQ ID NO: 266, SEQ ID NO: 268, SEQ ID NO: 270, SEQ ID NO: 272, SEQ ID NO: 274, SEQ ID NO: 276, SEQ ID NO: 278, SEQ ID NO: 280, SEQ ID NO: 282, SEQ ID NO: 284, SEQ ID NO: 286, SEQ ID NO: 288, SEQ ID NO: 290, SEQ ID NO: 292, SEQ ID NO: 294, SEQ ID NO: 296, or SEQ ID NO: 298.

[00232] In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 255 and the LC sequence is an LC sequence consisting of SEQ ID NO: 256. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 257 and the LC sequence is an LC sequence consisting of SEQ ID NO: 258. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 259 and the LC sequence is an LC sequence consisting of SEQ ID NO: 260. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 261 and the LC sequence is an LC sequence consisting of SEQ ID NO: 262. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 263 and the LC sequence is an LC sequence consisting of SEQ ID NO: 264. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 265 and the LC sequence is an LC sequence consisting of SEQ ID NO: 266. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 267 and the LC sequence is an LC sequence consisting of SEQ ID NO: 268. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 269 and the LC sequence is an LC sequence consisting of SEQ ID NO: 270. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 271 and the LC sequence is an LC sequence consisting of SEQ ID NO: 272. In

some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 273 and the LC sequence is an LC sequence consisting of SEQ ID NO: 274. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 275 and the LC sequence is an LC sequence consisting of SEQ ID NO: 276. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 277 and the LC sequence is an LC sequence consisting of SEQ ID NO: 278. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 279 and the LC sequence is an LC sequence consisting of SEQ ID NO: 280. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 281 and the LC sequence is an LC sequence consisting of SEQ ID NO: 282. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 283 and the LC sequence is an LC sequence consisting of SEQ ID NO: 284. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 285 and the LC sequence is an LC sequence consisting of SEQ ID NO: 286. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 287 and the LC sequence is an LC sequence consisting of SEQ ID NO: 288. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 289 and the LC sequence is an LC sequence consisting of SEQ ID NO: 290. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 291 and the LC sequence is an LC sequence consisting of SEQ ID NO: 292. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 293 and the LC sequence is an LC sequence consisting of SEQ ID NO: 294. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 295 and the LC sequence is an LC sequence consisting of SEQ ID NO: 296. In some embodiments, the HC sequence is an HC sequence consisting of SEQ ID NO: 297 and the LC sequence is an LC sequence consisting of SEQ ID NO: 298.

2.8. Consensus Sequences

[00233] In some embodiments, provided herein are anti-CD39 antibodies comprising one or more sequences defined by consensus sequences. Each consensus sequence is based, at least in part, on one or more alignments of two or more useful anti-CD39 CDR sequences provided in this disclosure. Based on such alignments, a person of skill in the art would recognize that different amino acid residues may useful in certain positions of the CDRs. Accordingly, each consensus sequence encompasses two or more useful anti-CD39 CDR sequences.

2.8.1. CDR-H3 Consensus Sequences

[00234] In some embodiments, the antibody comprises a CDR-H3 sequence defined by

the consensus sequence G-K-R-E-G-G-T-E-Y-L-R-$У_{12}$ (SEQ ID NOS: 82-86), where $У_{12}$ is H, K, S, N, or V.

[00235] In some aspects, $У_{12}$ is H. In some aspects, $У_{12}$ is K. In some aspects, $У_{12}$ is S. In some aspects, $У_{12}$ is N. In some aspects, $У_{12}$ is V.

[00236] In some embodiments, the antibody comprises a CDR-H3 sequence defined by the consensus sequence E-S-G-$Ф_4$-Y-R-D-H-R-L-$Ф_{11}$-V (SEQ ID NOS: 94-96), where $Ф_4$ is G or T and $Ф_{11}$ is D or G.

[00237] In some aspects, $Ф_4$ is G when $Ф_{11}$ is D or G. In some aspects, $Ф_{11}$ is D when $Ф_4$ is G or T.

[00238] In some aspects, $Ф_4$ is G and $Ф_{11}$ is D. In some aspects, $Ф_4$ is T and $Ф_{11}$ is D. In some aspects, $Ф_4$ is G and $Ф_{11}$ is G.

[00239] In some embodiments, the antibody comprises a CDR-H3 sequence defined by the consensus sequence G-G-A-K-Y-A-$Э_7$-$Э_8$-$Э_9$-G-M-D-V (SEQ ID NOS: 87-93), where $Э_7$ is S, V, G, or R; $Э_8$ is T, Q, K, G, or R; and $Э_9$ is Y, H, L, or W.

[00240] In some aspects, $Э_7$ is S when $Э_8$ is T, Q, or K and $Э_9$ is Y, H, L, or W. In some aspects, $Э_8$ is T when $Э_7$ is S or R and $Э_9$ is Y or H. In some aspects, $Э_9$ is Y when $Э_7$ is S, V, G, or R and $Э_8$ is T, G, or R.

[00241] In some aspects, $Э_7$ is S when $Э_8$ is T and $Э_9$ is Y. In some aspects, $Э_7$ is S when $Э_8$ is T and $Э_9$ is H. In some aspects, $Э_7$ is S when $Э_8$ is Q and $Э_9$ is L. In some aspects, $Э_7$ is S when $Э_8$ is K and $Э_9$ is W. In some aspects, $Э_7$ is V when $Э_8$ is G and $Э_9$ is Y. In some aspects, $Э_7$ is G when $Э_8$ is R and $Э_9$ is Y. In some aspects, $Э_7$ is R when $Э_8$ is T and $Э_9$ is Y.

2.8.2. Chothia CDR-H2 Consensus Sequences

[00242] In some embodiments, the antibody comprises a Chothia CDR-H2 sequence defined by the consensus sequence N-P-$ε_5$-$ε_6$-G-S-T (SEQ ID NOS: 46-48), where $ε_5$ is L, R, or S and $ε_6$ is G or V.

[00243] In some aspects, when $ε_5$ is S, $ε_6$ is G or V. In some aspects, when $ε_6$ is G, $ε_5$ is S, L, or R.

[00244] In some aspects, when $ε_5$ is L, $ε_6$ is G. In some aspects, when $ε_5$ is S, $ε_6$ is G. In some aspects, when $ε_5$ is S, $ε_6$ is V. In some aspects, when $ε_5$ is R, $ε_6$ is G.

[00245] In some embodiments, the antibody comprises a Chothia CDR-H2 sequence

defined by the consensus sequence α_3-α_4-α_5-α_6-G-T-A (SEQ ID NOS: 51-54), where α_3 is I or L or is absent; α_4 is P or is absent; and α_5 is I, G, or R; and α_6 is A, F, or G.

[00246] In some aspects, when α_3, is I, α_4 is P; α_5 is I or R; and α_6 is F or G. In some aspects, when α_3, is L, α_4 is P; α_5 is I; and α_6 is A or G. In some aspects, when α_4, is P, α_3 is I or L; α_5 is I or R; and α_6 is A, F, or G. In some aspects, when α_5, is I, α_3 is I or L; α_4 is P; and α_6 is A, F, or G. In some aspects, when α_6, is F, α_3 is I or is absent; α_4 is P or is absent; and α_5 is I or G. In some aspects, when α_6, is G, α_3 is I or L; α_4 is P; and α_5 is I or R.

[00247] In some aspects, when α_3 is L, α_4 is P; α_5 is I; and α_6 is A. In some aspects, when α_3 is I, α_4 is P; α_5 is I; and α_6 is F. In some aspects, when α_3 is absent, α_4 is absent; α_5 is G; and α_6 is F. In some aspects, when α_3 is L, α_4 is P; α_5 is I; and α_6 is G. In some aspects, when α_3 is I, α_4 is P; α_5 is R; and α_6 is G.

[00248] In some embodiments, the antibody comprises a Chothia CDR-H2 sequence defined by the consensus sequence I-P-β_5-β_6-G-β_8-A (SEQ ID NOS: 56-60), where β_5 is I, E, S, or T; β_6 is F, I, or S; and β_8 is I or T.

[00249] In some aspects, when β_5 is I, β_6 is F or S and β_8 is T. In some aspects, when β_6 is F, β_5 is E, I, or T and β_8 is I or T. In some aspects, when β_8 is T, β_5 is I, S, or T and β_6 is F, I, or S.

[00250] In some aspects, when β_5 is I, β_6 is F and β_8 is T. In some aspects, when β_5 is E, β_6 is F and β_8 is I. In some aspects, when β_5 is S, β_6 is I and β_8 is T. In some aspects, when β_5 is I, β_6 is S and β_8 is T. In some aspects, when β_5 is T, β_6 is S and β_8 is T.

2.8.3. Chothia CDR-H1 Consensus Sequences

[00251] In some embodiments, the antibody comprises a Chothia CDR-H1 sequence defined by the consensus sequence G-Y-T-F-Ω_5-S-Y (SEQ ID NOS: 1-2 and 4-6), where Ω_5 is T, K, Q, F, or V.

[00252] In some aspects, Ω_5 is T. In some aspects, Ω_5 is K. In some aspects, Ω_5 is Q. In some aspects, Ω_5 is F. In some aspects, Ω_5 is V.

[00253] In some embodiments, the antibody comprises a Chothia CDR-H1 sequence defined by the consensus sequence G-G-T-F-ν_5- ν_6-Y (SEQ ID NOS: 17-22 and 24), where ν_5 is S, G, or E and ν_6 is S, K, R, or S.

[00254] In some aspects, ν_5 is S when ν_6 is S or K. In some aspects, ν_6 is S when ν_5 is S or E.

[00255] In some aspects, v_5 is S when v_6 is S. In some embodiments, v_5 is S when v_6 is K. In some aspects, v_5 is G when v_6 is R. In some aspects v_5 is E when v_6 is S.

[00256] In some embodiments, the antibody comprises a Chothia CDR-H1 sequence defined by the consensus sequence G-G-T-F-κ_5-κ_6-κ_7 (SEQ ID NOS: 7-16), where κ_5 is S, Q, P, or A; κ_6 is S, K, H, L, A, or W; and κ_7 is Y, L, T, N, or M.

[00257] In some aspects, when κ_5 is S, κ_6 is S, K, H, L, A, or W and κ_7 is Y, L, T, or M. In some aspects, when κ_6 is S, κ_5 is S, Q, P, or A and κ_7 is Y, L, or N. In some aspects, when κ_7 is L, κ_5 is S, Q, or A and κ_6 is S, K, L, or W.

[00258] In some aspects, when κ_5 is S, κ_6 is S and κ_7 is Y. In some aspects, when κ_5 is S, κ_6 is S and κ_7 is L. In some aspects, when κ_5 is S, κ_6 is K and κ_7 is L. In some aspects, when κ_5 is S, κ_6 is H and κ_7 is T. In some aspects, when κ_5 is S, κ_6 is L and κ_7 is L. In some aspects, when κ_5 is Q, κ_6 is S and κ_7 is L. In some aspects, when κ_5 is P, κ_6 is S and κ_7 is N. In some aspects, when κ_5 is S, κ_6 is A and κ_7 is M. In some aspects, when κ_5 is A, κ_6 is S and κ_7 is L. In some aspects, when κ_5 is S, κ_6 is W and κ_7 is L.

2.8.4. Kabat CDR-H2 Consensus Sequences

[00259] In some embodiments, the antibody comprises a Kabat CDR-H2 sequence defined by the consensus sequence ε_1-I-N-P-ε_5-ε_6-G-S-T-ε_{10}-Y-A-Q-K-F-Q-G (SEQ ID NOS: 63-66 and 68), where ε_1 is K, S, R, or V; ε_5 is L, R, or S; ε_6 is G or V; and ε_{10} is S or W.

[00260] In some aspects, when ε_1 is V; ε_5 is L or S; ε_6 is G; and ε_{10} is S. In some aspects, when ε_1 is R; ε_5 is S; ε_6 is V or G; and ε_{10} is W. In some aspects, when ε_5 is S; ε_1 is R or V; ε_6 is G or V; and ε_{10} is S or W. In some aspects, when ε_6 is G; ε_1 is R or V; ε_5 is S; and ε_{10} is S or W. In some aspects, when ε_{10} is S; ε_1 is V or S; ε_5 is L, R, or S; and ε_6 is G. In some aspects, when ε_{10} is W; ε_1 is K or R; ε_5 is S; and ε_6 is G or V.

[00261] In some aspects, when ε_1 is V; ε_5 is L; ε_6 is G; and ε_{10} is S. In some aspects, when ε_1 is V; ε_5 is S; ε_6 is G; and ε_{10} is S. In some aspects, when ε_1 is R; ε_5 is S; ε_6 is V; and ε_{10} is W. In some aspects, when ε_1 is R; ε_5 is S; ε_6 is G; and ε_{10} is W. In some aspects, when ε_1 is K; ε_5 is S; ε_6 is G; and ε_{10} is W. In some aspects, when ε_1 is S; ε_5 is R; ε_6 is G; and ε_{10} is S.

[00262] In some embodiments, the antibody comprises a Kabat CDR-H2 sequence defined by the consensus sequence G-I-α_3-α_4-α_5-α_6-G-T-A-N-Y-A-Q-K-F-Q-G (SEQ ID NOS: 69-72), where α_3 is I or L or is absent; α_4 is P or is absent; and α_5 is I, G, or R; and α_6 is A, F,

or G.

[00263] In some aspects, when α_3, is I, α_4 is P; α_5 is I or R; and α_6 is F or G. In some aspects, when α_3, is L, α_4 is P; α_5 is I; and α_6 is A or G. In some aspects, when α_4, is P, α_3 is I or L; α_5 is I or R; and α_6 is A, F, or G. In some aspects, when α_5, is I, α_3 is I or L; α_4 is P; and α_6 is A, F, or G. In some aspects, when α_6, is F, α_3 is I or is absent; α_4 is P or is absent; and α_5 is I or G. In some aspects, when α_6, is G, α_3 is I or L; α_4 is P; and α_5 is I or R.

[00264] In some aspects, when α_3 is L, α_4 is P; α_5 is I; and α_6 is A. In some aspects, when α_3 is I, α_4 is P; α_5 is I; and α_6 is F. In some aspects, when α_3 is absent, α_4 is absent; α_5 is G; and α_6 is F. In some aspects, when α_3 is L, α_4 is P; α_5 is I; and α_6 is G. In some aspects, when α_3 is I, α_4 is P; α_5 is R; and α_6 is G.

[00265] In some embodiments, the antibody comprises a Kabat CDR-H2 sequence defined by the consensus sequence β_1-I-I-P-β_5-β_6-G-β_8-A-N-Y-A-Q-K-F-G-Q (SEQ ID NOS: 74 and 76-79) where β_1 is S or G; β_5 is I, E, S, or T; β_6 is F, I, or S; and β_8 is I or T.

[00266] In some aspects, when β_1 is S, β_5 is E, I, or S; β_6 is I or F; and β_8 is I or T. In some aspects, when β_1 is G, β_5 is I or T; β_6 is F or S; and β_8 is T. In some aspects, when β_5 is I, β_1 is G or S; β_6 is F or S; and β_8 is T. In some aspects, when β_6 is F, β_1 is G or S; β_5 is E, I, or T; and β_8 is I or T. In some aspects, when β_8 is T, β_1 is G or S; β_5 is I, S, or T; and β_6 is F, I, or S.

[00267] In some aspects, when β_1 is S, β_5 is I; β_5 is F; and β_8 is T. In some aspects, when β_1 is S, β_5 is E; β_5 is F; and β_8 is I. In some aspects, when β_1 is S, β_5 is S; β_5 is I; and β_8 is T. In some aspects, when β_1 is G, β_5 is I; β_5 is F; and β_8 is T. In some aspects, when β_1 is G, β_5 is I; β_5 is S; and β_8 is T. In some aspects, when β_1 is G, β_5 is T; β_5 is F; and β_8 is T.

2.8.5. Kabat CDR-H1 Consensus Sequences

[00268] In some embodiments, the antibody comprises a Kabat CDR-H1 sequence defined by the consensus sequence S-Y-Δ_3-M-Δ_5 (SEQ ID NOS: 25-29 and 44-45), where Δ_3 is E, F, Q, or Y and Δ_5 is H or Y.

[00269] In some aspects, when Δ_3 is Y, Δ_5 is H or Y. In some aspects, when Δ_5 is H, Δ_3 is E, F, Q, or Y.

[00270] In some aspects, Δ_3 is Y when Δ_5 H. In some aspects, Δ_3 is Y when Δ_5 is Y. In some aspects, Δ_3 is E when Δ_5 is H. In some aspects, Δ_3 is Q when Δ_5 is H. In some aspects, Δ_3 is F when Δ_5 is H.

[00271] In some embodiments, the antibody comprises a Kabat CDR-H1 sequence defined by the consensus sequence θ_1-θ_2-θ_3-I-S (SEQ ID NOS: 30-37), where θ_1 is A, H, K, L, S, or W; θ_2 is L, M, N, or T; and θ_3 is A or P.

[00272] In some aspects, when θ_1 is S, θ_2 is L or N and θ_3 is A or P. In some aspects, when θ_2 is L, θ_1 is K, L, S, or W and θ_3 is A or P. In some aspects, when θ_3 is A, θ_1 is A, H, K, L, S, or W and θ_2 is L, M, N, or T.

[00273] In some aspects, θ_1 is S, when θ_2 is L and θ_3 is A. In some aspects, θ_1 is K, when θ_2 is L and θ_3 is A. In some aspects, θ_1 is H when θ_2 is T and θ_3 is A. In some aspects, θ_1 is S when θ_2 is L and θ_3 is P. In some aspects, θ_1 is L when θ_2 is L and θ_3 is A. In some aspects, θ_1 is S when θ_2 is N and θ_3 is A. In some aspects, θ_1 is A when θ_2 is M and θ_3 is A. In some aspects, θ_1 is W when θ_2 is L and θ_3 is A.

[00274] In some embodiments, the antibody comprises a Kabat CDR-H1 sequence defined by the consensus sequence η_1-Y-η_3-I-S SEQ ID NOS: 38-41), where η_1 is S, K, N, or R and η_3 is A or G.

[00275] In some aspects, η_1 is S where η_3 is A or G. In some aspects, η_3 is A where η_1 is N or S. In some aspects, η_3 is G where η_1 is K, R, or S.

[00276] In some aspects, when η_1 is S, η_3 is A. In some aspects, when η_1 is S, η_3 is G. In some aspects, when η_1 is K, η_3 is G. In some aspects, when η_1 is R, η_3 is G. In some aspects, when η_1 is N, η_3 is A.

2.8.6. CDR-L3 Consensus Sequences

[00277] In some embodiments, the antibody comprises a CDR-L3 sequence defined by the consensus sequence Q-Q-Y-π_4- π_5-π_6-π_7-T (SEQ ID NOS: 141-147), where π_4 is G, H, or Y; π_5 is S, N, F, G, or R; π_6 is S, Y, A, G, or R; and π_7 is P, I, or L.

[00278] In some aspects, π_4 is H when π_5 is S, N, G, or R; π_6 is Y, A, G, or R; and π_7 is I or L. In some aspects, π_5 is S, when π_4 is G or H; π_6 is S, Y, or A; and π_7 is P, I or L. In some aspects, π_6 is Y, when π_4 is H or Y; π_5 is S or F; and π_7 is I. In some aspects, π_6 is A when π_4 is H; π_5 is N or S; and π_7 is I or L. In some aspects, π_7 is I when π_4 is H or Y; π_5 is S, N, F, G, or R; and π_6 is Y, A, G, or R.

[00279] In some aspects, π_4 is G when π_5 is S; π_6 is S; and π_7 is P. In some aspects, π_4 is H when π_5 is S; π_6 is Y; and π_7 is I. In some aspects, π_4 is H when π_5 is N; π_6 is I; and π_7 is A. In some aspects, π_4 is Y when π_5 is F; π_6 is Y; and π_7 is I. In some aspects, π_4 is H when π_5 is

S; π_6 is A; and π_7 is L. In some aspects, π_4 is H when π_5 is G; π_6 is G; and π_7 is I. In some aspects, π_4 is H when π_5 is R; π_6 is R; and π_7 is I.

[00280] In some embodiments, the antibody comprises a CDR-L3 sequence defined by consensus sequence Q-Q-λ_3-λ_4-λ_5-λ_6-P-T (SEQ ID NOS: 148-150), where λ_3 is R, F, H, S, L, D, Y, or V; λ_4 is S, V, T, G, L, Y, or N; λ_5 is N, L, F, K, or V; and λ_6 is W, F, Y, or L.

[00281] In some aspects, λ_3 is R, when λ_4 is S or N; λ_5 is N or F; and λ_6 is W or Y. In some aspects, λ_3 is H when λ_4 is V or T; λ_5 is N or V; and λ_6 is F or W. In some aspects, λ_3 is S when λ_4 is V or Y; λ_5 is F; and λ_6 is W or L. In some aspects, λ_4 is V when λ_3 is F, H, S, or D; λ_5 is L, N, or F; and λ_6 is W or F. In some aspects, λ_4 is T when λ_3 is L or H; λ_5 is K or V; and λ_6 is W. In some aspects, λ_5 is N when λ_3 is R, H, or V; λ_4 is S, V, or L; and λ_6 is W, F, or Y. In some aspects, λ_5 is L when λ_3 is F, D, or Y; λ_4 is V or G; and λ_6 is W or F. In some aspects, λ_5 is F when λ_3 is S or R; λ_4 is V, Y, or N; and λ_6 is W, L, or Y. In some aspects, λ_6 is W when λ_3 is R, F, S, L, D, or H; λ_4 is S, V, or T; and λ_5 is N, L, F, K, or V. In some aspects, λ_6 is F when λ_3 is H or Y; λ_4 is V or G; and λ_5 is N or L. In some aspects, λ_6 is Y when λ_3 is V or R; λ_4 is L or N; and λ_5 is N or F.

[00282] In some aspects, λ_3 is R when λ_4 is S; λ_5 is N; and λ_6 is W. In some aspects, λ_3 is F when λ_4 is V; λ_5 is L; and λ_6 is W. In some aspects, λ_3 is H when λ_4 is V; λ_5 is N; and λ_6 is F. In some aspects, λ_3 is S when λ_4 is V; λ_5 is F; and λ_6 is W. In some aspects, λ_3 is L when λ_4 is T; λ_5 is K; and λ_6 is W. In some aspects, λ_3 is D when λ_4 is V; λ_5 is L; and λ_6 is W. In some aspects, λ_3 is Y when λ_4 is G; λ_5 is L; and λ_6 is F. In some aspects, λ_3 is H when λ_4 is T; λ_5 is V; and λ_6 is W. In some aspects, λ_3 is V when λ_4 is L; λ_5 is N; and λ_6 is Y. In some aspects, λ_3 is S when λ_4 is Y; λ_5 is F; and λ_6 is L. In some aspects, λ_3 is R when λ_4 is N; λ_5 is F; and λ_6 is Y.

[00283] In some embodiments, the antibody comprises a CDR-L3 sequence defined by the consensus sequence Q-Q-Y-ρ_3-ρ_4-W-P-L-T (SEQ ID NOS: 151 and 152), where ρ_3 is N or L and ρ_4 is N or L.

[00284] In some aspects, ρ_3 is N when ρ_4 is L. In some aspects, ρ_3 is L when ρ_4 is L.

[00285] In some embodiments, the antibody comprises a CDR-L3 sequence defined by the consensus sequence Q-Q-ω_3-ω_4-ω_5-ω_6-P- ω_8-T (SEQ ID NOS: 153-156), where ω_3 is Y or F; ω_4 is Y or W; ω_5 is S, L, T, or F; ω_6 is T, Y, or F; and ω_8 is L or P.

[00286] In some aspects, ω_3 is Y when ω_4 is Y or W; ω_5 is S, L, or T; ω_6 is T or Y; and ω_8 is L. In some aspects, ω_4 is Y when ω_3 is Y or F; ω_5 is S, L, or F; ω_6 is T or Y; and ω_8 is L

or P. In some aspects, ω_6 is Y when ω_3 is Y; ω_4 is Y or W; ω_5 is L or T; and ω_8 is L. In some aspects, ω_8 is L when ω_3 is Y; ω_4 is Y or W; ω_5 is S, L, or T; and ω_6 is T or Y.

[00287] In some aspects, ω_3 is Y when ω_4 is Y; ω_5 is S; ω_6 is T; and ω_8 is L. In some aspects, ω_3 is Y when ω_4 is Y; ω_5 is L; ω_6 is Y; and ω_8 is L. In some aspects, ω_3 is Y when ω_4 is W; ω_5 is T; ω_6 is Y; and ω_8 is L. In some aspects, ω_3 is F when ω_4 is Y; ω_5 is F; ω_6 is F; and ω_8 is P.

2.8.7. CDR-L2 Consensus Sequences

[00288] In some embodiments, the antibody comprises a CDR-L2 sequence defined by the consensus sequence ψ_1-A-S-ψ_4-R-ψ_6-ψ_7 (SEQ ID NOS: 125-136), where ψ_1 is G or Y, ψ_4 is S or N; ψ_6 is A or H; and ψ_7 is T, Y, or N.

[00289] In some aspects, ψ_1 is G when ψ_4 is S or N; ψ_6 is A or H; and ψ_7 is T or N. In some aspects, ψ_1 is Y when is S or N; ψ_6 is A; and ψ_7 is Y or T. In some aspects, ψ_4 is S when ψ_1 is G or Y; ψ_6 is A; and ψ_7 is T, Y, or N. In some aspects, ψ_4 is N when ψ_1 is G or Y; ψ_6 is H or A; and ψ_7 is T. In some aspects, ψ_6 is A when ψ_1 is G or Y; ψ_4 is S or N; and ψ_7 is T, Y, or N. In some aspects, ψ_7 is T when ψ_1 is G or Y; ψ_4 is S or N; and ψ_6 is A or H.

[00290] In some aspects, ψ_1 is G when ψ_4 is S; ψ_6 is A; and ψ_7 is T. In some aspects, ψ_1 is G when ψ_4 is N; ψ_6 is H; and ψ_7 is T. In some aspects, ψ_1 is Y when ψ_4 is S; ψ_6 is A; and ψ_7 is Y. In some aspects, ψ_1 is G when ψ_4 is S; ψ_6 is A; and ψ_7 is N. In some aspects, ψ_1 is Y when ψ_4 is N; ψ_6 is A; and ψ_7 is T.

[00291] In some embodiments, the antibody comprises a CDR-L2 sequence defined by the consensus sequence D-A-S- χ_4-R-A-T (SEQ ID NOS: 138 and 139), where £4 is N or K.

[00292] In some aspects, χ_4 is N. In some aspects, χ_4 is K.

[00293] In some embodiments, the antibody comprises a CDR-L2 sequence defined by the consensus sequence W-A-S-T-R-σ_6-S (SEQ ID NOS: 131 and 133-134), where σ_6 is A, E, or Q.

[00294] In some aspects, σ_6 is A. In some aspects, σ_6 is E. In some aspects, σ_6 is Q.

2.8.8. CDR-L1 Consensus Sequences

[00295] In some embodiments, the antibody comprises a CDR-L1 sequence defined by the consensus sequence ϕ_1-A-S-ϕ_4-ϕ_5-V-ϕ_7-ϕ_8-ϕ_9-Y-L-A (SEQ ID NOS: 1101-114), where ϕ_1 is E, K, or R; ϕ_4 is Q or E; ϕ_5 is S or Y; ϕ_7 is S or A; ϕ_8 is S or Y; and ϕ_9 is D or S.

[00296] In some aspects, ϕ_1 is R when ϕ_4 is Q or E; ϕ_5 is S or Y; ϕ_7 is S or A; ϕ_8 is S or Y; and ϕ_9 is S or D. In some aspects, ϕ_4 is E when ϕ_1 is K or R; ϕ_5 is S; ϕ_7 is S; ϕ_8 is S; and ϕ_9 is S. In some aspects, ϕ_4 is Q when ϕ_1 is E or R; ϕ_5 is S or Y; ϕ_7 is S or A; ϕ_8 is S or Y; and ϕ_9 is S or D. In some aspects, ϕ_5 is S when ϕ_1 is E, K, or R; ϕ_4 is E or Q; ϕ_7 is S or A; ϕ_8 is S or Y; and ϕ_9 is S or D. In some aspects, ϕ_7 is S when ϕ_1 is E, K, or R; ϕ_4 is E or Q; ϕ_5 is S or Y; ϕ_8 is S or Y; and ϕ_9 is S or D. In some aspects, ϕ_8 is S when ϕ_1 is K or R; ϕ_4 is E or Q; ϕ_5 is S or 5; ϕ_7 is A or S; and ϕ_9 is S or D. In some aspects, ϕ_8 is R when ϕ_1 is E or R; ϕ_4 is Q; ϕ_5 is S; ϕ_7 is S; and ϕ_9 is S. In some aspects, ϕ_9 is S when ϕ_1 is E, K, or R; ϕ_4 is E or Q; ϕ_5 is S or Y; ϕ_7 is A or S; and ϕ_8 is S or Y.

[00297] In some aspects, ϕ_1 is K when ϕ_4 is E; ϕ_5 is S; ϕ_7 is S; ϕ_8 is S; and ϕ_9 is S. In some aspects, ϕ_1 is E, when ϕ_4 is Q; ϕ_5 is S; ϕ_7 is S; ϕ_8 is Y; and ϕ_9 is S. In some aspects, ϕ_1 is R when ϕ_4 is Q; ϕ_5 is S; ϕ_7 is S; ϕ_8 is S; and ϕ_9 is D. In some aspects, ϕ_1 is R when ϕ_4 is Q; ϕ_5 is S; ϕ_7 is S; ϕ_8 is S; and ϕ_9 is S. In some aspects, ϕ_1 is R when ϕ_4 is Q; ϕ_5 is S; ϕ_7 is A; ϕ_8 is S; and ϕ_9 is S. In some aspects, ϕ_1 is R when ϕ_4 is Q; ϕ_5 is S; ϕ_7 is S; ϕ_8 is Y; and ϕ_9 is S. In some aspects, ϕ_1 is R when ϕ_4 is E; ϕ_5 is S; ϕ_7 is S; ϕ_8 is S; and ϕ_9 is S. In some aspects, ϕ_1 is R when ϕ_4 is Q; ϕ_5 is Y; ϕ_7 is S; ϕ_8 is S; and ϕ_9 is S.

[00298] In some embodiments, the antibody comprises a CDR-L1 sequence defined by the consensus sequence $б_1$-A-S-Q-$б_5$-$б_6$-$б_7$-$б_8$-$б_9$-L-$б_{11}$ (SEQ ID NOS: 118 and 120-123), where $б_1$ is Q or Rl; $б_5$ is D or S; $б_6$ is I or V; $б_7$ is G or S; $б_8$ is N, R, or S; $б_9$ is N, Y, or W; and $б_{11}$ is A or N.

[00299] In some aspects, when $б_1$ is R, $б_5$ is S; $б_6$ is I or V; $б_7$ is G or S; $б_8$ is R or S; $б_9$ is N, Y, or W; and $б_{11}$ is A. In some aspects, when $б_5$ is S, $б_1$ is R; $б_6$ is I or V; $б_7$ is G or S; $б_8$ is R or S; $б_9$ is N, Y, or W; and $б_{11}$ is A. In some aspects, when $б_6$ is I, $б_1$ is Q or R; $б_5$ is D or S; $б_7$ is S; $б_8$ is N or S; $б_9$ is Y or W; and $б_{11}$ is A or N. In some aspects, when $б_6$ is V, $б_1$ is R; $б_5$ is S; $б_7$ is G or S; $б_8$ is R or S; $б_9$ is N or W; and $б_{11}$ is A. In some aspects, when $б_7$ is S, $б_1$ is Q or R; $б_5$ is D or S; $б_6$ is I or V; $б_8$ is N, S, or R; $б_9$ is Y or W; and $б_{11}$ is A or N. In some aspects, when $б_8$ is S, $б_1$ is R; $б_5$ is S; $б_6$ is I or V; $б_7$ is S; $б_9$ is N, Y, or W; and $б_{11}$ is A. In some aspects, when $б_9$ is Y, $б_1$ is Q or R; $б_5$ is D or S; $б_6$ is I or V; $б_7$ is S; $б_8$ is N, S, or R; and $б_{11}$ is A or N. In some aspects, when $б_{11}$ is A, $б_1$ is R; $б_5$ is S; $б_6$ is I or V; $б_7$ is S or G; $б_8$ is S, or R; and $б_9$ is N, W, or Y.

[00300] In some aspects, when $б_1$ is R, $б_5$ is S; $б_6$ is V; $б_7$ is S; $б_8$ is S; $б_9$ is Y; and $б_{11}$ is A. In some aspects, when $б_1$ is Q, $б_5$ is D; $б_6$ is I; $б_7$ is S; $б_8$ is N; $б_9$ is Y; and $б_{11}$ is N. In

some aspects, when Б1 is R, Б5 is S; Б6 is V; Б7 is S; Б8 is R; Б9 is Y; and Б11 is A. In some aspects, when Б1 is R, Б5 is S; Б6 is V; Б7 is G; Б8 is S; Б9 is N; and Б11 is A. In some aspects, when Б1 is R, Б5 is S; Б6 is I; Б7 is S; Б8 is S; Б9 is W; and Б11 is A.

[00301] In some embodiments, the antibody comprises a CDR-L1 sequence defined by the consensus sequence K-S-S-Г4-S-V-L- Г8-S- Г10-N-N-K-N-Y-L-A (SEQ ID NOS: 115-117), where Г4 is Q, R or K; Г8 is F or Y; and Г10 is S or N.

[00302] In some aspects, Г4 is Q when Г8 is F or Y and Г10 is S. In some aspects, Г8 is F when Г4 is Q or R and Г10 is S. In some aspects, Г8 is Y when Г4 is K or Q and Г10 is S or N. In some aspects, Г10 is S when Г4 is R or Q and Г8 is F or Y.

[00303] In some aspects, Г4 is Q when Г8 is Y and Г10 is S. In some aspects, Г4 is K when Г8 is Y and Г10 is N. In some aspects, Г4 is Q when Г8 is F and Г10 is S. In some aspects, Г4 is R when Г8 is F and Г10 is S.

3. Germline

[00304] In some embodiments, the antibody that specifically binds CD39 is an antibody comprising a variable region that is encoded by a particular germline gene, or a variant thereof. The illustrative antibodies provided herein comprise variable regions that are encoded by the heavy chain variable region germline genes VH1-46, VH1-69, 1-69, and VH1-46, or variants thereof; and the light chain variable region germline genes VK3-20, VK3-11, VK4-01, VK3, and VK3-15, or variants thereof. One of skill in the art would recognize that the CDR sequences provided herein may also be useful when combined with variable regions encoded by other variable region germline genes, or variants thereof. In particular, the CDR sequences provided herein may be useful when combined with variable regions encoded by variable region germline genes, or variants thereof, that are structurally similar to the variable region germline genes recited above. For example, in some embodiments, a CDR-H sequence provided herein may be combined with a variable region encoded by a variable region germline gene selected from the VH1 or VH3 family, or a variant thereof. In some embodiments, a CDR-L sequence provided herein may be combined with a variable region encoded by a variable region germline gene selected from the Vλ3, Vκ1, Vκ3, and Vκ4 families, or a variant thereof.

4. Affinity

[00305] In some embodiments, the affinity of the antibody for CD39, as indicated by K_D, is less than about 10^{-5} M, less than about 10^{-6} M, less than about 10^{-7} M, less than about 10^{-8} M, less than about 10^{-9} M, less than about 10^{-10} M, less than about 10^{-11} M, or less than

about 10^{-12} M. In some embodiments, the affinity of the antibody is between about 10^{-7} M and 10^{-11} M. In some embodiments, the affinity of the antibody is between about 10^{-7} M and 10^{-10} M. In some embodiments, the affinity of the antibody is between about 10^{-7} M and 10^{-9} M. In some embodiments, the affinity of the antibody is between about 10^{-7} M and 10^{-8} M. In some embodiments, the affinity of the antibody is between about 10^{-8} M and 10^{-11} M. In some embodiments, the affinity of the antibody is between about 10^{-8} M and 10^{-10} M. In some embodiments, the affinity of the antibody is between about 10^{-9} M and 10^{-11} M. In some embodiments, the affinity of the antibody is between about 10^{-10} M and 10^{-11} M.

[00306] In some embodiments, the affinity of the antibody for human CD39 is between about 4.09×10^{-7} M and 7.31×10^{-11} M. In some embodiment, the affinity of the antibody for human CD39 is about 1.14×10^{-7} M, about 1.31×10^{-7} M, about 1.67×10^{-7} M, about 1.43×10^{-7} M, about 1.30×10^{-8} M, about 1.27×10^{-8} M, about 1.13×10^{-8} M, about 1.60×10^{-8} M, about 1.34×10^{-9} M, about 1.16×10^{-9} M, about 7.31×10^{-11} M, about 7.60×10^{-10} M, about 2.66×10^{-10} M, about 9.22×10^{-10} M, about 6.72×10^{-10} M, about 9.24×10^{-10} M, about 5.58×10^{-10} M, about 5.48×10^{-8} M, about 3.37×10^{-8} M, about 3.11×10^{-8} M, about 1.88×10^{-8} M, about 1.63×10^{-8} M about 1.64×10^{-8} M, about 1.01×10^{-8} M, about 2.44×10^{-7} M, about 4.09×10^{-7} M, about 3.35×10^{-8} M, about 1.91×10^{-8} M, about 1.73×10^{-8} M, or about 2.39×10^{-8} M.

[00307] In some embodiments the antibody has a k_{on} when associating with human CD39 of between about 1.93×10^{4} $M^{-1}\times sec^{-1}$ and about 1.72×10^{6} $M^{-1}\times sec^{-1}$. In some embodiments the antibody has a k_a when associating with human CD39 of about 6.59×10^{4} $M^{-1}\times sec^{-1}$, about 1.93×10^{4} $M^{-1}\times sec^{-1}$, about 4.44×10^{5} $M^{-1}\times sec^{-1}$, about 2.72×10^{5} $M^{-1}\times sec^{-1}$, about 6.39×10^{5} $M^{-1}\times sec^{-1}$, about 8.93×10^{5} $M^{-1}\times sec^{-1}$, about 9.55×10^{5} $M^{-1}\times sec^{-1}$, about 2.11×10^{5} $M^{-1}\times sec^{-1}$, about 1.17×10^{5} $M^{-1}\times sec^{-1}$, about 2.02×10^{5} $M^{-1}\times sec^{-1}$, about 1.76×10^{5} $M^{-1}\times sec^{-1}$, about 1.72×10^{5} $M^{-1}\times sec^{-1}$, about 2.73×10^{5} $M^{-1}\times sec^{-1}$, about 1.43×10^{5} $M^{-1}\times sec^{-1}$, about 9.01×10^{5} $M^{-1}\times sec^{-1}$, about 3.13×10^{5} $M^{-1}\times sec^{-1}$, about 5.03×10^{5} $M^{-1}\times sec^{-1}$, about 3.02×10^{5} $M^{-1}\times sec^{-1}$, about 2.73×10^{5} $M^{-1}\times sec^{-1}$, about 1.78×10^{5} $M^{-1}\times sec^{-1}$, about 2.98×10^{5} $M^{-1}\times sec^{-1}$, about 4.31×10^{5} $M^{-1}\times sec^{-1}$, about 2.27×10^{5} $M^{-1}\times sec^{-1}$, about 3.14×10^{5} $M^{-1}\times sec^{-1}$, about 2.81×10^{5} $M^{-1}\times sec^{-1}$, about 4.73×10^{5} $M^{-1}\times sec^{-1}$, about 3.26×10^{5} $M^{-1}\times sec^{-1}$, about 1.73×10^{5} $M^{-1}\times sec^{-1}$, about 2.68×10^{5} $M^{-1}\times sec^{-1}$, about 2.63×10^{5} $M^{-1}\times sec^{-1}$, about 3.82×10^{5} $M^{-1}\times sec^{-1}$, about 2.46×10^{5} $M^{-1}\times sec^{-1}$, about 3.11×10^{5} $M^{-1}\times sec^{-1}$, about 4.53×10^{5} $M^{-1}\times sec^{-1}$, about 4.63×10^{5} $M^{-1}\times sec^{-1}$, about 9.01×10^{5} $M^{-1}\times sec^{-1}$, about 1.03×10^{6} $M^{-1}\times sec^{-1}$, about 1.52×10^{6} $M^{-1}\times sec^{-1}$, or about 3.53×10^{5} $M^{-1}\times sec^{-1}$.

[00308] In some embodiments the antibody has a k_{off} of about 7.51×10^{-3} sec^{-1}, about

6.33×10^{-2} sec^{-1}, about 4.70×10^{-2} sec^{-1}, about 7.82×10^{-4} sec^{-1}, about 4.70×10^{-2} sec^{-1}, about 1.05×10^{-2} sec^{-1}, about 3.65×10^{-1} sec^{-1}, about 1.60×10^{-1} sec^{-1}, about 7.11×10^{-3} sec^{-1}, about 6.44×10^{-3} sec^{-1}, about 3.85×10^{-2} sec^{-1}, about 2.30×10^{-2} sec^{-1}, about 5.33×10^{-2} sec^{-1}, about 9.14×10^{-2} sec^{-1}, about 1.80×10^{-3} sec^{-1}, about 8.15×10^{-3} sec^{-1}, about 3.85×10^{-4} sec^{-1}, about 1.34×10^{-4} sec^{-1}, about 2.29×10^{-4} sec^{-1}, about 4.37×10^{-3} sec^{-1}, about 3.71×10^{-3} sec^{-1}, about 4.06×10^{-3} sec^{-1}, about 6.66×10^{-2} sec^{-1}, about 2.02×10^{-3} sec^{-1}, about 2.00×10^{-4} sec^{-1}, about 5.26×10^{-3} sec^{-1}, about 1.13×10^{-2} sec^{-1}, about 3.28×10^{-3} sec^{-1}, about 2.76×10^{-3} sec^{-1}, about 2.86×10^{-4} sec^{-1}, about 2.43×10^{-4} sec^{-1}, about 2.13×10^{-4} sec^{-1}, about 6.09×10^{-4} sec^{-1}, about 8.39×10^{-4} sec^{-1}, about 8.15×10^{-3} sec^{-1}, about 1.32×10^{-4} sec^{-1}, about 1.11×10^{-4} sec^{-1}, about 2.43×10^{-4} sec^{-1}, about 2.13×10^{-4} sec^{-1}, about 6.09×10^{-4} sec^{-1}, about 8.15×10^{-3} sec^{-1}, about 1.32×10^{-4} sec^{-1}, or about 1.11×10^{-4} sec^{-1}.

[00309] In some aspects, the K_D, k_a, and k_d are determined at 25°C. In some embodiments, the K_D, k_a, and k_d are determined by surface plasmon resonance. In some embodiments, the K_D, k_a, and k_d are determined according to the methods described in the examples.

5. Inhibition of CD39

[00310] In some aspects, the antibody decreases affinity of CD39 to its substrate. In some aspects, the antibody inhibits CD39 function on tumor cells. In some aspects, the antibody inhibits or impedes the release of ADP or AMP from CD39. In some aspects, the antibody inhibits or impedes CD39 processivity.

[00311] In some aspects, the antibody binds CD39 but does not inhibit ATPase. In some aspects, the antibody binds CD39 and inhibits extracellular CD39 activity but not cellular ATPase activity. In some aspects, the antibody binds both the extracellular domain of CD39 and cellular CD39 and can inhibit both the extracellular domain of CD39 and cellular CD39. In some aspects, the antibodies do not compete with A1 and/or others in binding to the extracellular domain.

6. CD39 Assays

[00312] In some embodiments, the antibody binds to an epitope of CD39. In some aspects, CD39 has a sequence identical to the amino acid sequence set forth in SEQ ID NO: 249. In some aspects, the epitope has an amino acid sequence that is identical to the amino acid sequence set forth in SEQ ID NO: 249. In some aspects, the epitope is in an extracellular domain of CD39. In some aspects, the extracellular domain corresponds to all or at least a

portion of amino acids 38-478 of SEQ ID NO: 249. In some aspects, the epitope has an amino acid sequence that is 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95% identical to the sequence set forth in SEQ ID NO: 249 or all or a portion of the extracellular domain. In some aspects, the epitope has a sequence that is identical or corresponds to residues 143-158 and/or residues 274-277 of SEQ ID NO: 249. In some aspects, the epitope is in the region of E143 to N158 on the human CD39 polypeptide having the sequence set forth in SEQ ID NO: 249. In some aspects, the epitope has a sequence that has a 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95% identity to residues 143-158 or 274-277 of the sequence set forth in SEQ ID NO: 249. In some aspects, the epitope has 1, 2, 3, 4, 5, 6, 7, 8, or 9 substitutions from residues 143-158 of the sequence forth in SEQ ID NO: 249. In some aspects, the epitope has 1, 2 or 3 substitutions from residues 274-277 of SEQ ID NO: 249. In some aspects, the antibody makes contact with any of the residues set forth in FIG. 14E, Table 1. In some aspects, the antibody makes contact with any of the residues set forth in FIG. 14E, Table 2. In some aspects, the antibody binds to D150, E153, and/or R154 or to N99 and none, one, two, or three of D150, E153, and R154 or to any of the above alone or in combination.

[00313] In some aspects, the antibody competes with 1, 2, 3, 4, or 5 of antibodies 27536, 27571, 28347, 27579, or 27597 as set forth in FIG. 14A. In some aspects, the antibody competes with 1, 2, 3, 4, or 5 antibodies 27536, 27571, 28347, 27579, or 27597 as set forth in FIG. 14A. In some aspects, the antibody competes with 1, 2, or 3 of antibodies 25571, 27536, or 27549 as set forth in FIG. 14C. In some aspects, the antibody competes with 1, 2, or 3 of antibodies 25571, 27536, or 27549 set forth in FIG. 14C.

[00314] In some aspects, the antibody inhibits conversion by CD39 of ATP to ADP and/or ADP to AMP. In some aspects, the antibody inhibits platelet aggregation. In some aspects, the antibody decreases or prevents activation of phospho antigen specific T cells selected from MAIT cells and γδ T cells. In some aspects, the antibody inhibits angiogenesis. In some aspects, the antibody decreases levels of phosphate, ADP, AMP, and/or adenosine and/or increasing levels of ATP. In some aspects, the antibody increases T effector cell function. In some aspects, the antibody decreases the number of regulatory T cells in tissues or in circulation. In some aspects, the antibody decreases the regulatory T cells or regulatory T cell activity. In some aspects, the antibody increases B cell function. In some aspects, the antibody increases antigen presenting cell function. In some aspects, the antibody inhibits processing of at least one of phospho-antigen from phosphorylated isoprenoid, phosphorylated vitamin B metabolite, and/or phosphorylated riboflavin.

[00315] In some aspects, the antibody has limited ability to limit ATPase of the soluble or extracellular domain. In some aspects, the antibody has limited ability to inhibit ATPase of the cellular and/or extracellular domain of CD39.

7. Glycosylation Variants

[00316] In certain embodiments, an antibody may be altered to increase, decrease or eliminate the extent to which it is glycosylated. Glycosylation of polypeptides is typically either "N-linked" or "O-linked."

[00317] "N-linked" glycosylation refers to the attachment of a carbohydrate moiety to the side chain of an asparagine residue. The tripeptide sequences asparagine-X-serine and asparagine-X-threonine, where X is any amino acid except proline, are the recognition sequences for enzymatic attachment of the carbohydrate moiety to the asparagine side chain. Thus, the presence of either of these tripeptide sequences in a polypeptide creates a potential glycosylation site.

[00318] "O-linked" glycosylation refers to the attachment of one of the sugars N-acetylgalactosamine, galactose, or xylose to a hydroxyamino acid, most commonly serine or threonine, although 5-hydroxyproline or 5-hydroxylysine may also be used.

[00319] Addition or deletion of N-linked glycosylation sites to the antibody may be accomplished by altering the amino acid sequence such that one or more of the above-described tripeptide sequences is created or removed. Addition or deletion of O-linked glycosylation sites may be accomplished by addition, deletion, or substitution of one or more serine or threonine residues in or to (as the case may be) the sequence of an antibody.

[00320] In certain embodiments, the antibody is glycosylated. In certain embodiments, the antibody is deglycosylated. Carbohydrates may be removed by standard techniques. In certain embodiments, the antibody is aglycosylated, for instance by expression in a system that does not glycosylate.

8. Fc Variants

[00321] In certain embodiments, amino acid modifications may be introduced into the Fc region of an antibody provided herein to generate an Fc region variant. In certain embodiments, the Fc region variant possesses some, but not all, effector functions. Such antibodies may be useful, for example, in applications in which the half-life of the antibody *in vivo* is important, yet certain effector functions are unnecessary or deleterious. Examples of effector functions include complement-dependent cytotoxicity (CDC) and antibody-directed

complement-mediated cytotoxicity (ADCC). Numerous substitutions or substitutions or deletions with altered effector function are known in the art.

[00322] An alteration in in CDC and/or ADCC activity can be confirmed using *in vitro* and/or *in vivo* assays. For example, Fc receptor (FcR) binding assays can be conducted to measure FcγR binding. The primary cells for mediating ADCC, NK cells, express FcγRIII only, whereas monocytes express FcγRI, FcγRII and FcγRIII. FcR expression on hematopoietic cells is summarized in Ravetch and Kinet, *Ann. Rev. Immunol.*, 1991, 9:457-492.

[00323] Non-limiting examples of *in vitro* assays to assess ADCC activity of a molecule of interest are provided in U.S. Patent Nos. 5,500,362 and 5,821,337; Hellstrom et al., *Proc. Natl. Acad. Sci. U.S.A.*, 1986, 83:7059-7063; Hellstrom et al., *Proc. Natl. Acad. Sci. U.S.A.*, 1985, 82:1499-1502; and Bruggemann et al., *J. Exp. Med.*, 1987, 166:1351-1361. Useful effector cells for such assays include peripheral blood mononuclear cells (PBMC) and Natural Killer (NK) cells. Alternatively, or additionally, ADCC activity of the molecule of interest may be assessed *in vivo*, using an animal model such as that disclosed in Clynes et al. *Proc. Natl. Acad. Sci. U.S.A.*, 1998, 95:652-656.

[00324] C1q binding assays may also be carried out to confirm that the antibody is unable to bind C1q and hence lacks CDC activity. Examples of C1q binding assays include those described in WO 2006/029879 and WO 2005/100402.

[00325] Complement activation assays include those described, for example, in Gazzano-Santoro et al., *J. Immunol. Methods*, 1996, 202:163-171; Cragg et al., *Blood*, 2003, 101:1045-1052; and Cragg and Glennie, *Blood*, 2004, 103:2738-2743.

[00326] FcRn binding and *in vivo* clearance (half-life determination) can also be measured, for example, using the methods described in Petkova et al., *Intl. Immunol.*, 2006, 18:1759-1769.

9. Preparation of Antibodies

9.1. Antigen Preparation

[00327] The CD39 antigen to be used for production of antibodies may be intact CD39 or a fragment of CD39. The intact CD39, or fragment of CD39, may be in the form of an isolated protein or expressed by a cell. Other forms of CD39 useful for generating antibodies will be apparent to those skilled in the art.

9.2. Monoclonal Antibodies

[00328] Monoclonal antibodies may be obtained, for example, using the hybridoma method first described by Kohler et al., *Nature*, 1975, 256:495-497, and/or by recombinant DNA methods (*see e.g.*, U.S. Patent No. 4,816,567). Monoclonal antibodies may also be obtained, for example, using phage or yeast-based libraries. *See e.g.*, U.S. Patent Nos. 8,258,082 and 8,691,730.

[00329] In the hybridoma method, a mouse or other appropriate host animal is immunized to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the protein used for immunization. Alternatively, lymphocytes may be immunized *in vitro*. Lymphocytes are then fused with myeloma cells using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell. *See* Goding J.W., *Monoclonal Antibodies: Principles and Practice* 3rd ed. (1986) Academic Press, San Diego, CA.

[00330] The hybridoma cells are seeded and grown in a suitable culture medium that contains one or more substances that inhibit the growth or survival of the unfused, parental myeloma cells. For example, if the parental myeloma cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine (HAT medium), which substances prevent the growth of HGPRT-deficient cells.

[00331] Useful myeloma cells are those that fuse efficiently, support stable high-level production of antibody by the selected antibody-producing cells, and are sensitive media conditions, such as the presence or absence of HAT medium. Among these, preferred myeloma cell lines are murine myeloma lines, such as those derived from MOP-21 and MC-11 mouse tumors (available from the Salk Institute Cell Distribution Center, San Diego, CA), and SP-2 or X63-Ag8-653 cells (available from the American Type Culture Collection, Rockville, MD). Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies. *See e.g.*, Kozbor, *J. Immunol.*, 1984, 133:3001.

[00332] After the identification of hybridoma cells that produce antibodies of the desired specificity, affinity, and/or biological activity, selected clones may be subcloned by limiting dilution procedures and grown by standard methods. *See* Goding, *supra*. Suitable culture media for this purpose include, for example, D-MEM or RPMI-1640 medium. In addition, the hybridoma cells may be grown *in vivo* as ascites tumors in an animal.

[00333] DNA encoding the monoclonal antibodies may be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are

capable of binding specifically to genes encoding the heavy and light chains of the monoclonal antibodies). Thus, the hybridoma cells can serve as a useful source of DNA encoding antibodies with the desired properties. Once isolated, the DNA may be placed into expression vectors, which are then transfected into host cells such as bacteria (e.g., *E. coli*), yeast (e.g., *Saccharomyces* or *Pichia* sp.), COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce antibody, to produce the monoclonal antibodies.

9.3. Humanized Antibodies

[00334] Humanized antibodies may be generated by replacing most, or all, of the structural portions of a monoclonal antibody with corresponding human antibody sequences. Consequently, a hybrid molecule is generated in which only the antigen-specific variable, or CDR, is composed of non-human sequence. Methods to obtain humanized antibodies include those described in, for example, Winter and Milstein, *Nature*, 1991, 349:293-299; Rader et al., *Proc. Nat. Acad. Sci. U.S.A.*, 1998, 95:8910-8915; Steinberger et al., *J. Biol. Chem.*, 2000, 275:36073-36078; Queen et al., *Proc. Natl. Acad. Sci. U.S.A.*, 1989, 86:10029-10033; and U.S. Patent Nos. 5,585,089, 5,693,761, 5,693,762, and 6,180,370.

9.4. Human Antibodies

[00335] Human antibodies can be generated by a variety of techniques known in the art, for example by using transgenic animals (e.g., humanized mice). *See, e.g.,* Jakobovits et al., *Proc. Natl. Acad. Sci. U.S.A.*, 1993, 90:2551; Jakobovits et al., *Nature*, 1993, 362:255-258; Bruggermann et al., *Year in Immuno.*, 1993, 7:33; and U.S. Patent Nos. 5,591,669, 5,589,369 and 5,545,807. Human antibodies can also be derived from phage-display libraries (*see e.g.,* Hoogenboom et al., *J. Mol. Biol.*, 1991, 227:381-388; Marks et al., *J. Mol. Biol.*, 1991, 222:581-597; and U.S. Pat. Nos. 5,565,332 and 5,573,905). Human antibodies may also be generated by *in vitro* activated B cells (*see e.g.,* U.S. Patent. Nos. 5,567,610 and 5,229,275). Human antibodies may also be derived from yeast-based libraries (*see e.g.,* U.S. Patent No. 8,691,730).

10. Vectors, Host Cells, and Recombinant Methods

[00336] The invention also provides isolated nucleic acids encoding anti-CD39 antibodies, vectors and host cells comprising the nucleic acids, and recombinant techniques for the production of the antibodies.

[00337] For recombinant production of the antibody, the nucleic acid encoding it may be isolated and inserted into a replicable vector for further cloning (i.e., amplification of the

DNA) or expression. In some aspects, the nucleic acid may be produced by homologous recombination, for example as described in U.S. Patent No. 5,204,244.

[00338] Many different vectors are known in the art. The vector components generally include, but are not limited to, one or more of the following: a signal sequence, an origin of replication, one or more marker genes, an enhancer element, a promoter, and a transcription termination sequence, for example as described in U.S. Patent No. 5,534,615.

[00339] Illustrative examples of suitable host cells are provided below. these host cells are not meant to be limiting.

[00340] Suitable host cells include any prokaryotic (e.g., bacterial) , lower eukaryotic (e.g., yeast), or higher eukaryotic (e.g., mammalian) cells. Suitable prokaryotes include eubacteria, such as Gram-negative or Gram-positive organisms, for example, Enterobacteriaceae such as *Escherichia* (*E. coli*), *Enterobacter*, *Erwinia*, *Klebsiella*, *Proteus*, *Salmonella* (*S. typhimurium*), *Serratia* (*S. marcescans*), *Shigella*, *Bacilli* (*B. subtilis* and *B. licheniformis*), *Pseudomonas* (*P. aeruginosa*), and *Streptomyces*. One useful *E. coli* cloning host is *E. coli* 294, although other strains such as *E. coli* B, *E. coli* X1776, and *E. coli* W3110 are suitable.

[00341] In addition to prokaryotes, eukaryotic microbes such as filamentous fungi or yeast are also suitable cloning or expression hosts for anti-CD39 antibody-encoding vectors. *Saccharomyces cerevisiae*, or common baker's yeast, is a commonly used lower eukaryotic host microorganism. However, a number of other genera, species, and strains are available and useful, such as *Schizosaccharomyces pombe*, *Kluyveromyces* (*K. lactis*, *K. fragilis*, *K. bulgaricus K. wickeramii*, *K. waltii*, *K. drosophilarum*, *K. thermotolerans*, and *K. marxianus*), *Yarrowia*, *Pichia pastoris*, *Candida* (*C. albicans*), *Trichoderma reesia*, *Neurospora crassa*, *Schwanniomyces* (*S. occidentalis*), and filamentous fungi such as, for example *Penicillium*, *Tolypocladium*, and *Aspergillus* (*A. nidulans* and *A. niger*).

[00342] Useful mammalian host cells include COS-7 cells, HEK293 cells; baby hamster kidney (BHK) cells; Chinese hamster ovary (CHO); mouse sertoli cells; African green monkey kidney cells (VERO-76), and the like.

[00343] The host cells used to produce the anti-CD39 antibody of this invention may be cultured in a variety of media. Commercially available media such as, for example, Ham's F10, Minimal Essential Medium (MEM), RPMI-1640, and Dulbecco's Modified Eagle's Medium (DMEM) are suitable for culturing the host cells. In addition, any of the media described in

Ham et al., *Meth. Enz.*, 1979, 58:44; Barnes et al., *Anal. Biochem.*, 1980, 102:255; and U.S. Patent Nos. 4,767,704, 4,657,866, 4,927,762, 4,560,655, and 5,122,469, or WO 90/03430 and WO 87/00195 may be used.

[00344] Any of these media may be supplemented as necessary with hormones and/or other growth factors (such as insulin, transferrin, or epidermal growth factor), salts (such as sodium chloride, calcium, magnesium, and phosphate), buffers (such as HEPES), nucleotides (such as adenosine and thymidine), antibiotics, trace elements (defined as inorganic compounds usually present at final concentrations in the micromolar range), and glucose or an equivalent energy source. Any other necessary supplements may also be included at appropriate concentrations that would be known to those skilled in the art.

[00345] The culture conditions, such as temperature, pH, and the like, are those previously used with the host cell selected for expression, and will be apparent to the ordinarily skilled artisan.

[00346] When using recombinant techniques, the antibody can be produced intracellularly, in the periplasmic space, or directly secreted into the medium. If the antibody is produced intracellularly, as a first step, the particulate debris, either host cells or lysed fragments, is removed, for example, by centrifugation or ultrafiltration. For example, Carter et al. (*Bio/Technology*, 1992, 10:163-167) describes a procedure for isolating antibodies which are secreted to the periplasmic space of *E. coli*. Briefly, cell paste is thawed in the presence of sodium acetate (pH 3.5), EDTA, and phenylmethylsulfonylfluoride (PMSF) over about 30 minutes. Cell debris can be removed by centrifugation.

[00347] In some embodiments, the antibody is produced in a cell-free system. In some aspects, the cell-free system is an *in vitro* transcription and translation system as described in Yin et al., *mAbs*, 2012, 4:217-225, incorporated by reference in its entirety. In some aspects, the cell-free system utilizes a cell-free extract from a eukaryotic cell or from a prokaryotic cell. In some aspects, the prokaryotic cell is *E. coli*. Cell-free expression of the antibody may be useful, for example, where the antibody accumulates in a cell as an insoluble aggregate, or where yields from periplasmic expression are low.

[00348] Where the antibody is secreted into the medium, supernatants from such expression systems are generally first concentrated using a commercially available protein concentration filter, for example, an Amicon® or Millipore® Pellcon® ultrafiltration unit. A protease inhibitor such as PMSF may be included in any of the foregoing steps to inhibit

proteolysis and antibiotics may be included to prevent the growth of adventitious contaminants.

[00349] The antibody composition prepared from the cells can be purified using, for example, hydroxylapatite chromatography, gel electrophoresis, dialysis, and affinity chromatography, with affinity chromatography being a particularly useful purification technique. The suitability of protein A as an affinity ligand depends on the species and isotype of any immunoglobulin Fc domain that is present in the antibody. Protein A can be used to purify antibodies that are based on human γ1, γ2, or γ4 heavy chains (Lindmark et al., *J. Immunol. Meth.*, 1983, 62:1-13). Protein G is useful for all mouse isotypes and for human γ3 (Guss et al., *EMBO J.*, 1986, 5:1567-1575).

[00350] The matrix to which the affinity ligand is attached is most often agarose, but other matrices are available. Mechanically stable matrices such as controlled pore glass or poly(styrenedivinyl)benzene allow for faster flow rates and shorter processing times than can be achieved with agarose. Where the antibody comprises a C_{H3} domain, the BakerBond ABX® resin is useful for purification.

[00351] Other techniques for protein purification, such as fractionation on an ion-exchange column, ethanol precipitation, Reverse Phase HPLC, chromatography on silica, chromatography on heparin Sepharose®, chromatofocusing, SDS-PAGE, and ammonium sulfate precipitation are also available, and can be applied by one of skill in the art.

[00352] Following any preliminary purification step(s), the mixture comprising the antibody of interest and contaminants may be subjected to low pH hydrophobic interaction chromatography using an elution buffer at a pH between about 2.5 to about 4.5, generally performed at low salt concentrations (e.g., from about 0 to about 0.25 M salt).

11. Pharmaceutical Compositions and Methods of Administration

[00353] Any of the antibodies provided herein can be provided in any appropriate pharmaceutical composition and be administered by any suitable route of administration. Suitable routes of administration include, but are not limited to, the inhalation, intraarterial, intradermal, intramuscular, intraperitoneal, intravenous, nasal, parenteral, pulmonary, and subcutaneous routes.

[00354] The pharmaceutical composition may comprise one or more pharmaceutical excipients. Any suitable pharmaceutical excipient may be used, and one of ordinary skill in the art is capable of selecting suitable pharmaceutical excipients. Accordingly, the pharmaceutical excipients provided below are intended to be illustrative, and not limiting. Additional

pharmaceutical excipients include, for example, those described in the *Handbook of Pharmaceutical Excipients*, Rowe et al. (Eds.) 6th Ed. (2009), incorporated by reference in its entirety.

[00355] In some embodiments, the pharmaceutical composition comprises an anti-foaming agent. Any suitable anti-foaming agent may be used. In some aspects, the anti-foaming agent is selected from an alcohol, an ether, an oil, a wax, a silicone, a surfactant, and combinations thereof. In some aspects, the anti-foaming agent is selected from a mineral oil, a vegetable oil, ethylene bis stearamide, a paraffin wax, an ester wax, a fatty alcohol wax, a long chain fatty alcohol, a fatty acid soap, a fatty acid ester, a silicon glycol, a fluorosilicone, a polyethylene glycol-polypropylene glycol copolymer, polydimethylsiloxane-silicon dioxide, ether, octyl alcohol, capryl alcohol, sorbitan trioleate, ethyl alcohol, 2-ethyl-hexanol, dimethicone, oleyl alcohol, simethicone, and combinations thereof.

[00356] In some embodiments, the pharmaceutical composition comprises a cosolvent. Illustrative examples of cosolvents include ethanol, poly(ethylene) glycol, butylene glycol, dimethylacetamide, glycerin, and propylene glycol.

[00357] In some embodiments, the pharmaceutical composition comprises a buffer. Illustrative examples of buffers include acetate, borate, carbonate, lactate, malate, phosphate, citrate, hydroxide, diethanolamine, monoethanolamine, glycine, methionine, guar gum, and monosodium glutamate.

[00358] In some embodiments, the pharmaceutical composition comprises a carrier or filler. Illustrative examples of carriers or fillers include lactose, maltodextrin, mannitol, sorbitol, chitosan, stearic acid, xanthan gum, and guar gum.

[00359] In some embodiments, the pharmaceutical composition comprises a surfactant. Illustrative examples of surfactants include *d*-alpha tocopherol, benzalkonium chloride, benzethonium chloride, cetrimide, cetylpyridinium chloride, docusate sodium, glyceryl behenate, glyceryl monooleate, lauric acid, macrogol 15 hydroxystearate, myristyl alcohol, phospholipids, polyoxyethylene alkyl ethers, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene stearates, polyoxylglycerides, sodium lauryl sulfate, sorbitan esters, and vitamin E polyethylene(glycol) succinate.

[00360] In some embodiments, the pharmaceutical composition comprises an anti-caking agent. Illustrative examples of anti-caking agents include calcium phosphate (tribasic), hydroxymethyl cellulose, hydroxypropyl cellulose, and magnesium oxide.

[00361] Other excipients that may be used with the pharmaceutical compositions include, for example, albumin, antioxidants, antibacterial agents, antifungal agents, bioabsorbable polymers, chelating agents, controlled release agents, diluents, dispersing agents, dissolution enhancers, emulsifying agents, gelling agents, ointment bases, penetration enhancers, preservatives, solubilizing agents, solvents, stabilizing agents, and sugars. Specific examples of each of these agents are described, for example, in the *Handbook of Pharmaceutical Excipients*, Rowe et al. (Eds.) 6th Ed. (2009), The Pharmaceutical Press, incorporated by reference in its entirety.

[00362] In some embodiments, the pharmaceutical composition comprises a solvent. In some aspects, the solvent is saline solution, such as a sterile isotonic saline solution or dextrose solution. In some aspects, the solvent is water for injection.

[00363] In some embodiments, the pharmaceutical compositions are in a particulate form, such as a microparticle or a nanoparticle. Microparticles and nanoparticles may be formed from any suitable material, such as a polymer or a lipid. In some aspects, the microparticles or nanoparticles are micelles, liposomes, or polymersomes. In certain embodiments, a composition provided herein is a pharmaceutical composition or a single unit dosage form. Pharmaceutical compositions and single unit dosage forms provided herein comprise a prophylactically or therapeutically effective amount of one or more prophylactic or therapeutic antibodies.

[00364] Further encompassed herein are anhydrous pharmaceutical compositions and dosage forms comprising an antibody, since water can facilitate the degradation of some antibodies.

[00365] Anhydrous pharmaceutical compositions and dosage forms provided herein can be prepared using anhydrous or low moisture containing ingredients and low moisture or low humidity conditions. Pharmaceutical compositions and dosage forms that comprise lactose and at least one active ingredient that comprises a primary or secondary amine can be anhydrous if substantial contact with moisture and/or humidity during manufacturing, packaging, and/or storage is expected.

[00366] An anhydrous pharmaceutical composition should be prepared and stored such that its anhydrous nature is maintained. Accordingly, anhydrous compositions can be packaged using materials known to prevent exposure to water such that they can be included in suitable formulary kits. Examples of suitable packaging include, but are not limited to, hermetically

sealed foils, plastics, unit dose containers (*e.g.*, vials), blister packs, and strip packs.

11.1. Parenteral Dosage Forms

[00367] In certain embodiments, provided are parenteral dosage forms. Parenteral dosage forms can be administered to subjects by various routes including, but not limited to, subcutaneous, intravenous (including bolus injection), intramuscular, and intraarterial. Because their administration typically bypasses subjects' natural defenses against contaminants, parenteral dosage forms are typically, sterile or capable of being sterilized prior to administration to a subject. Examples of parenteral dosage forms include, but are not limited to, solutions ready for injection, dry products ready to be dissolved or suspended in a pharmaceutically acceptable vehicle for injection, suspensions ready for injection, and emulsions.

[00368] Suitable vehicles that can be used to provide parenteral dosage forms are well known to those skilled in the art. Examples include, but are not limited to: Water for Injection USP; aqueous vehicles such as, but not limited to, Sodium Chloride Injection, Ringer's Injection, Dextrose Injection, Dextrose and Sodium Chloride Injection, and Lactated Ringer's Injection; water miscible vehicles such as, but not limited to, ethyl alcohol, polyethylene glycol, and polypropylene glycol; and non-aqueous vehicles such as, but not limited to, corn oil, cottonseed oil, peanut oil, sesame oil, ethyl oleate, isopropyl myristate, and benzyl benzoate.

[00369] Excipients that increase the solubility of one or more of the antibodies disclosed herein can also be incorporated into the parenteral dosage forms.

11.2. Dosage and Unit Dosage Forms

[00370] In human therapeutics, the doctor will determine the posology which he considers most appropriate according to a preventive or curative treatment and according to the age, weight, condition and other factors specific to the subject to be treated.

[00371] The amount of the antibody or composition which will be effective in the prevention or treatment of a disorder or one or more symptoms thereof will vary with the nature and severity of the disease or condition, and the route by which the antibody is administered. The frequency and dosage will also vary according to factors specific for each subject depending on the specific therapy (*e.g.*, therapeutic or prophylactic agents) administered, the severity of the disorder, disease, or condition, the route of administration, as well as age, body, weight, response, and the past medical history of the subject. Effective doses may be

extrapolated from dose-response curves derived from *in vitro* or animal model test systems.

[00372] In certain embodiments, exemplary doses of a composition include milligram or microgram amounts of the antibody per kilogram of subject or sample weight (*e.g.*, about 10 micrograms per kilogram to about 50 milligrams per kilogram, about 100 micrograms per kilogram to about 25 milligrams per kilogram, or about 100 microgram per kilogram to about 10 milligrams per kilogram). In certain embodiment, the dosage of the antibody provided herein, based on weight of the antibody, administered to prevent, treat, manage, or ameliorate a disorder, or one or more symptoms thereof in a subject is 0.1 mg/kg, 1 mg/kg, 2 mg/kg, 3 mg/kg, 4 mg/kg, 5 mg/kg, 6 mg/kg, 10 mg/kg, or 15 mg/kg or more of a subject's body weight. In another embodiment, the dosage of the composition or a composition provided herein administered to prevent, treat, manage, or ameliorate a disorder, or one or more symptoms thereof in a subject is 0.1 mg to 200 mg, 0.1 mg to 100 mg, 0.1 mg to 50 mg, 0.1 mg to 25 mg, 0.1 mg to 20 mg, 0.1 mg to 15 mg, 0.1 mg to 10 mg, 0.1 mg to 7.5 mg, 0.1 mg to 5 mg, 0.1 to 2.5 mg, 0.25 mg to 20 mg, 0.25 to 15 mg, 0.25 to 12 mg, 0.25 to 10 mg, 0.25 mg to 7.5 mg, 0.25 mg to 5 mg, 0.25 mg to 2.5 mg, 0.5 mg to 20 mg, 0.5 to 15 mg, 0.5 to 12 mg, 0.5 to 10 mg, 0.5 mg to 7.5 mg, 0.5 mg to 5 mg, 0.5 mg to 2.5 mg, 1 mg to 20 mg, 1 mg to 15 mg, 1 mg to 12 mg, 1 mg to 10 mg, 1 mg to 7.5 mg, 1 mg to 5 mg, or 1 mg to 2.5 mg.

[00373] The dose can be administered according to a suitable schedule, for example, once, two times, three times, or for times weekly. It may be necessary to use dosages of the antibody outside the ranges disclosed herein in some cases, as will be apparent to those of ordinary skill in the art. Furthermore, it is noted that the clinician or treating physician will know how and when to interrupt, adjust, or terminate therapy in conjunction with subject response.

[00374] Different therapeutically effective amounts may be applicable for different diseases and conditions, as will be readily known by those of ordinary skill in the art. Similarly, amounts sufficient to prevent, manage, treat or ameliorate such disorders, but insufficient to cause, or sufficient to reduce, adverse effects associated with the antibodies provided herein are also encompassed by the herein described dosage amounts and dose frequency schedules. Further, when a subject is administered multiple dosages of a composition provided herein, not all of the dosages need be the same. For example, the dosage administered to the subject may be increased to improve the prophylactic or therapeutic effect of the composition or it may be decreased to reduce one or more side effects that a particular subject is experiencing.

[00375] In certain embodiments, treatment or prevention can be initiated with one or more loading doses of an antibody or composition provided herein followed by one or more maintenance doses.

[00376] In certain embodiments, a dose of an antibody or composition provided herein can be administered to achieve a steady-state concentration of the antibody in blood or serum of the subject. The steady-state concentration can be determined by measurement according to techniques available to those of skill or can be based on the physical characteristics of the subject such as height, weight and age.

[00377] In certain embodiments, administration of the same composition may be repeated and the administrations may be separated by at least 1 day, 2 days, 3 days, 5 days, 10 days, 15 days, 30 days, 45 days, 2 months, 75 days, 3 months, or 6 months. In other embodiments, administration of the same prophylactic or therapeutic agent may be repeated and the administration may be separated by at least 1 day, 2 days, 3 days, 5 days, 10 days, 15 days, 30 days, 45 days, 2 months, 75 days, 3 months, or 6 months.

12. Therapeutic Applications

[00378] For therapeutic applications, the antibodies of the invention are administered to a mammal, generally a human, in a pharmaceutically acceptable dosage form such as those known in the art and those discussed above. For example, the antibodies of the invention may be administered to a human intravenously as a bolus or by continuous infusion over a period of time, by intramuscular, intraperitoneal, intra-cerebrospinal, subcutaneous, intra-articular, intrasynovial, intrathecal, or intratumoral routes. The antibodies also are suitably administered by peritumoral, intralesional, or perilesional routes, to exert local as well as systemic therapeutic effects. The intraperitoneal route may be particularly useful, for example, in the treatment of ovarian tumors.

[00379] The antibodies provided herein may be useful for the treatment of any disease or condition involving CD39, such as cancer, autoimmune disease, and infection.

[00380] Any suitable cancer may be treated with the antibodies provided herein. Illustrative suitable cancers include, for example, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), adrenocortical carcinoma, anal cancer, appendix cancer, astrocytoma, basal cell carcinoma, brain tumor, bile duct cancer, bladder cancer, bone cancer, breast cancer, bronchial tumor, Burkitt Lymphoma, carcinoma of unknown primary origin, cardiac tumor, cervical cancer, chordoma, chronic lymphocytic leukemia (CLL), chronic

myelogenous leukemia (CML), chronic myeloproliferative neoplasm, colon cancer, colorectal cancer, craniopharyngioma, cutaneous T-cell lymphoma, ductal carcinoma, embryonal tumor, endometrial cancer, ependymoma, esophageal cancer, esthesioneuroblastoma, fibrous histiocytoma, Ewing sarcoma, eye cancer, germ cell tumor, gallbladder cancer, gastric cancer, gastrointestinal carcinoid tumor, gastrointestinal stromal tumor, gestational trophoblastic disease, glioma, head and neck cancer, hairy cell leukemia, hepatocellular cancer, histiocytosis, Hodgkin lymphoma, hypopharyngeal cancer, intraocular melanoma, islet cell tumor, Kaposi sarcoma, kidney cancer, Langerhans cell histiocytosis, laryngeal cancer, leukemia, lip and oral cavity cancer, liver cancer, lobular carcinoma in situ, lung cancer, lymphoma, macroglobulinemia, malignant fibrous histiocytoma, melanoma, Merkel cell carcinoma, mesothelioma, metastatic squamous neck cancer with occult primary, midline tract carcinoma involving *NUT* gene, mouth cancer, multiple endocrine neoplasia syndrome, multiple myeloma, mycosis fungoides, myelodysplastic syndrome, myelodysplastic/myeloproliferative neoplasm, nasal cavity and par nasal sinus cancer, nasopharyngeal cancer, neuroblastoma, non-Hodgkin lymphoma, non-small cell lung cancer, oropharyngeal cancer, osteosarcoma, ovarian cancer, pancreatic cancer, papillomatosis, paraganglioma, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytomas, pituitary tumor, pleuropulmonary blastoma, primary central nervous system lymphoma, prostate cancer, rectal cancer, renal cell cancer, renal pelvis and ureter cancer, retinoblastoma, rhabdoid tumor, salivary gland cancer, Sezary syndrome, skin cancer, small cell lung cancer, small intestine cancer, soft tissue sarcoma, spinal cord tumor, stomach cancer, T-cell lymphoma, teratoid tumor, testicular cancer, throat cancer, thymoma and thymic carcinoma, thyroid cancer, urethral cancer, uterine cancer, vaginal cancer, vulvar cancer, and Wilms tumor.

[00381] Any suitable autoimmune disease may be treated with the antibodies provided herein. Illustrative suitable autoimmune diseases, or diseases with an autoimmune component, include, for example, acute disseminated encephalomyelitis (ADEM), acute necrotizing hemorrhagic leukoencephalitis, Addison's disease, agammaglobulinemia, alopecia areata, amyloidosis, ankylosing spondylitis, anti-GBM/anti-TBM nephritis, antiphospholipid syndrome (APS), autoimmune angioedema, autoimmune aplastic anemia, autoimmune dysautonomia, autoimmune hepatitis, autoimmune hyperlipidemia, autoimmune immunodeficiency, autoimmune inner ear disease (AIED), autoimmune myocarditis, autoimmune oophoritis, autoimmune pancreatitis, autoimmune retinopathy, autoimmune thrombocytopenic purpura (ATP), autoimmune thyroid disease, autoimmune urticarial, axonal

& neuronal neuropathies, Balo disease, Behcet's disease, bullous pemphigoid, cardiomyopathy, Castleman disease, Celiac disease, Chagas disease, chronic fatigue syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), chronic recurrent multifocal ostomyelitis (CRMO), Churg-Strauss syndrome, cicatricial pemphigoid/benign mucosal pemphigoid, Crohn's disease, Cogans syndrome, cold agglutinin disease, colitis, congenital heart block, coxsackie myocarditis, CREST disease, essential mixed cryoglobulinemia, demyelinating neuropathies, dermatitis herpetiformis, dermatomyositis, Devic's disease (neuromyelitis optica), discoid lupus, Dressler's syndrome, endometriosis, eosinophilic esophagitis, eosinophilic fasciitis, erythema nodosum, experimental allergic encephalomyelitis, Evans syndrome, fibromyalgia, fibrosing alveolitis, giant cell arteritis (temporal arteritis), giant cell myocarditis, glomerulonephritis, Goodpasture's syndrome, granulomatosis with polyangiitis (GPA) (formerly called Wegener's Granulomatosis), Graves' disease, Guillain-Barre syndrome, Hashimoto's encephalitis, Hashimoto's thyroiditis, hemolytic anemia, Henoch-Schonlein purpura, herpes gestationis, hypogammaglobulinemia, idiopathic thrombocytopenic purpura (ITP), IgA nephropathy, IgG4-related sclerosing disease, immunoregulatory lipoproteins, inclusion body myositis, inflammatory bowel disease. interstitial cystitis, juvenile arthritis, juvenile diabetes (Type 1 diabetes), juvenile myositis, Kawasaki syndrome, Lambert-Eaton syndrome, leukocytoclastic vasculitis, lichen planus, lichen sclerosus, ligneous conjunctivitis, linear IgA disease (LAD), lupus (SLE), Lyme disease (chronic), Meniere's disease, microscopic polyangiitis, mixed connective tissue disease (MCTD), Mooren's ulcer, Mucha-Habermann disease, multiple sclerosis, myasthenia gravis, myositis, narcolepsy, neuromyelitis optica (Devic's), neutropenia, ocular cicatricial pemphigoid, optic neuritis, palindromic rheumatism, PANDAS (Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus), paraneoplastic cerebellar degeneration, paroxysmal nocturnal hemoglobinuria (PNH), Parry Romberg syndrome, Parsonnage-Turner syndrome, pars planitis (peripheral uveitis), pemphigus, peripheral neuropathy, perivenous encephalomyelitis, pernicious anemia, POEMS syndrome, polyarteritis nodosa, type I, II, & III autoimmune polyglandular syndromes, polymyalgia rheumatic, polymyositis, postmyocardial infarction syndrome, postpericardiotomy syndrome, progesterone dermatitis, primary biliary cirrhosis, rimary sclerosing cholangitis, psoriasis, psoriatic arthritis, idiopathic pulmonary fibrosis, pyoderma gangrenosum, pure red cell aplasia, Raynauds phenomenon, reactive arthritis, reflex sympathetic dystrophy, Reiter's syndrome, relapsing polychondritis, restless legs syndrome, retroperitoneal fibrosis, rheumatic fever,

rheumatoid arthritis, sarcoidosis, Schmidt syndrome, scleritis, scleroderma, Sjogren's syndrome, sperm & testicular autoimmunity, stiff person syndrome, subacute bacterial endocarditis (SBE), Susac's syndrome, sympathetic ophthalmia, Takayasu's arteritis, temporal arteritis/giant cell arteritis, thrombotic disease, thrombocytopenic purpura (TTP), Tolosa-Hunt syndrome, transverse myelitis, type 1 diabetes, ulcerative colitis, undifferentiated connective tissue disease (UCTD), uveitis, vasculitis, vesiculobullous dermatosis, vitiligo, and Wegener's granulomatosis (now termed Granulomatosis with Polyangiitis (GPA).

[00382] Any suitable infection may be treated with the antibodies provided herein. Illustrative suitable infections include, for example, hepatitis A virus, hepatitis B virus, hepatitis C virus (HCV), human immunodeficiency virus (HIV), and other viral infections.

13. Diagnostic Applications

[00383] In some embodiments, the antibodies provided herein are used in diagnostic applications. For example, an ant-CD39 antibody may be useful in assays for CD39 protein. In some aspects, the antibody can be used to detect the expression of CD39 in various cells and tissues. These assays may be useful, for example, evaluating cancer and autoimmune disease.

[00384] In some diagnostic applications, the antibody may be labeled with a detectable moiety. Suitable detectable moieties include, but are not limited to radioisotopes, fluorescent labels, and enzyme-substrate labels. In another embodiment of the invention, the anti-CD39 antibody need not be labeled, and the presence thereof can be detected using a labeled antibody which specifically binds to the anti-CD39 antibody.

14. Affinity Purification Reagents

[00385] The antibodies of the invention may be used as affinity purification agents. In this process, the antibodies may be immobilized on a solid phase such a resin or filter paper, using methods well known in the art. The immobilized antibody is contacted with a sample containing the CD39 protein (or fragment thereof) to be purified, and thereafter the support is washed with a suitable solvent that will remove substantially all the material in the sample except the CD39 protein, which is bound to the immobilized antibody. Finally, the support is washed with another suitable solvent, such as glycine buffer, pH 5.0, that will release the CD39 protein from the antibody.

15. Kits

[00386] In some embodiments, an anti-CD39 antibody provided herein is provided in the form of a kit, i.e., a packaged combination of reagents in predetermined amounts with

instructions for performing a procedure. In some embodiments, the procedure is a diagnostic assay. In other embodiments, the procedure is a therapeutic procedure.

[00387] In some embodiments, the kit further comprises a solvent for the reconstitution of the anti-CD39 antibody. In some embodiments, the anti-CD39 antibody is provided in the form of a pharmaceutical composition.

EXAMPLES

Example 1: Selection of CD39 Antigen-Binding Proteins

[00388] CD39 ABPs were selected from a synthetic library of human antibodies presented on the surface of yeast cells in IgG format, as generally described, e.g., in WO2009036379; WO2010105256; WO2012009568; and Xu et al., Protein Eng. Des. Sel., 2013, 26:663-670 (each incorporated by reference in its entirety), and more specifically as provided below. The sequences and characteristics of the ABPs isolated from the recombinant library are provided in Table S.

[00389] Eight naïve human synthetic yeast libraries each of ~10E+09 diversity were propagated as described in WO2009036379; WO2010105256; WO2012009568; and Xu et al., Protein Eng. Des. Sel., 2013, 26:663-670; each incorporated by reference in its entirety. For the first two rounds of selection, a magnetic bead sorting technique utilizing the Miltenyi MACS® system was performed, as described in Siegel et al., J. Immunol. Meth., 2004, 286:141-153. The following rounds of selection were performed using flow cytometry based sorting. For all round of selection, the antigen was biotinylated human CD39 extracellular domain (heretofore "ECD"), and decreasing concentrations of antigen were used in each subsequent round of selection. In addition to selection on antigen, some rounds of selection were employed in order to reduce the number of non-specific binders utilizing soluble membrane proteins from CHO cells (see WO2014179363 and Xu et al., Protein Eng. Des. Sel., 2013, 26:663-670, each incorporated by reference in its entirety). After the final round of sorting, yeast were plated and individual colonies were picked for characterization and for nomination of clones for affinity maturation.

[00390] Antibody variable domains of interest were synthesized, with codon optimization to maximize transient expression in host cells. The variable regions were cloned in to expression vectors containing human immunoglobulin constant domains and their sequence confirmed. Antibody heavy and light chain vector pairings were transfected into

Expi293 cells using the Expifectamine system (Invitrogen). Transient cultures were harvested on day 4 and clarified cell culture supernatant IgG titer was estimated using Bio-Layer Interferometry (BLI) using Octet (ForteBio) alongside standards. Antibodies were subsequently purified on a Protein A column and eluted using low pH glycine. Purified antibody samples were then buffer-exchanged or dialyzed into downstream assay-compatible buffers.

[00391] Antibody purity was assessed by running samples on SDS-PAGE and on an analytical size exclusion chromatography column.

[00392] Light Chain Shuffling: Heavy chain plasmids were extracted from naïve outputs (described herein) and transformed into a pre-made naïve light chain library with a diversity of 10E+06. Selections were performed as described above with one round of MACS sorting and three rounds of FACS sorting using decreasing amounts of biotinylated ECD antigen for respective rounds. Selected individual heavy chains from the primary discovery process were also independently transformed into separate pre-made light chain libraries with a diversity of 10E+06 and selections performed as described above with one round of MACS sorting and three rounds of FACS sorting using decreasing amount of biotinylated ECD antigen for respective rounds.

Example 2: Affinity Maturation

[00393] Optimization of naïve clones was carried out utilizing three maturation strategies; diversification of CDR-H1 and CDR-H2; diversification of CDR-H3; diversification of CDR-L1, L2 and L3; shuffling of diversified heavy and light chains.

[00394] CDR-H1 and CDR-H2 Selection: The CDR-H3s from clones selected from each of the light chain batch diversification, light chain diversification, and naive discovery efforts were independently recombined into premade libraries with CDR-H1 and CDR-H2 variants of a diversity of >10E+8 and selections were performed using ECD antigen. Affinity pressures were applied by using decreasing concentrations of antigen.

[00395] CDR-H3 Selection: Clones obtained from the CDR-H1 and CDR-H2 selection procedure were subject to additional rounds of affinity maturation via walking dimer mutagenesis of the heavy chain. Selections were performed using ECD as antigen generally as described above but with the addition of employing FACS sorting for all selection rounds.

[00396] CDR-L1, L2, L3 Selection: Clones obtained from the CDR-H1 and CDR-H2

selection procedure were subject to additional rounds of affinity maturation via mutagenesis of the light chain. The CDR-L1 and CDR-L2 diversity derived from a pre-made library while CDR-L3 diversity derived from walking dimer mutagenesis. Selections were performed using ECD as antigen generally as described above but with the addition of employing FACS sorting for all selection rounds, with one round of MACS followed by three rounds of FACS in the CDR-L1, L2, L3 process described here.

[00397] Diversified Heavy Chain and Light Chain Shuffling: Outputs from heavy chain diversification and light diversification described above were recombined and selections were performed using ECD as antigen generally as described above but with the addition of employing FACS sorting for all selection rounds.

Example 3: Monovalent Affinity Of Anti-hCD39 Antibodies To Recombinant CD39 Extracellular Domain

[00398] Binding kinetics were measured using the Octet Red96 system (ForteBio) at 25°C in running buffer (1x Pall ForteBio Kinetics Buffer diluted into PBS or Tris pH 7.4). In brief, 1.25 mg/ml of unlabeled anti-hCD39 antibodies were immobilized onto anti-human Fc sensors. After a short baseline step in running buffer, the sensors were exposed to varying concentrations (10-300 nM) of rhCD39-ECD-His (R&D Systems) for the association step. Dissociation of the complex was monitored upon exposure of the sensors to running buffer once again. Data was processed using ForteBio Octet software with baseline subtraction, global fit and 1:1 binding model to obtain association and dissociation rates. K_D was calculated from the ratio of k_d to k_a.

[00399] Data shown in FIG. 1 had R^2 >0.980. PF= poor fit. The association and dissociation time course data was globally fit with a simple 1:1 Langmuir binding model to yield on-rate (kon) and off-rate (koff) values. The equilibrium dissociation constants (K_D) were calculated from the kon and koff values. The kon values ranged from 1.93E+04 to 1.72E+06 $M^{-1}s^{-1}$ and the off rate values ranges from 3.65E-01 to 1.11E-04 s^{-1}. The K_D values ranged from 4.09E-07 to 7.31E-011 molar indicating that all of the antibodies bound with moderate or high affinity to human CD39 ECD.

[00400] The paralog specificity of the anti-CD39 antibodies was assessed by biolayer interferometry using soluble recombinant human ENTDP2 and soluble recombinant human ENTDP3 (both from R&D Systems). ENTDP2 and ENTDP3 are enzymes with functions similar to CD39. None of the antibodies exhibited detectable binding to ENTDP2 or ENTDP3

(data not shown). Thus all of the antibodies exhibit specific binding to human CD39.

Example 4: Inhibition Of Recombinant Human CD39 Extracellular Domain

[00401] The inhibition of recombinant human CD39 ECD by anti-CD39 antibodies was measured as follows. Recombinant human CD39/ENTPD1 (4397-EN from R&D systems), (either 5 or 10 nM final concentration) was combined with anti-CD39 IgGs (0.25 or 1 micromolar final concentration) in 25 mM Tris, 5 mM $CaCl_2$, pH 7.5 in a 96-well plate and incubated at room temperature for 2 hrs. ATP (Sigma A1852-1VL) was then added to a final concentration of 500 micromolar and incubated at 37°C for 60 minutes. The plate was then placed at room temperature and CellTiter-Glo Luminescent Cell Viability Assay solution was added to each well of the assay plate, mixed and read on a microplate reader using "CellTiter-Glo luminescent" preset. Control reactions consisting of negative control IgG, IgG only (no ATP), ATP only (no CD39) were run using the same method. Data values are the average of 2 replicates.

[00402] Inhibition of human CD39 ECD enzymatic activity by anti-CD39 antibodies was determined by measuring ATP levels using the CellTiter-Glo assay (FIG.s 2 A-E). The enzymatic catabolism of ATP by CD39 ECD was observed in the presence of an isotype control antibody or no IgG with average RLU values ranging from 38 to 857. All of the anti-CD39 antibodies showed marked inhibition ATP catabolism by CD39, having much higher average RLU values than the isotype control antibody (average RLU values range from 4890 to 20329). In contrast, Benchmark antibody BY40va did not show significant inhibition of CC39 ECD in this assay having RLU values similar to the isotype control antibody (average RLU values 11 and 415).

Example 5: Antibodies Bind To CHO Cells Expressing Human And Cyno CD39

[00403] Binding of anti-CD39 IgGs to Chinese Hamster Ovary K1 (CHO) CD39 cells. 100 nanomolar IgGs (each antibody is indicated as a unique clone number in the FIG.) were incubated at 25°C for 30 minutes on ice in phosphate buffered saline (PBS) with parental CHO cells or CHO cells engineered to express either human or cynomolgus macaque (Macaca fascicularis) CD39 (CHO CD39 cells). Cells were then washed with ice cold PBS and incubated with a fluorescently labeled goat-anti-human IgG for 20 minutes on ice. Cells were washed and resuspended in ice cold PBS prior to analysis by flow cytrometry. Fold over background binding levels represent the ratio of median fluorescence intensity (MFI) values for anti-CD39 antibodies binding to CHO CD39 to MFI values for anti-CD39 antibodies binding to the parental CHO cells.

[00404] The anti-CD39 antibodies bound to CHO cells expressing cellular human CD39 (CHO CD39 cells) and did not exhibit significant binding to parental CHO cells (FIGS. 2F-J). The binding of these antibodies to CHO CD39 cells ranged from 10 to 2033-fold over background. Antibodies 28337 and 27575 did not show significant binding to CHO CD39 cells (only 2 to 4-fold over background) (FIGS. 2F-J) indicating that these antibodies do not have low affinity for the cellular form of human CD39.

[00405] The ortholog specificity of the anti-CD39 antibodies was assessed with flow cytrometry using CHO cells engineered to express either cynomolgus macaque or mouse CD39. The anti-CD39 antibodies bound to cynomolgus macaque CD39 to a similar extent as human CD39 (FIGS. 2 F-J). None of the anti-CD39 antibodies showed detectable binding to mouse CD39. Thus, the anti-CD39 antibodies are cross reactive to cynomolgus macaque CD39 but not to mouse CD39.

Example 6: Binding Of Antibodies To Cell Surface CD39 In MEL-28 Or 721 Cells And Antibodies That Inhibit CD39 On MEL-28 Cells A Short Term ATPAse Assay

[00406] Cells were incubated with serially diluted anti-CD39 antibodies for 30 minutes at 4 degrees C. Cells were washed 3 times in FACS buffer (PS, 2% FBS, and 2 mM EDTA) and next incubated with secondary antibody (goat anti-human IgG Southern Biotech) at 1:100 for 30 minutes at 4 degrees C. Cells were washed, resuspended in FACS buffer, and analyzed for binding by flow cytometry analysis on BD Celesta.

[00407] $3.5x10^4$ MEL-28 cells/well were washed with Tris buffer and incubated with serially diluted (100-0.00013nM) antibody for 30 minutes at 37 degrees C. 50 μM ATP was added to each well and incubated with cells for 15 minutes. The supernatants were collected and analyzed in Malachite Green Assay (R&D) according to manufacturer's protocol. Phosphate released from CD39 processing of ATP was used as a readout of enzyme activity. Palivizumab was used as an isotype control and ARL (Tocris) and POM-1 (Alpha Aesar), non-specific small molecule inhibitors of CD39, were used as positive controls at 100 μm.

[00408] All antibodies bound to endogenously expressed CD39 on both cell lines with similar affinity with EC50 ranges from 0.05-0.28 μg/ml on MEL-28 (*see* Fig. 3 A) and with EC50 ranges of 0.2-7.5 μg/ml on 721.22 cell line (*see* Fig.3B). Maximum signal (MFI) differed between antibodies tested even when EC50 values were similar (FIGS. 3A-B).

[00409] After confirmation of cellular binding, anti-CD39 antibodies were evaluated for inhibition of ATPase activity on MEL-28 cell in short term 30 minute Malachite Green

phosphate readout assay. Isotype control was used to establish maximum possible signal from ATP processing in MEL-28 cells–50 μm ATP addition to cells typically resulted in 55-60 μM phosphate signal in this assay (*see* Fig.4A and B). Anti-CD39 antibodies inhibited ATPase activity in MEL-28 cells by 60-80% at the highest concentration of antibodies tested (100nM) – this level of inhibition was similar to non-specific ATPase inhibitors ARL and POM1 (*see* Fig.4A). IC50 values for anti-CD39 antibodies in MEL-28 malachite green assay were all in sub-nanomolar range (*see* Fig. 4B).

Example 7: ATP Preservation Quantified When MEL-28 Cells Are Treated With CD39 Enzymatic Inhibitors

[00410] $3.5x10^4$ MEL-28 cells were plated overnight at 37 degrees C. Cells were washed with Tris assay buffer to remove phosphate. 100nM titrated down to 0.005pM of monoclonal antibodies were incubated with cells for 30 minutes at 37 degrees C. 50 μM ATP was added and incubated for 15 minutes. Supernates were harvested and frozen. Supernates were thawed and evaluated for ATP using the EnzyLight (EnzyLight ATP Assay Kit, BioAssay Systems). Palivizumab was used as an isotype control and ARL (Tocris) and POM-1 (Alpha Aesar) used at a concentration of 100 μM are non-specific small molecule inhibitors of CD39 as positive controls.

[00411] ATP was almost undetectable after 30 minutes post ATP addition to the cells in untreated and/or isotype treated samples (*see* Fig.5 A) while all of the anti-CD39 antibodies tested prevented processing of ATP in dose dependent manner (*see* Fig.5 A, B). Most of the anti-CD39 antibodies tested in this assay prevented ATP processing by CD39 to a similar extent as ARL (*see* Fig.5A). IC50s of anti-CD39 antibodies in ATP preservation assay ranged from 0.02-0.1nM. Overall potency of antibodies in this assay was consistent with what was observed in Malachite Green phosphate readout assay.

Example 8: Antibodies Inhibit CD39 Activity On MEL-28 In An Overnight Assay

[00412] $3.5x10^4$ MEL-28 cells/well were plated and incubated with antibodies overnight at 37 degrees C. Cells were washed to remove FBS. Cells next were pre-treated with antibodies in X-VIVO 15 FBS free media overnight at 37 degrees C. ATP was then spiked in at 50 μM for 15 minutes. Supernatants were collected and analyzed using AMP-Glo kit according to manufacturer's instructions (Promega). Palivizumab was used as an isotype control and POM-1 (Alpha Aesar), a non-specific small molecule inhibitor of CD39, was used as positive control at 100 μM.

[00413] Anti-CD39 antibodies tested in overnight AMPGlo assay in MEL-28 cells demonstrated sustained inhibition of ATPase activity as indicated by decreased AMP levels present in the supernatants (*see* FIG. 6A). Inhibition of CD39 activity by antibodies was equivalent to or more potent compared to POM-1 treatment. The data is consistent with results obtained in CD39 short-term Malachite Green assay in MEL-28 (*see* FIG 4). Antibodies tested in an overnight assay had IC50 values in an AMPGlo CD39 inhibition assay ranging from 0.01 to 0.3nM. (*see* Fig.6 B)

Example 9: Anti-CD 39 Antibodies Bind To Primary Human And Cyno B Cells

[00414] B cells were isolated from human donor leukopak using EasySep B cell isolation kit (STEMCELL Technologies). Cyno monocytes were purified from fresh cyno blood using NHP CD14 positive selection kit (Miltenyi) and flow through was collected and stained with CD4, CD8, CD20, CD16, and CD3 antibodies (BD). Human B cells or cyno cells were incubated with serially diluted anti-CD39 antibodies (15 μg/ml 7.5fold serial dilution, 8-point) for 30 minutes at 4 degrees C. Cell were washed 3 times in FACS buffer (PS, 2% FBS, and 2 mM EDTA) and incubated with secondary antibody (mouse anti-human IgG southern biotech) at 1:100 for 30 minutes at 4 degrees C. Cells were washed 2 times in FACS buffer and resuspended in FACS buffer and analyzed on BD Celesta.

[00415] Detection of antibody binding is as described in FIG. 7 where B cells were incubated with serially diluted antibodies and detected using a fluorescently tagged antibody and analyzed by flow cytometry. The results are shown in FIG. 7 and appear to indicate that the antibodies bind specifically to both human and cyno B cells with EC50s that range from 0.02 μg/ml to 3.18 μg/ml (human) and .03 μg/ml to .17 μg/ml (cyno). Similar binding was observed on human tumor cells lines (FIG. 3) where subset of the antibodies had a low maximal MFI and a subset had a high MFI to both the human and cyno B cells.

Example 10: Antibodies Inhibit CD39 Activity On Human B Cells

[00416] B cells were isolated from human leukopak using EasySep B cell isolation kit (STEMCELL Technologies). $5x10^4$ B cells/well were washed with Tris buffer and incubated with serially diluted (100-0.00013nM) antibodies for 30 minutes at 37 degrees C. 50 μM ATP was added to each well and incubated with cells for 2 hrs. The supernatants were collected and analyzed in Malachite Green Assay (R&D) according to manufacturer's protocol. Phosphate released from CD39 processing of ATP was used as a readout of enzyme activity. Palivizumab was used as an isotype control and ARL (Tocris) and POM-1 (Alpha Aesar), non-specific small

molecule inhibitors of CD39, were used as positive controls at 100 μM.

[00417] The antibodies were demonstrated to bind to primary human and cyno B cells (*see* FIG. 7) and the next step was to evaluate the inhibition of ATP hydrolysis by detection of free phosphate (Pi) using a malachite green assay. The results are shown in FIG. 8 and indicate the anti-CD39 antibodies inhibit the enzymatic inhibition/dephosphorylation of ATP by primary human B cells. The ability of the antibodies to inhibit enzymatic activity was comparable regardless of high vs. low max MFI detected in the binding to human B cells (FIG. 7).

Example 11: Anti-CD39 Antibodies Inhibit ATPAse Activity On Human And Cyano Monocytes

[00418] Human monocytes were purified from leukopak using EasySep Human monocytes isolation kit (STEMCELL). Cyno monocytes were isolated from whole cyno blood using NHP CD14 positive selection kit (Miltenyi). Monocytes at $5x10^4$ cells/well were washed with Tris buffer and incubated with serially diluted (100-0.00013nM) anti-CD39 antibodies for 30 minutes at 37C. 50 μM ATP was added to the cells for 15minutes at 37C and supernatants were harvested and analyzed in Malachite Green Assay (R&D) for phosphate levels. Palivizμmab was used as an isotype control and ARL (Tocris) and POM-1 (Alpha Aesar), non-specific small molecule inhibitors of CD39, were used as positive controls at 100 μM.

[00419] CD39 expression has been detected on human leukocytes with the highest expression detected on monocytes (Thromb Res. 2007;121(3):309-17). Because of this information, it was important to evaluate the ability of the anti-CD39 antibodies to inhibit ATPase activity on the cell surface. As demonstrated in FIG. 7, anti-CD39 antibodies bind to both human and cyno B cells. It is appropriate to evaluate the inhibition of enzymatic activity on human and cyno monocytes. The results indicate that all the antibodies are able to inhibit ATPase activity of CD39 on human and cyno monocytes with similar potencies.

Example 12: Anti-CD39 Antibodies Bind To Primary Human TRegs And Inhibit CD39 Enzymatic Activity

[00420] Treg cells were isolated from human donor leukopak using $CD4^+CD25^+CD127^{dim}$ regulatory T cell isolation kit II (Miltenyi). Human Treg cells were incubated with serially diluted anti-CD39 antibodies (100nM-0.00064nM) for 30 minutes at 4 degrees C. Cell were washed 3 times in FACS buffer (PS, 2% FBS, and 2 mM EDTA) and incubated with secondary antibody (mouse anti-human IgG southern biotech) at 1:100 for 30

minutes at 4 degrees C. Cells were washed 2 times in FACS buffer, resuspended in FACS buffer and analyzed on BD Fortessa.

[00421] $CD4^+CD25^+CD127^{dim}$ human Treg cells were washed 3x with Tris buffer. Cells were incubated with anti-CD39 antibodies (100nM-0.00064nM) for 30 minutes at 37C. The cells were spiked with 50 μM ATP and supernatants were collected after 15 minutes incubation at 37C. Supernatants were analyzed for phosphate levels in Malachite Green Assay kit (R&D). Palivizumab was used as an isotype control and ARL (Tocris) and POM-1 (Alpha Aesar), non-specific small molecule inhibitors of CD39, were used as positive controls at 100 μM.

[00422] CD39 had been shown to be expressed on human regulatory T cells (Treg) and important for their suppressive function by hydrolysis of ATP to immune suppressive adenosine. (Blood. 2007 Aug 15;110(4):1225-32, *Cellular & Molecular Immunology* (2017) 14, 521–528; doi:10.1038/cmi.2016.30). In order to determine whether the anti-CD39 antibodies were capable of inhibiting CD39 enzymatic activity, it was important to evaluate the binding to human Tregs. Tregs were isolated from human PBMCs and the Tregs were purified and the anti-bodies were evaluated for binding by flow cytometry. The result indicate that the anti-CD39 antibodies bind to human Tregs (FIG. 10). Of note, both the high maximum MFI and low MFI profiles were observed similar to the human B cell staining (*see* FIG. 8). The ability of the antibodies to inhibit the ATPase activity on human Tregs was also evaluated. All the antibodies inhibit Treg CD39 enzymatic activity (*see* FIG. 11) equally well regardless of the maximal MFI staining observed.

Example 13: Anti-CD39 Antibodies Increase $CD8^+$ T Cell Response In A CMV Recall Response Assay

[00423] Frozen PBMCs are thawed and resuspended at $3x10^6$/ml and cultured in presence of CMV peptides (Miltenyi, PeptTivator CMV pp65) for 3 days in complete (10% FBS) media at 37 degrees C. T cells were then purified (STEMCELL, EasyStep) and rested for 24 hours at 37 degrees C. APCs were generated by depleting CD2 positive cells (STEMCELL, Easystep) from PBMCs from the same donor and plated at $5x10^4$/well overnight at 37degreesC. The following day $5x10^4$ rested T cells were added to the APCs. Antibodies were added at 25 μg/ml plus 100μ M ATP +1 μM EHNA and Golgi plug/stop with CMV peptides and incubated at 37 degrees C for 5 hours. T cells were stained and analyzed for intracellular IFN gamma on a Fortessa (Becton Dickinson) flow cytometer.

[00424] Adenosine has been shown to inhibit T cell activation. (Int J Oncol. 2008

Mar;32(3):527-35). As the rate-limiting enzyme in ATP/ADP-AMP-adenosine pathway, inhibiting CD39 would diminish the levels of immune suppressive adenosine and increase immune activating ATP resulting in enhanced T cell activity. In order to evaluate the role of anti-CD39 antibodies inhibiting ATP/ADP-AMP hydrolysis, preventing the generation of adenosine which could result in an increased T cell response, a CMV recall assay was used. PBMCs were cultured in the presence of a pool of CMV peptides for 3 days and then the T cells were purified cultured with autologous PBMC plus CMV peptides and ATP + EHNA. After 5 hours the T cells were evaluated for the production of IFN gamma. The results indicate that some of the anti-CD39 antibodies were able to increase $CD8^+$ T cells activity in a CMV recall responses assay. This demonstrates that inhibiting the enzymatic activity of CD39 prevents the generation of adenosine and preserves ATP levels and allowing for a robust T cell response to a peptide:MHC complex. In addition, not all antibodies that bind to CD39 and inhibit cell surface enzymatic activity are capable of increasing T cell response and the specific interaction of the antibody to CD39 is important.

Example 14: Evaluation of Antibodies For Inhibition Of CD39 Activity On Mel-28 And Human Monocytes

[00425] $3.5x10^4$ MEL-28 cells/well were incubated with 100nM down to 0.32 pM of monoclonal antibodies for 30 minutes. 50 μM ATP was added and incubated for 15 minutes. Supernate was evaluated for free phosphate (Pi) using the Malachite Green Phosphate Detection Kit (R&D Systems cat#DY996). Palivizumab was used as an isotype control and ARL (Tocris) and POM-1 (Alpha Aesar) used at a concentration of 100 μM as non-specific small molecule inhibitors of CD39 as positive controls. Cyno monocytes were isolated from whole cyno blood using NHP CD14 positive selection kit (Miltenyi). Monocytes at $5x10^4$ cells/well were washed with Tris buffer and incubated as described above.

[00426] When comparing anti-CD39 antibodies for enzymatic inhibition in short term assays, differences were observed. Some were able to block the release of free phosphate (Pi) measured in a malachite green assay and others demonstrated very little activity. For example, BY40v9 and 9-8B have little to no enzymatic inhibition at concentrations of 100 nM using both the MEL-28 cell or primary human monocyte compared to other anti-CD39 antibodies (e.g., 29579 and 28347) that are able to inhibit ATPase activity at low nM concentrations.

[00427] 9-8B was produced as described in US 2017/ 0335007 A1, using SEQ ID Nos. 22 and 23, as hIgG4. BY40v9 is an engineered variant of the antibody BY40 described in WO

2009/095478 A1 SEQ ID Nos. 1 and 5. We tried to express BY40 as described as a human IgG4 but repeated attempts failed. The VH described in SEQ No.1 appears to be missing several N-terminal residues compared to germline VH's, so we engineered in the missing residues with closest germline sequence from IMGT (http://imgt.org/), resulting in BY40-v9, which expressed and was determined to specifically bind rhCD39-ECD and cellular ECD.

Example 15: Design of Chimera and Region Of Distinct Binding

(a) Examples of antibodies that bind soluble recombinant CD39 ECD and cellular CD39 but do not inhibit ATPase activity and do not compete with cellular inhibitors for binding to ECD inhibitors

[00428] 0.04-3.3 nM rhCD39-ECD (R&D Systems) was incubated with buffer, 50 μg/ml antibody or 100 μM POM-1 (Alpha Aesar) for 1 hr at 37°C in assay buffer (25 mM Tris pH 7.5, 5 mM $CaCl_2$) at which point ATP (Sigma) was spiked in to a final concentration of 10 μM, and the reaction further incubated for 30 min 37°C. Production of free phosphate (Pi) was subsequently measured using Malachite Green Phosphate Detection kit (R&D Systems).

[00429] Indicated cells were incubated in assay buffer with 10-25 μg/ml antibody, 100 μM POM-1 or 100 μM ARL for 30 min at 37 ° C 5% CO_2. ATP was added to a final concentration of 50 μM and the incubation continued for 15 min. Supernatant was evaluated for free phosphate (Pi) using the Malachite Green Phosphate Detection kit. Palivizumab is used as an isotype control and POM-1 and ARL are non-specific small molecule inhibitors of CD39.

[00430] A1 antibody was immobilized onto an Anti-Mouse IgG Fc Capture (AMC) biosensor (ForteBio). Association of hCD39-ECD was then monitored for 180 seconds via Bio-Layer Interferometry (BLI) using the Octet system (ForteBio), at which point the biosensor was dipped into competitor antibody and monitored for another 180 seconds. Association of the second antibody was recorded as an upward shift in the interference pattern and indicates that the antibodies bind to different epitopes on CD39. No change in the interference pattern indicated that A1 blocks the second antibody from binding to CD39.

[00431] Although A1 does bind hCD39 ECD (FIG. 1), it does not inhibit its ATPase activity. Although A1 does bind cellular CD39 (FIG. 2), it does not appreciably directly inhibit the ATPase activity of CD39 expressed on OAW42. Capture of hCD39 ECD by A1 blocks subsequent binding by A1 (FIG. 14A, bottom right hand sensorgram), but does not block binding of inhibitory antibodies such as 27536, 27571, 27579, 27597, or 38347.

[00432] The commercially available A1 antibody represents a group of anti-human CD39 monoclonal antibodies that do not directly inhibit the ATPase activity of CD39 and do not bin with any of the other anti-CD39 antibodies described here. More than 30 antibodies were discovered that do not inhibit ECD ATPase activity, do not inhibit cellular CD39 ATPase activity, but do compete with A1 for binding to ECD. These antibodies may be considered to bin with anti-hCD39 antibody A1.

(b) Example of antibodies that have limited ability to inhibit the ATPase activity of both soluble recombinant and cellular CD39 and bin separately from other cellular CD39 inhibitors

[00433] The methods are the same as set forth above except that instead of A1, the representative antibody was immobilized using anti-human IgG Fc Capture (AHC) biosensor.

[00434] Anti-hCD39 antibodies exemplified by 27536 and 28337 represent a group of antibodies that bind both soluble ECD and cellular CD39 and have the ability to inhibit their ATPase activity yet do not compete with other inhibitors for CD39 binding. Both 27536 and 28337 are able to inhibit the hydrolysis of ATP by hCD39 ECD compared to isotype or buffer controls as shown by μM Pi, as described herein (top left panel). 27536 and 28337 inhibit the hydrolysis of CD39 expressed on MEL-28 and OAW42 cells, as shown, compared to isotype control. Antibodies 27536 and 28337 represent a distinct bin group of anti-hCD39 inhibitory antibodies since they are blocked from binding CD39 ECD by another bin member that does not block other inhibitory antibodies such as 27571, 27579, 27597, or 38347 (*see* insert (c) at the bottom of FIG. 14B).

(c) Example of antibodies that inhibit the ATPase activity of soluble recombinant CD39ECD but do not inhibit cellular CD39 and bin separately from other CD39 ECD inibitors

[00435] The methods are as provided above, with the addition of experimental design where inhibition of 0.37 nM CD39 by 50 μg/ml antibody was challenged by ATP concentrations of 3-100 μM. Also, an 18 hour incubation was used with the antibody or isotype control. Finally, an additional 30 second baseline dip in buffer between antigen capture and dipping into a second competitor antibody for 300 seconds was used.

[00436] Anti-hCD39 antibodies exemplified by 27549 represent a group of antibodies that can bind ECD and cellular CD39 but can only inhibit ECD ATPase activity and not cellular CD39 ATPase activity. As can be seen in FIG. 14C (top left), 27549 is able to inhibit the hydrolysis of ATP by hCD39 ECD compared to isotype or buffer controls. Also from FIG.

14C (top right), 27549 is unable to inhibit the hydrolysis of CD39 expressed on MEL-28 cells compared to isotype control. Antibodies 27536 and 28337 represent a distinct bin group of anti-hCD39 inhibitory antibodies since they are blocked from binding CD39 ECD by another bin member that does not block other inhibitory antibodies such as 27571, 27579, 27597, or 38347 (*see* FIG. 14C, bottom).

[00437] Antibody 27549 represents a group of anti-human CD39 monoclonal antibodies that directly inhibit the ATPase activity of sol CD39 ECD yet does inhibit cellular CD39 despite being able to bind to CD39 expressed on cells (Fig 2). It does not compete with A1 or with any of the other inhibitory anti-CD39 antibodies described here for binding to ECD, so 27549 represents another bin of anti-hCD39 antibodies (*see* FIG. 14C).

(d) Example of antibodies that inhibit the ATPase activity of ECD and cellular CD39 and bin separately from other CD39 ECD and/or cellular inhibitors

[00438] The methods are as provided above.

[00439] Antibodies 27571, 27579 and 28347 represent a group of anti-human CD39 antibodies that directly inhibit the ATPase activity of soluble CD39 ECD and inhibit cellular CD39 and yet do not compete with A1, cellular inhibitors 27536 or 28337, or ECD inhibitor 27549 (FIGS.14A-C) for binding to ECD. 27571, 27579, and 28347 are able to inhibit the hydrolysis of ATP by hCD39 ECD compared to isotype or buffer controls (*see* FIG. 14D, left). 27571, 27579, and 28347 also inhibit the hydrolysis of CD39 expressed on MEL-28 cells compared to isotype control (*see* FIG. 14D, right). These cellular inhibitors represent another bin of anti-hCD39 antibodies (*see* FIG. 14D).

(e) Examples of inhibitory antibodies that make distinct contacts with CD39

[00440] Chimeras were generated by replacing human CD39 with mouse CD39 sequence in mammalian expression vectors. The chimeras were expressed in CHO cells and the ability of anti-human CD39 antibodies to bind the chimeras tested via FACS. In brief, cells were washed and blocked in FACS buffer (PBS/ 2% FBS) for 30 min on ice. They were then incubated with 15 µg/ml anti-human CD39 antibodies diluted in FACS buffer x 1h on ice. After 2 washes, cells were incubated with fluorescently labeled anti-human Fc antibodies, anti-mouse Fc antibodies, or anti-mCD39 antibody (R&D Systems 495826) diluted in FACS buffer per manufacturers' instructions x 30 min on ice. After 2 washes, cells were resuspended in FACS buffer and analyzed on BD Fortessa. Data was processed with FlowJo. Positive binding was scored as "yes" and lack of binding was scored as "NO" and examples of FACS plots used to

generate this table are in Figs.14.F and 14.G.

[00441] Chimeras formed between human and mouse CD39 distinguish regions critical for antibody contact that are unique to inhibitory antibodies such as 31414, 31895, 31873, 31901, 31905, reference antibodies such as BY40v9 and 9-8B, and commercial antibodies such as A1 and 498403. Columns 1 and 3 describe the human CD39 sequences flanking the mouse CD39 sequence described in column 2. Column 4 lists the exact mouse amino sequence in the chimera.

[00442] The antibodies described thus far have no/minimal cross-reactivity to mouse CD39, which shares 78% percent identity with human CD39 in the extracellular domain. Chimeras were therefore made between human and mouse CD39 in order to identify those region(s) critical to antibody recognition and binding. To that end, 8 chimeras were generated with the sequence swaps chosen based on sequence diversity between human and mouse CD39 and potential for surface exposure based on rat ENTPD1 and rat ENTPD2 crystal structures. Thus, these 8 chimeras do not comprehensively interrogate all potential contact residues. All tested antibodies were able to bind Chimeras #1,3,5,6,7, and 8, suggesting that these chimeras maintained overall global structural integrity. A1 and 498403 lost the ability to bind Chimera #4, indicating that residues critical to their contact with human CD39 had been lost. A1, 498403, BY40v9 and 9-8B were able to bind Chimera #2, suggesting that this chimera maintained overall global structural integrity. In contrast, inhibitory antibodies 31414, 31895, 31901, 31905, and 31873 were able to bind all chimeras but Chimera #2. Thus, Chimera #2 has lost residues critical to making contacts with these antibodies and therefore E143-N158 constitute part or all of the human CD39 epitope for these antibodies. Notably, these antibodies belong to the bin group exemplified by 27571, 27579 and 28347 in Fig. 14D, i.e. they do not bin with anti-CD39 antibody bin groups represented by antibodies A1, 27536, or 27549.

[00443] Chimeras were generated by mutagenesis of Chimera #2 or WT hCD39 expression vectors. Residues for mutagenesis were chosen based on divergence between human and mouse CD39. The chimeras were expressed in CHO cells and the ability of anti-human CD39 antibodies to bind the chimeras tested via FACS, as described in Fig. 14E. Table 2. Positive binding was scored as "Yes" and lack of binding was scored as "No" and examples of FACS plots used to generate this table are in Figs.14.F and 14.G.

[00444] Specific residues critical for antibody contact can distinguish inhibitory antibodies 31414, 31418, and 31895 from 31901, 31905, and 31873. Individual amino acids

in the mouse sequence of human-mouse Chimera #2, when reverted back to the respective human residue (resulting in Chimera #9,10), restore the ability of antibodies 31895, 31414, 31418 to bind to CD39 but not the ability of 31901, 31905, or 31873 to bind CD39. Mutation of individual residues in the context of otherwise fully human CD39 (Chimeras #11,12) did not impair the binding ability of any of the tested antibodies. Co-mutation of two human residues to the cognate mouse residues (Chimeras #13,14) did not impair binding by antibodies 31414, 31418 or 31895. In stark contrast, antibodies 31901, 31905, and 31873 completely lost their ability to bind Chimeras #13 and 14. The ability of indicated antibodies to bind a given chimera was determined by FACS. In particular, FIG. 14F and FIG. 14G show representative FACS plots used to populate this table and FIG. 14G shows the importance of human CD39 residues N99, R154, and/or S153 in recognition by antibodies represented by 31901, 31905, and 31873.

[00445] As demonstrated in Fig. 14E, Table 1, inhibitory antibodies 31414, 31418, 31895, 31901, 31905 and 31873 can be distinguished from other monoclonal anti-CD39 antibodies based on their inability to recognize Chimera #2. In Table 2, these antibodies are further distinguished by the gain or loss of the ability to bind specific point mutants of hCD39 or Chimera #2. Thus, these antibodies, while binding the same general region of human CD39, form distinct contacts with different critical residues in hCD39. Since these antibodies share the requirement for residues E143-N158, they may share some common contact residues yet can be differentiated based on the demonstrated unique points of contact.

(f) FACS plots highlighting the importance of human CD39 residue D150 and/or E153 in recognition of antibodies represented by 31414, 31418, and 31895 and FACS plots highlighting the importance of human CD39 residues N99, R154, and/or E153 in recognition by antibodies represented by 31901, 31905, and 31873

[00446] The methods are as provided above for the examples of inhibitory antibodies that make distinct contacts with CD39.

[00447] The ability of indicated antibodies to bind to a given chimera was determined by FACS.

[00448] While antibodies 31414, 31418, 31895, 31873, 31901, and 31905 all share a common requirement for human CD39 residues E143-N158, these antibodies make different critical contacts with residues within and outside of this region. Thus, antibodies, which belong to the bin group represented, by antibodies 27571, 27579, and 28347 (FIG. 14.D) can be further distinguished into at least two more groups based on sensitivity to distinct residues. There are

at least 5 bin groups: (1) A1-like antibodies that compete each other for ECD binding yet do not inhibit ECD activity, but do not compete with antibodies in bin groups 2,3,4,or 5 for ECD binding and make critical contacts with N275-I277 as evidenced by loss of binding to Chimera #4; (2) 27536/28337-like antibodies that compete each other for ECD binding and can inhibit both ECD and cellular CD39 ATPase activity, but do not compete with antibodies in bin groups 1,3,4 or 5 for ECD binding; (3) 27549-like antibodies that compete each other for ECD binding and can inhibit CD39 ECD but not cellular CD39, and do not compete with antibodies in bin groups 1,2,4 or 5 for ECD binding; (4) 31414/31418/31895-like antibodies that make critical contacts with E143-N158 in cellular CD39 including (but not limited to) D150 and E153, inhibit the ATPase activity of both ECD and cellular CD39, compete with each other for ECD binding, but do not compete with antibodies in bins 1, 2 or 3 for ECD binding; and (5) 31873/31901/31905-like antibodies that make critical contacts with E143-N158 in cellular CD39 including (but not limited to) E153 and R154, as well as a sensitivity to residue N99, inhibit the ATPase activity of both ECD and cellular CD39, compete with each other for ECD binding, but do not compete with antibodies in bins 1, 2, or 3 for ECD binding. Thus, there are anti-human CD39 antibodies that can be distinguished based on their affinity for ECD, affinity for cells, ability to inhibit ECD ATPase activity, ability to inhibit cellular ATPase activity, and points of contact with CD39. For example, 27549 binds both ECD (FIG. 1) and cells well (FIG.2) yet can only inhibit ECD ATPase activity. 27579 binds ECD weakly but is a potent cellular CD39 inhibitor.

Example 16: Anti-CD39 Antibodies Are Reversible Allosteric, Not Competitive, Inhibitors Due To V_{max} Suppression of V_{max}

[00449] Anti-CD39 antibodies or isotype control antibody (100 nanomolar final concentration) were incubated with MEL-28 cells (35,000 MEL-28 cells/well) endogenously expressing human CD39 at 37°C for 20 minutes in the presence of EnzChek reagents (PNP & MESG). Immediately following the addition of ATP (final concentrations ranging from 0-450 micromolar), the rate of ATP hydrolysis to free phosphate (Pi) by CD39 was monitored over time at Abs360nm using SpectraMax i3x plate reader. The initial enzyme velocity, v0, was determined from the linear region of Pi vs. time curve for each ATP concentration. The plot of v0 vs. [ATP] was curve fit using non-linear regression of the Michaelis-Menten kinetic model.

[00450] The ATP hydrolysis rate by CD39 expressed on MEL-28 cells can be markedly reduced by the anti-CD39 antibodies (*see* FIG. 15). The ATP hydrolysis rate in the presence

of the anti-CD39 antibodies ranges from 1.2 to 2.7 micromolar Pi per minute, which is much less than the ATP hydrolysis rate observed in the presence of an isotype control antibody (7.7 micromolar Pi per minute) and similar in magnitude to the pan ATPase inhibitor ARL (1.2 micromolar Pi per minute).

[00451] The plot of initial velocity versus ATP concentration for multiple concentrations of the anti-CD39 antibody 29872 indicates that the mechanism of inhibition of this IgG antibody is not competitive (*see* FIG. 16 A.). The reduction in initial velocity is constant for ATP concentrations above 100 micromolar (100, 200, 300 and 500 micromolar) in the presence of 5 nanomolar 29872. 29872 could be a non-competitive inhibitor, an un-competitive inhibitor, or a mixed inhibitor of CD39 (having properties of both non-competitive and un-competitive inhibition). The monovalent Fab form of anti-CD39 antibody 29872 showed a very similar inhibition profile (*see* FIG. 16 B.), indicating that the CD39 inhibition activity of 29872 is not dependent on the bivalent structure of the IgG and the potential properties that could result from IgG bivalency such as CD39 crosslinking.

[00452] Many of the other anti-CD39 antibodies tested in this assay showed a similar profile for CD39 enzymatic inhibition (data not shown), indicating that they also may be non-competitive inhibitors, un-competitive inhibitors, or mixed inhibitors of CD39. The mechanism of enzymatic inhibition of these antibodies suggests that they retain their full inhibition of CD39 enzymatic inhibition at high ATP concentrations. The anti-CD39 antibodies appear to be reversible inhibitors.

Example 17: Anti-CD39 Can Induce Internalization of CD39 On Cyno Monocytes

[00453] Anti-CD39 antibodies were injected into cynomolgus monkeys to test for ability to downregulate CD39 on cell surface of cyno monocytes. CD39 internalization was assessed by FACS of whole blood samples collected pre-dose, Day 1, Day 7, and Day 14 after antibody treatment. Non-competing anti-CD39-PE antibody (clone A1) was used to measure CD39 levels on CD14+ gated monocytes. Data is shown as MFI of A1-PE on gated cyno monocytes in FIG. 17.

[00454] Cynomolgus monkeys were injected with anti-CD39 antibodies at 10mg/kg. Blood samples were collected prior to injection and on Day 1, Day 7, and Day 14 after treatment. For each time-point, 50 uL of cynomolgus whole blood was incubated with 30 uL of staining buffer (PBS, 2%FBS, 2mM EDTA, 3% mouse serum, 5% goat serum) containing CD14 and CD20 antibodies (eBioscience) and an Fc blocking reagent (BD) for 30 minutes at

4C. CD39 antibody (clone eBioA1, eBioscience) was added to the sample and incubated for an additional 40 minutes at 4 degrees C. Following incubation, the samples were treated with ACK lysis buffer (ThermoFisher) for 10 minutes at room temperature to lyse red blood cells. Samples were washed several times with staining buffer and fixed with 1% PFA (Sigma) before acquisition on a BD Fortessa X-20 flow cytometer. Total CD39 receptor expression on CD14 positive monocytes was determined by mean fluorescence intensity.

[00455] CD39 was highly expressed on cyno monocytes prior to antibody treatment in all blood samples tested (pre-dose). Anti-CD39 antibodies tested in vivo had distinct internalization profiles where antibody 1 treatment led to downregulation of CD39 on cell surface of monocytes and antibody 2 had no effect on overall CD39 levels. Apparent decrease of CD39 levels after antibody 1 treatment was not due to A1 antibody competing with antibody 1 for binding to CD39 as the epitopes for A1 and antibody 1 are distinct from each other.

Example 18: Anti-CD39 Antibody Increases Stimulated Human $CD4^+$ and $CD8^+$ T Cell in the Presence of Exogenous ATP

[00456] Anti-CD3 + anti-CD28 stimulated PBMCs were treated with anti-CD39 antibody 31895 or isotype control in the presence of 50μM ATP for 96 hours. Proliferation of $CD4^+$ and $CD8^+$ T cells was measured by Cell Trace Violet by flow cytometry.

[00457] FIG. 19 shows that anti-CD39 antibody increases proliferation of stimulated human $CD4^+$ and $CD8^+$ T cell in the presence of exogenous ATP. The left side shows $CD8^+$ T cells, with the x-axis showing antibody (nM) and the y-axis showing % $CD8^+$ T cell proliferation. The right side shows $CD4^+$ T cells, with the x-axis showing antibody (nM) and the y-axis showing % $CD4^+$ T cell proliferation. The inset to the right shows symbols for the respective antibodies and controls.

Example 19: Anti-CD39 Antibody Increase Stimulated PBMC Secretion of INF-γ, TNF-α and IL-2.

[00458] Human PBMCs were treated with anti-CD3 + anti-CD28 and incubated with anti-CD39 antibody 31895 or isotype control in presence (B) or absence (A) of exogenous ATP (50μM). Supernatants were harvested after 96 hours and cytokines were measured using a Meso Scale Discovery human cytokine kit.

[00459] FIG. 20 shows anti-CD39 antibody 31895 increases cytokine secretion by anti-CD3 + anti-CD28 activated PBMC in absence (A) or presence (B) of exogenous ATP in a dose

dependent manner. The top row shows results with exogenous ATP added and the bottom row shows results with no exogeonous ATP added. The x-axis shows antibody (nM) and the y-axis shows secretion of INF-γ, TNF-α and IL-2, respectively.

Example 20: Anti-CD39 Antibody Increases Stimulated PBMC Secretion of INF-γ, TNF-α, IL-2 and IL-1β.

[00460] Human PBMCs were stimulated with anti-CD3 + anti-CD28 and incubated with anti-CD39 antibodies 31895, HAO-391 (*See,* SEQ ID 10/SEQ ID 11 from WO 2017/089334), HAO mAb4 (*See* SEQ ID 12/ SEQ ID 13 from WO2017157948) or isotype control at a fixed concentration of 50 μg/ml in presence of ATP. Supernatants were harvested after 96 hours and analyzed by Meso Scale Discovery human cytokine kit.

[00461] FIG. 21 shows anti-CD39 antibody 31895 increased cytokine release by activated PBMCs to a higher degree compared to anti-CD39 antibodies HAO-391 (VL SEQ ID No. 10; VH SEQ ID No. 11 from WO 2017/089334) and HAO mAb4 (VL SEQ ID No. 12; VH SEQ ID No. 13 from WO2017157948). The x-axis indicates the andtibody and/or conditions and the y-axis shows INF-γ, TNF-α, IL-2 and IL-1β, respectively.

Example 21: Anti-39 Antibody 31895 Increase Extracellular ATP Accumulation and Reduces Adenosine Generation by $CD39^+CD73^+$ SK-MEL-28 Cells

[00462] SK-MEL-28 cells were treated with 31895, isotype control, or small molecule inhibitors (EHNA, ARL, or POM-1) for 1 hour and 50μM ATP was added for 15 min prior to harvesting of the supernatants. The supernatants were analyzed for ATP levels using AmpGlo Kit (A) and for adenosine levels using LC/MS analysis (B). % Adenosine levels were normalized to isotype control (100%) and SK-MEL-28 CD39 KO cells (0%).

[00463] The results are shown in FIG. 22. The left graph shows ATP accumulation and the right graph shows adenosine generation (LC/MC). The x-axis for each graph shows conditions. The y-axis for the left graph shows ATP (μM) and the y-axis for the right graph shows % of adenosine levels.

Example S: Sequences

[00464] Table S provides sequences referred to herein.

Table S Sequences.

SEQ ID NO:	Region	Scheme/Clone	Sequence
1	CDR-H1	Chothia	GYTFTSY
2	CDR-H1	Chothia	GYTFKSY
3	CDR-H1	Chothia	GYIFKSY
4	CDR-H1	Chothia	GYTFQSY
5	CDR-H1	Chothia	GYTFFSY
6	CDR-H1	Chothia	GYTFVSY
7	CDR-H1	Chothia	GGTFSSLAIS
8	CDR-H1	Chothia	GGTFSKLAIS
9	CDR-H1	Chothia	GGTFSHT
10	CDR-H1	Chothia	GGTFSSL
11	CDR-H1	Chothia	GGTFSLL
12	CDR-H1	Chothia	GGTFQSL
13	CDR-H1	Chothia	GGTFPSN
14	CDR-H1	Chothia	GGTFSAM
15	CDR-H1	Chothia	GGTFASL
16	CDR-H1	Chothia	GGTFSWL
17	CDR-H1	Chothia	GGTFSSY
18	CDR-H1	Chothia	GGTFGSY
19	CDR-H1	Chothia	GGTFSKY
20	CDR-H1	Chothia	GGTFGRY
21	CDR-H1	Chothia	GGTFESY
22	CDR-H1	Chothia	GGTFSNY
23	CDR-H1	Chothia	GGAFSSY

SEQ ID NO:	Region	Scheme/Clone	Sequence
24	CDR-H1	Chothia	GFTFSSY
25	CDR-H1	Kabat	SYYMH
26	CDR-H1	Kabat	SYEMH
27	CDR-H1	Kabat	SYQMH
28	CDR-H1	Kabat	SYYMY
29	CDR-H1	Kabat	SYFMH
30	CDR-H1	Kabat	SLAIS
31	CDR-H1	Kabat	KLAIS
32	CDR-H1	Kabat	HTAIS
33	CDR-H1	Kabat	SLPIS
34	CDR-H1	Kabat	LLAIS
35	CDR-H1	Kabat	SNAIS
36	CDR-H1	Kabat	AMAIS
37	CDR-H1	Kabat	WLAIS
38	CDR-H1	Kabat	SYAIS
39	CDR-H1	Kabat	SYGIS
40	CDR-H1	Kabat	KYGIS
41	CDR-H1	Kabat	NYAIS
42	CDR-H1	Kabat	SYATS
43	CDR-H1	Kabat	SYAIG
44	CDR-H1	Kabat	SYSMN
45	CDR-H1	Kabat	SYGMN
46	CDR-H2	Chothia	NPSGGST
47	CDR-H2	Chothia	NPSVGS

SEQ ID NO:	Region	Scheme/Clone	Sequence
48	CDR-H2	Chothia	NPSGGS
49	CDR-H2	Chothia	NPLGGG
50	CDR-H2	Chothia	NPRGGS
51	CDR-H2	Chothia	IPIFGT
52	CDR-H2	Chothia	GFGT
53	CDR-H2	Chothia	LPIGGT
54	CDR-H2	Chothia	LPIAGT
55	CDR-H2	Chothia	LPIFGE
56	CDR-H2	Chothia	IPRGGT
57	CDR-H2	Chothia	IPEFGI
58	CDR-H2	Chothia	IPSIGT
59	CDR-H2	Chothia	IPISGT
60	CDR-H2	Chothia	IPTFGT
61	CDR-H2	Chothia	SSSSSY
62	CDR-H2	Chothia	WYDGSN
63	CDR-H2	Kabat	VINPSGGSTSYAQKFQG
64	CDR-H2	Kabat	RINPSVGSTWYAQKFQG
65	CDR-H2	Kabat	RINPSGGSTWYAQKFQG
66	CDR-H2	Kabat	KINPSGGSTWYAQKFQG
67	CDR-H2	Kabat	VINPLGGGTSYAQKFQG
68	CDR-H2	Kabat	SINPRGGSTSYAQKFQG
69	CDR-H2	Kabat	GIIPIFGTANYAQKFQG
70	CDR-H2	Kabat	GI--GFGTANYAQKFQG
71	CDR-H2	Kabat	GILPIGGTANYAQKFQG

SEQ ID NO:	Region	Scheme/Clone	Sequence
72	CDR-H2	Kabat	GILPIAGTANYAQKFQG
73	CDR-H2	Kabat	GILPIFGEANYAQKFQG
74	CDR-H2	Kabat	GIIPRGGTANYAQKFQG
75	CDR-H2	Kabat	SIIPIFGTANYAQKFRG
76	CDR-H2	Kabat	SIIPEFGIANYAQKFQG
77	CDR-H2	Kabat	SIIPIFGTANYAQKFQG
78	CDR-H2	Kabat	GIIPISGTANYAQEFQG
79	CDR-H2	Kabat	GIIPTFGTANYAQKFQG
80	CDR-H2	Kabat	SISSSSSYIYYADSVKG
81	CDR-H2	Kabat	VIWYDGSNKYYADSVKG
82	CDR-H3		GKREGGTEYLRH
83	CDR-H3		GKREGGTEYLRK
84	CDR-H3		GKREGGTEYLRS
85	CDR-H3		GKREGGTEYLRN
86	CDR-H3		GKREGGTEYLRV
87	CDR-H3		GGAKYASTYGMDV
88	CDR-H3		GGAKYASTHGMDV
89	CDR-H3		GGAKYASQLGMDV

SEQ ID NO:	Region	Scheme/Clone	Sequence
90	CDR-H3		GGAKYASKWGMDV
91	CDR-H3		GGAKYAVGYGMDV
92	CDR-H3		GGAKYAGRYGMDV
93	CDR-H3		GGAKYARTYGMDV
94	CDR-H3		ESGGYRDHRLDV
95	CDR-H3		ESGTYRDHRLDV
96	CDR-H3		ESGGYRDHRLGV
97	CDR-H3		DFTDYSSGYSSGWTY
98	CDR-H3		DTLYSSGAYYGYNV
99	CDR-H3		AKRGYDSYGGVYFDY
100	CDR-H3		GPTVTATTSIGTHNWFDP
101	CDR-H3		EGRGYDSSRYYKFWFDPWGQGTLVTVSS
102	CDR-H3		DGGGYRHHYFDL
103	CDR-H3		ESGGYRDHKLDV
104	CDR-H3		DGGGYQHHYFDL
105	CDR-H3		DSGYHRHYSDY

SEQ ID NO:	Region	Scheme/Clone	Sequence
106	CDR-H3		DPLGIRKHWFDP
107	CDR-H3		DTPRWRYHYFDY
108	CDR-H3		ERRGSLALGMDV
109	CDR-H3		DLGGYSYGEPYYYYYGMDV
110	CDR-L1		RASQSVSSSYLA
111	CDR-L1		RASQSVASSYLA
112	CDR-L1		EASQSVSYSYLA
113	CDR-L1		KASESVSSSYLA
114	CDR-L1		RASQYVSSSYLA
115	CDR-L1		KSSQSVLFSSNNKNYLA
116	CDR-L1		KSSRSVLFSSNNKNYLA
117	CDR-L1		KSSKSVLYSNNNKNYLA
118	CDR-L1		RASQSVGSNLA
119	CDR-L1		KSSQSVLYSSNNKNYLA
120	CDR-L1		QASQDISNYLN
121	CDR-L1		RASQSVSSYLA

SEQ ID NO:	Region	Scheme/Clone	Sequence
122	CDR-L1		RASQSVSRYLA
123	CDR-L1		RASQSISSWLA
124	CDR-L1		RASQSVSSDYLA
125	CDR-L2		GASSRAT
126	CDR-L2		GASNRHT
127	CDR-L2		YASSRAY
128	CDR-L2		GASSRAN
129	CDR-L2		YASSRAT
130	CDR-L2		YASNRAT
131	CDR-L2		WASTRES
132	CDR-L2		WASSRES
133	CDR-L2		WASTRQS
134	CDR-L2		WASTRAS
135	CDR-L2		GASTRAT
136	CDR-L2		GASTRAS
137	CDR-L2		DASNLET

SEQ ID NO:	Region	Scheme/Clone	Sequence
138	CDR-L2		DASNRAT
139	CDR-L2		DASKRAT
140	CDR-L2		KASSLES
141	CDR-L3		QQYHSYIT
142	CDR-L3		QQYHNAIT
143	CDR-L3		QQYYFYIT
144	CDR-L3		QQYHSALT
145	CDR-L3		QQYHGGIT
146	CDR-L3		QQYHRRIT
147	CDR-L3		QQYHSGIT
148	CDR-L3		QQYYLYPLT
149	CDR-L3		QQYWTYPLT
150	CDR-L3		QQYLLYPLT
151	CDR-L3		QQYLIWPLT
152	CDR-L3		QQYLLWPLT
153	CDR-L3		QQFYFFPPT

SEQ ID NO:	Region	Scheme/Clone	Sequence
154	CDR-L3		QQAYTFPPT
155	CDR-L3		QQYYIFPPT
156	CDR-L3		QQRNFYPPT
157	CDR-L3		QQFVLWPRT
158	CDR-L3		QQHVNFPLT
159	CDR-L3		QQSVFWPIT
160	CDR-L3		QQLTKWPLT
161	CDR-L3		QQDVLWPLT
162	CDR-L3		QQYGLFPIT
163	CDR-L3		QQHTVWPIT
164	CDR-L3		QQVLNYPLT
165	CDR-L3		QQSYFLPPT
166	CDR-L3		QQAHSSPYT
167	Leader for scFV, scFv-Fc	Leader	MKYLLPTAAAGLLLLAAQPAMA
168	Linker for scFV, scFV-FC	Linker	GGGGSGGGGSGGGGS

SEQ ID NO:	Region	Scheme/Clone	Sequence
169	C-Term Tag for scFV, scFV-FC	C-Term Tag	GPGGQHHHHHH
170	C-Term Tag for scFv, scFV-FC	C-Term Tag	PKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKD TLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPIEKTISKAKGQPREPQV YTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
171	scFv	29872	MKYLLPTAAAGLLLLAAQPAMAQVQLVQSGAEV KEPGASVKVSCKAPGYTFTSYYMHWVRQAPGQG LEWMGVINPSGGSTSYAQKFQGRVTMTRDTSTS TVYMELSSLRSEDTAVYYCARGKREGGTEYLRH WGQGTLVTVSSGGGGSGGGGSGGGGSEIVLTQS PGTLSLSPGERATLSCRASQSVSSSYLAWYQQK PGQAPRLLIYGASSRATGIPDRFSGSGSGTDFT LTISRLEPEDFAVYYCQQYHSYITFGGGTKVEI KGPGGQHHHHHH
172	scFv	31895	MKYLLPTAAAGLLLLAAQPAMAQVQLVQSGAEV KKPGASVKVSCKASGYTFKSYEMHWVRQAPGQG LEWMGRINPSVGSTWYAQKFQGRVTMTRDTSTS TVYMELSSLRSEDTAVYYCARGKREGGTEYLRK WGQGTLVTVSSGGGGSGGGGSGGGGSEIVLTQS PGTLSLSPGERATLSCRASQSVASSYLAWYQQK PGQAPRLLIYGASNRHTGIPDRFSGSGSGTDFT LTISRLEPEDFAVYYCQQYHNAITFGGGTKVEI K GPGGQHHHHHH
173	scFv	31414	MKYLLPTAAAGLLLLAAQPAMAQVQLVQSGAEV KKPGASVKVSCKASGYTFKSYEMHWVRQAPGQG LEWMGRINPSVGSTWYAQKFQGRVTMTRDTSTS TVYMELSSLRSEDTAVYYCARGKREGGTEYLRN WGQGTLVTVSSGGGGSGGGGSGGGGSEIVLTQS PGTLSLSPGERATLSCRASQSVSSSYLAWYQQK PGQAPRLLIYGASSRATGIPDRFSGSGSGTDFT LTISRLEPEDFAVYYCQQYHSYITFGGGTKVEI KGPGGQHHHHHH

SEQ ID NO:	Region	Scheme/Clone	Sequence
174	scFv	31905	MKYLLPTAAAGLLLLAAQPAMAQVQLVQSGAEV KKPGSSVKVSCKASGGTFPSNAISWVRQAPGQG LEWMGGIGFGTANYAQKFQGRVTITADESTSTA YMELSSLRSEDTAVYYCARGGAKYARTYGMDVW GQGTTVTVSSGGGGSGGGGSGGGGSDIVMTQSP DSLAVSLGERATINCKSSKSVLYSNNNKNYLAW YQQKPGQPPKLLIYWASTRQSGVPDRFSGSGSG TDFTLTISSLQAEDVAVYYCQQYLLYPLTFGGG TKVEIKGPGGQHHHHHH
175	scFv-Fc	29872	MKYLLPTAAAGLLLLAAQPAMAQVQLVQSGAEV KEPGASVKVSCKAPGYTFTSYYMHWVRQAPGQG LEWMGVINPSGGSTSYAQKFQGRVTMTRDTSTS TVYMELSSLRSEDTAVYYCARGKREGGTEYLRH WGQGTLVTVSSGGGGSGGGGSGGGGSEIVLTQS PGTLSLSPGERATLSCRASQSVSSSYLAWYQQK PGQAPRLLIYGASSRATGIPDRFSGSGSGTDFT LTISRLEPEDFAVYYCQQYHSYITFGGGTKVEI KPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPK DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVD KSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG K
176	scFv-Fc	31895	MKYLLPTAAAGLLLLAAQPAMAQVQLVQSGAEV KKPGASVKVSCKASGYTFKSYEMHWVRQAPGQG LEWMGRINPSVGSTWYAQKFQGRVTMTRDTSTS TVYMELSSLRSEDTAVYYCARGKREGGTEYLRK WGQGTLVTVSSGGGGSGGGGSGGGGSEIVLTQS PGTLSLSPGERATLSCRASQSVASSYLAWYQQK PGQAPRLLIYGASNRHTGIPDRFSGSGSGTDFT LTISRLEPEDFAVYYCQQYHNAITFGGGTKVEI KPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPK DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVD KSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG K
177	scFv-Fc	31414	MKYLLPTAAAGLLLLAAQPAMAQVQLVQSGAEV KKPGASVKVSCKASGYTFKSYEMHWVRQAPGQG LEWMGRINPSVGSTWYAQKFQGRVTMTRDTSTS TVYMELSSLRSEDTAVYYCARGKREGGTEYLRN WGQGTLVTVSSGGGGSGGGGSGGGGSEIVLTQS PGTLSLSPGERATLSCRASQSVSSSYLAWYQQK PGQAPRLLIYGASSRATGIPDRFSGSGSGTDFT LTISRLEPEDFAVYYCQQYHSYITFGGGTKVEI KPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPK DTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG

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			VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWL NGKEYKCKVSNKALPAPIEKTISKAKGQPREPQ VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVE WESNGQPENNYKTTPPVLDSDGSFFLYSKLTVD KSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG K
178	scFv-Fc	31905	MKYLLPTAAAGLLLLAAQPAMAQVQLVQSGAEV KKPGSSVKVSCKASGGTFPSNAISWVRQAPGQG LEWMGGIGFGTANYAQKFQGRVTITADESTSTA YMELSSLRSEDTAVYYCARGGAKYARTYGMDVW GQGTTVTVSSGGGGSGGGGSGGGGSDIVMTQSP DSLAVSLGERATINCKSSKSVLYSNNNKNYLAW YQQKPGQPPKLLIYWASTRQSGVPDRFSGSGSG TDFTLTISSLQAEDVAVYYCQQYLLYPLTFGGG TKVEIKPKSCDKTHTCPPCPAPELLGGPSVFLF PPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLICLVKGFYPS DIAVEWESNGQPENNYKTTPPVLDSDGSFFLYS KLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL SLSPGK
179	VH	27579	QVQLVQSGAEVKEPGASVKVSCKAPGYTFTSYY MHWVRQAPGQGLEWMGVINPSGGSTSYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRHWGQGTLVTVSS
180	VH	31895	QVQLVQSGAEVKKPGASVKVSCKASGYTFKSYE MHWVRQAPGQGLEWMGRINPSVGSTWYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRKWGQGTLVTVSS
181	VH	31415	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYQ MHWVRQAPGQGLEWMGRINPSGGSTWYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRSWGQGTLVTVSS
182	VH	31414	QVQLVQSGAEVKKPGASVKVSCKASGYTFKSYE MHWVRQAPGQGLEWMGRINPSVGSTWYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRNWGQGTLVTVSS
183	VH	31891	QVQLVQSGAEVKKPGASVKVSCKASGYIFKSYE MHWVRQAPGQGLEWMGRINPSVGSTWYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRVWGQGTLVTVSS

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184	VH	29871	QVQLVQSGAEVKKPGASVKVSCKASGYTFQSYY MHWVRQAPGQGLEWMGKINPSGGSTWYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRHWGQGTLVTVSS
185	VH	31418	QVQLVQSGAEVKKPGASVKVSCKASGYTFKSYE MHWVRQAPGQGLEWMGRINPSGGSTWYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRHWGQGTLVTVSS
186	VH	31431	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYQ MHWVRQAPGQGLEWMGRINPSGGSTWYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRHWGQGTLVTVSS
187	VH	31421	QVQLVQSGAEVKKPGASVKVSCKASGYTFFSYY MYWVRQAPGQGLEWMGVINPLGGGTSYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRHWGQGTLVTVSS
188	VH	31429	QVQLVQSGAEVKKPGASVKVSCKASGYTFVSYF MHWVRQAPGQGLEWMGSINPRGGSTSYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRHWGQGTLVTVSS
189	VH	29872	QVQLVQSGAEVKKPGASVKVSCKASGYTFKSYE MHWVRQAPGQGLEWMGRINPSVGSTWYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRHWGQGTLVTVSS
190	VH	28347	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSLA ISWVRQAPGQGLEWMGGIIPIFGTANYAQKFQG RVTITADESTNTAYMELSSLRSEDTAVYYCARG GAKYASTYGMDVWGQGTTVTVSS
191	VH	31896	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSKLA ISWVRQAPGQGLEWMGGIGFGTANYAQKFQGRV TITADESASTAYMELSSLRSEDTAVYYCARGGA KYASTHGMDVWGQGTTVTVSS
192	VH	31432	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSHTA ISWVRQAPGQGLEWMGGILPIGGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARG GAKYASQLGMDVWGQGTTVTVSS

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193	VH	31915	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSLP ISWVRQAPGQGLEWMGGIGFGTANYAQKFQGRV TITADESTSTAYMELSSLRSEDTAVYYCARGGA KYASKWGMDVWGQGTTVTVSS
194	VH	31436	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSLLA ISWVRQAPGQGLEWMGGILPIAGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARG GAKYAVGYGMDVWGQGTTVTVSS
195	VH	31437	QVQLVQSGAEVKKPGASVKVSCKASGGTFQSLA ISWVRQAPGQGLEWMGGILPIGGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARG GAKYAGRYGMDVWGQGTTVTVSS
196	VH	31905	QVQLVQSGAEVKKPGSSVKVSCKASGGTFPSNA ISWVRQAPGQGLEWMGGIGFGTANYAQKFQGRV TITADESTSTAYMELSSLRSEDTAVYYCARGGA KYARTYGMDVWGQGTTVTVSS
197	VH	31901	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSLP ISWVRQAPGQGLEWMGGIGFGTANYAQKFQGRV TITADESTSTAYMELSSLRSEDTAVYYCARGGA KYAGRYGMDVWGQGTTVTVSS
198	VH	29852	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSAMA ISWVRQAPGQGLEWMGGILPIAGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARG GAKYASTYGMDVWGQGTTVTVSS
199	VH	29851	QVQLVQSGAEVKKPGSSVKVSCKASGGTFASLA ISWVRQAPGQGLEWMGGILPIFGEANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARG GAKYASTYGMDVWGQGTTVTVSS
200	VH	29857	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSWLA ISWVRQAPGQGLEWMGGIIPRGGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARG GAKYASTYGMDVWGQGTTVTVSS
201	VH	27571	QVQLVQSGAEVKKPGSSVKASCKASGGTFSSYA ISWVRQAPGQGLEWMGSIIPIFGTANYAQKFRG RVTITADESTSTTYMELSSLRSEDTAVYYCARE SGGYRDHRLDVWGQGTMVTVSS

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202	VH	31861	QVQLVQSGAEVKKPGSSVKVSCKASGGTFGSYG ISWVRQAPGQGLEWMGSIIPEFGIANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARE SGTYRDHRLDVWGQGTMVTVSS
203	VH	31873	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSKYG ISWVRQAPGQGLEWMGSIIPEFGIANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARE SGGYRDHRLGVWGQGTMVTVSS
204	VH	31393	QVQLVQSGAEVKKPGSSVKVSCKASGGTFESYG ISWVRQAPGQGLEWMGSIIPEFGIANYAQKFQG RVTITADESTSTTYMELSSLRSEDTAVYYCARE SGGYRDHRLDVWGQGTMVTVSS
205	VH	27534	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYA ISWVRQAPGQGLEWMGGIIPIFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARD FTDYSSGYSSGWTYWGQGTLVTVSS
206	VH	27536	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSNYA ISWVRQAPGQGLEWMGGIIPIFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARD TLYSSGAYYGYNVWGQGTMVTVSS
207	VH	27588	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSNYA ISWVRQAPGQGLEWMGGIIPIFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARA KRGYDSYGGVYFDYWGQGTLVTVSS
208	VH	27590	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSNYA ISWVRQAPGQGLEWMGGIIPIFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARG PTVTATTSIGTHNWFDPWGQGILVTVSS
209	VH	27597	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYA ISWVRQAPGQGLEWMGSIIPIFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARE GRGYDSSRYYKFWFDPWGQGTLVTVSS
210	VH	27575	QVQLVQSGAEVKEPGSSVKVSCKASGGTFSSYA TSWVRQAPGQGLEWMGGIIPISGTANYAQEFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARD GGGYRHHYFDLWGRGTLVTVSS

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211	VH	27568	QVQLVQSGAEVKKPGSSVKVPCKASGGTFSSYA ISWVRQAPEQGLEWMGSIIPIFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCAGE SGGYRDHKLDVWGQGTVVTVSS
212	VH	27577	QVQLVQSGAEVKKPGSSVKVSCKASGGAFSSYA IGWVRQAPGQGLEWMGGIIPTFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARD GGGYQHHYFDLWGRGTLVTVSS
213	VH	27587	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYA ISWVRQAPGQGLEWMGSIIPIFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARE SGGYRDHKLDVWGQGTMVTVSS
214	VH	27589	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYA ISWVRQAPGQGLEWMGGIIPIFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARD SGYHRHYSDYWGQGTLVTVSS
215	VH	27596	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYA ISWVRQAPGQGLEWMGGIIPIFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARD PLGIRKHWFDPWGQGTLVTVSS
216	VH	27535	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYA ISWVRQAPGQGLEWMGGIIPIFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARD TPRWRYHYFDYWGQGTLVTVSS
217	VH	27550	EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYS MNWVRQAPGKGLEWVSSISSSSSYIYYADSVKG RFTISRDNAKNSLYLQMNSLRAEDTAVYYCARE RRGSLALGMDVWGQGTLVTVSS
218	VH	27549	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYG MNWVRQAPGKGLEWVAVIWYDGSNKYYADSVKG RFTISRDNSKNTLYLQMNSLRAEDTAVYYCARD LGGYSYGEPYYYYYGMDVWGQGTTVTVSS
219	VL	27579	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSY LAWYQQKPGQAPRLLIYGASSRATGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYHSYITFG GGTKVEIK

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220	VL	31895	EIVLTQSPGTLSLSPGERATLSCRASQSVASSY LAWYQQKPGQAPRLLIYGASNRHTGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYHNAITFG GGTKVEIK
221	VL	31891	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSY LAWYQQKPGQAPRLLIYYASSRAYGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYHNAITFG GGTKVEIK
222	VL	31418	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSY LAWYQQKPGQAPRLLIYGASSRATGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYYFYITFG GGTKVEIK
223	VL	31430	EIVLTQSPGTLSLSPGERATLSCEASQSVSYSY LAWYQQKPGQAPRLLIYGASSRANGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYHSALTFG GGTKVEIK
224	VL	31431	EIVLTQSPGTLSLSPGERATLSCRASQSVASSY LAWYQQKPGQAPRLLIYGASNRHTGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYHGGITFG GGTKVEIK
225	VL	31421	EIVLTQSPGTLSLSPGERATLSCKASESVSSSY LAWYQQKPGQAPRLLIYYASSRATGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYHRRITFG GGTKVEIK
226	VL	31429	EIVLTQSPGTLSLSPGERATLSCRASQYVSSSY LAWYQQKPGQAPRLLIYYASNRATGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYHSGITFG GGTKVEIK
227	VL	28347	DIVMTQSPDSLAVSLGERATINCKSSQSVLFSS NNKNYLAWYQQKPGQPPKLLIYWASTRESGVPD RFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYL YPLTFGGGTKVEIK
228	VL	31896	DIVMTQSPDSLAVSLGERATINCKSSRSVLFSS NNKNYLAWYQQKPGQPPKLLIYWASTRESGVPD RFSGSGSGTDFTLTISSLQAEDVAVYYCQQYWT YPLTFGGGTKVEIK

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229	VL	31915	DIVMTQSPDSLAVSLGERATINCKSSQSVLFSS NNKNYLAWYQQKPGQPPKLLIYWASSRESGVPD RFSGSGSGTDFTLTISSLQAEDVAVYYCQQYWT YPLTFGGGTKVEIK
230	VL	31905	DIVMTQSPDSLAVSLGERATINCKSSKSVLYSN NNKNYLAWYQQKPGQPPKLLIYWASTRQSGVPD RFSGSGSGTDFTLTISSLQAEDVAVYYCQQYLL YPLTFGGGTKVEIK
231	VL	31901	GIVMTQSPDSLAVSLGERATINCKSSQSVLFSS NNKNYLAWYQQKPGQPPKLLIYWASTRASGVPD RFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYL YPLTFGGGTKVEIK
232	VL	27571	EIVMTQSPATLSVSPGERATLSCRASQSVGSNL AWYQQKPGQAPRLLIYGASTRATGIPARFSGSG SGTEFTLTISSLQSEDFAVYYCQQYLIWPLTFG GGTKVEIK
233	VL	31861	EIVMTQSPATLSVSPGERATLSCRASQSVGSNL AWYQQKPGQAPRLLIYGASTRATGIPARFSGSG SGTEFTLTISSLQSEDFAVYYCQQYLLWPLTFG GGTKVEIK
234	VL	31873	EIVMTQSPATLSVSPGERATLSCRASQSVGSNL AWYQQKPGQAPRLLIYGASTRASGIPARFSGSG SGTEFTLTISSLQSEDFAVYYCQQYLLWPLTFG GGTKVEIK
235	VL	28337	DIVMTQSPDSLAVSLGERATINCKSSQSVLFSS NNKNYLAWYQQKPGQPPKLLIYWASTRESGVPD RFSGSGSGTDFTLTISSLQAEDVAVYYCQQFYF YPPTFGGGTKVEIK
236	VL	27536	DIVMTQSPDSLAVSLGERATINCKSSQSVLYSS NNKNYLAWYQQKPGQPPKLLIYWASTRESGVPD RFSGSGSGTDFTLTISSLQAEDVAVYYCQQAYT FPPTFGGGTKVEIK
237	VL	27588	DIQMTQSPSSLSASVGDRVTITCQASQDISNYL NWYQQKPGKAPKLLIYDASNLETGVPSRFSGSG SGTDFTFTISSLQPEDIATYYCQQYYIFPPTFG GGTKVEIK

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238	VL	27590	EIVLTQSPATLSLSPGERATLSCRASQSVSSYL AWYQQKPGQAPRLLIYDASNRATGIPARFSGSG SGTDFTLTISSLEPEDFAVYYCQQRNFYPPTFG GGTKVEIK
239	VL	27597	EIVLTQSPATLSLSPGERATLSCRASQSVSSYL AWYQQKPGQAPRLLIYDASNRATGIPARFSGSG SGTDFTLTISSLEPEDFAVYYCQQFVLWPRTFG GGTKVEIK
240	VL	27575	EIVLTQSPATLSLSPGERATLSCRASQSVSRYL AWYQQKPGQAPRLLIYDASNRATGIPARFSGSG SGTDFTLTISSLEPEDFAVYYCQQHVNFPLTFG GGTKVEIK
241	VL	27568	EIVLTQSPATLSLSPGERATLSCRASQSVSSYL AWYQQKPGQAPRLLIYDASNRATGIPARFSGSG SGTDFTLTISSLEPEDFAVYYCQQSVFWPITFG GGTKVEIK
242	VL	27577	EIVMTQSPATLSVSPGERATLSCRASQSVGSNL AWYQQKPGQAPRLLIYGASTRATGIPARFSGSG SGTEFTLTISSLQSEDFAVYYCQQLTKWPLTFG GGTKVEIK
243	VL	27587	EIVLTQSPATLSLSPGERATLSCRASQSVSSYL AWYQQKPGQAPRLLIYDASKRATGIPARFSGSG SGTDFTLTISSLEPEDFAVYYCQQDVLWPLTFG GGTKVEIK
244	VL	27589	DIQMTQSPSTLSASVGDRVTITCRASQSISSWL AWYQQKPGKAPKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQQYGLFPITFG GGTKVEIK
245	VL	27596	EIVMTQSPATLSLSPGERATLSCRASQSVSSYL AWYQQKPGQAPRLLIYDASNRATGIPARFSGSG SGTDFTLTISSLEPEDFAVYYCQQHTVWPITFG GGTKVEIK
246	VL	27535	EIVLTQSPATLSLSPGERATLSCRASQSVSSYL AWYQQKPGQAPRLLIYDASKRATGIPARFSGSG SGTDFTLTISSLEPEDFAVYYCQQVLNYPLTFG GGTKVEIK

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247	VL	27550	DIQMTQSPSSLSASVGDRVTITCQASQDISNYL NWYQQKPGKAPKLLIYDASNLETGVPSRFSGSG SGTDFTFTISSLQPEDIATYYCQQSYFLPPTFG GGTKVEIK
248	VL	27549	EIVLTQSPGTLSLSPGERATLSCRASQSVSSDY LAWYQQKPGQAPRLLIYGASSRATGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQAHSSPYTF GGGTKVEIK
249		hCD39	MEDTKESNVKTFCSKNILAILGFSSIIAVIALL AVGLTQNKALPENVKYGIVLDAGSSHTSLYIYK WPAEKENDTGVVHQVEECRVKGPGISKFVQKVN EIGIYLTDCMERAREVIPRSQHQETPVYLGATA GMRLLRMESEELADRVLDVVERSLSNYPFDFQG ARIITGQEEGAYGWITINYLLGKFSQKTRWFSI VPYETNNQETFGALDLGGASTQVTFVPQNQTIE SPDNALQFRLYGKDYNVYTHSFLCYGKDQALWQ KLAKDIQVASNEILRDPCFHPGYKKVVNVSDLY KTPCTKRFEMTLPFQQFEIQGIGNYQQCHQSIL ELFNTSYCPYSQCAFNGIFLPPLQGDFGAFSAF YFVMKFLNLTSEKVSQEKVTEMMKKFCAQPWEE IKTSYAGVKEKYLSEYCFSGTYILSLLLQGYHF TADSWEHIHFIGKIQGSDAGWTLGYMLNLTNMI PAEQPLSTPLSHSTYVFLMVLFSLVLFTVAIIG LLIFHKPSYFWKDMV
250		mCD39	MEDIKDSKVKRFCSKNILIILGFTSILAVIALI AVGLTQNKPLPENVKYGIVLDAGSSHTNLYIYK WPAEKENDTGVVQQLEECQVKGPGISKYAQKTD EIGAYLAECMELSTELIPTSKHHQTPVYLGATA GMRLLRMESEQSADEVLAAVSTSLKSYPFDFQG AKIITGQEEGAYGWITINYLLGRFTQEQSWLSL ISDSQKQETFGALDLGGASTQITFVPQNSTIES PENSLQFRLYGEDYTVYTHSFLCYGKDQALWQK LAKDIQVSSGGVLKDPCFNPGYEKVVNVSELYG TPCTKRFEKKLPFDQFRIQGTGDYEQCHQSILE LFNNSHCPYSQCAFNGVFLPPLHGSFGAFSAFY FVMDFFKKVAKNSVISQEKMTEITKNFCSKSWE ETKTSYPSVKEKYLSEYCFSGAYILSLLQGYNF TDSSWEQIHFMGKIKDSNAGWTLGYMLNLTNMI PAEQPLSPPLPHSTYIGLMVLFSLLLVAVAITG LFIYSKPSYFWKEAV

SEQ ID NO:	Region	Scheme/Clone	Sequence
251		Macaca fascicularis cCD39	MLFDSILSTVGLSKLVSVVSSPAAALSKSNVKT FCSKNILAILGFSSIIAVIALLAVGLTQNKALP ENIKYGIVLDAGSSHTSLYIYKWPAEKENDTGV VHQVEECRVKGPGISKYVQKVNEIGIYLTDCME RAREVIPRSQHQETPVYLGATAGMRLLRMESEE LADRVLDVVERSLSNYPFDFQGARIITGQEEGA YGWITINYLLGKFSQKTRWFSIVPYETNNQETF GALDLGGASTQITFVPQNQTTESPDNALQFRLY GKDYNVYTHSFLCYGKDQALWQKLAKDIQVASN EILRDPCFHPGYKKVVNVSDLYKTPCTKRFEMT LPFQQFEIQGIGNYQQCHQSVLELFNTSYCPYS QCAFNGIFLPPLQGDFGAFSAFYFVMNFLNLTS EKVSQEKVTEMMKKFCSQPWEEIKTSYAGVKEK YLSEYCFSGTYILSLLLQGYHFTADSWEHIHFI GKIQGSDAGWTLGYMLNLTNMIPAEQPLSTPLS HSTYVFLMVLFSLVLVIVAIIGLLIFHKPSYFW KDMV
252		hCD39 ECD	TQNKALPENVKYGIVLDAGSSHTSLYIYKWPAE KENDTGVVHQVEECRVKGPGISKFVQKVNEIGI YLTDCMERAREVIPRSQHQETPVYLGATAGMRL LRMESEELADRVLDVVERSLSNYPFDFQGARII TGQEEGAYGWITINYLLGKFSQKTRWFSIVPYE TNNQETFGALDLGGASTQVTFVPQNQTIESPDN ALQFRLYGKDYNVYTHSFLCYGKDQALWQKLAK DIQVASNEILRDPCFHPGYKKVVNVSDLYKTPC TKRFEMTLPFQQFEIQGIGNYQQCHQSILELFN TSYCPYSQCAFNGIFLPPLQGDFGAFSAFYFVM KFLNLTSEKVSQEKVTEMMKKFCAQPWEEIKTS YAGVKEKYLSEYCFSGTYILSLLLQGYHFTADS WEHIHFIGKIQGSDAGWTLGYMLNLTNMIPAEQ PLSTPLSHSTYVFLMVLFSLVLFTVAIIGLLIF HKPSYFWKDMV
253		mCD39 ECD	TQNKPLPENVKYGIVLDAGSSHTNLYIYKWPAE KENDTGVVQQLEECQVKGPGISKYAQKTDEIGA YLAECMELSTELIPTSKHHQTPVYLGATAGMRL LRMESEQSADEVLAAVSTSLKSYPFDFQGAKII TGQEEGAYGWITINYLLGRFTQEQSWLSLISDS QKQETFGALDLGGASTQITFVPQNSTIESPENS LQFRLYGEDYTVYTHSFLCYGKDQALWQKLAKD IQVSSGGVLKDPCFNPGYEKVVNVSELYGTPCT KRFEKKLPFDQFRIQGTGDYEQCHQSILELFNN SHCPYSQCAFNGVFLPPLHGSFGAFSAFYFVMD FFKKVAKNSVISQEKMTEITKNFCSKSWEETKT SYPSVKEKYLSEYCFSGAYILSLLQGYNFTDSS WEQIHFMGKIKDSNAGWTLGYMLNLTNMIPAEQ

SEQ ID NO:	Region	Scheme/Clone	Sequence
			PLSPPLPHSTYIGLMVLFSLLLVAVAITGLFIY SKPSYFWKEAV
254		cCD39 ECD	TQNKALPENIKYGIVLDAGSSHTSLYIYKWPAE KENDTGVVHQVEECRVKGPGISKYVQKVNEIGI YLTDCMERAREVIPRSQHQETPVYLGATAGMRL LRMESEELADRVLDVVERSLSNYPFDFQGARII TGQEEGAYGWITINYLLGKFSQKTRWFSIVPYE TNNQETFGALDLGGASTQITFVPQNQTTESPDN ALQFRLYGKDYNVYTHSFLCYGKDQALWQKLAK DIQVASNEILRDPCFHPGYKKVVNVSDLYKTPC TKRFEMTLPFQQFEIQGIGNYQQCHQSVLELFN TSYCPYSQCAFNGIFLPPLQGDFGAFSAFYFVM NFLNLTSEKVSQEKVTEMMKKFCSQPWEEIKTS YAGVKEKYLSEYCFSGTYILSLLLQGYHFTADS WEHIHFIGKIQGSDAGWTLGYMLNLTNMIPAEQ PLSTPLSHSTYVFLMVLFSLVLVIVAIIGLLIF HKPSYFWKDMV
255	HC	31895	QVQLVQSGAEVKKPGASVKVSCKASGYTFKSYE MHWVRQAPGQGLEWMGRINPSVGSTWYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRKWGQGTLVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK

SEQ ID NO:	Region	Scheme/Clone	Sequence
256	LC	31895	EIVLTQSPGTLSLSPGERATLSCRASQSVASSY LAWYQQKPGQAPRLLIYGASNRHTGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYHNAITFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC
257	HC	31415	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYQ MHWVRQAPGQGLEWMGRINPSGGSTWYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRSWGQGTLVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
258	LC	31415	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSY LAWYQQKPGQAPRLLIYGASSRATGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYHSYITFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC
259	HC	31891	QVQLVQSGAEVKKPGASVKVSCKASGYIFKSYE MHWVRQAPGQGLEWMGRINPSVGSTWYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRVWGQGTLVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP

SEQ ID NO:	Region	Scheme/Clone	Sequence
			PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
260	LC	31891	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSY LAWYQQKPGQAPRLLIYYASSRAYGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYHNAITFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC
261	HC	31418	QVQLVQSGAEVKKPGASVKVSCKASGYTFKSYE MHWVRQAPGQGLEWMGRINPSGGSTWYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRHWGQGTLVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
262	LC	31418	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSY LAWYQQKPGQAPRLLIYGASSRATGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYYFYITFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC

SEQ ID NO:	Region	Scheme/Clone	Sequence
263	HC	31430	QVQLVQSGAEVKKPGASVKVSCKASGYTFKSYE MHWVRQAPGQGLEWMGRINPSGGSTWYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRHWGQGTLVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
264	LC	31430	EIVLTQSPGTLSLSPGERATLSCEASQSVSYSY LAWYQQKPGQAPRLLIYGASSRANGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYHSALTFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC
265	HC	31915	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSLP ISWVRQAPGQGLEWMGGIGFGTANYAQKFQGRV TITADESTSTAYMELSSLRSEDTAVYYCARGGA KYASKWGMDVWGQGTTVTVSSASTKGPSVFPLA PCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT KTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPA PEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFN STYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPS SIEKTISKAKGQPREPQVYTLPPSQEEMTKNQV SLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMH EALHNHYTQKSLSLSLGK

SEQ ID NO:	Region	Scheme/Clone	Sequence
266	LC	31915	DIVMTQSPDSLAVSLGERATINCKSSQSVLFSS NNKNYLAWYQQKPGQPPKLLIYWASSRESGVPD RFSGSGSGTDFTLTISSLQAEDVAVYYCQQYWT YPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLK SGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
267	HC	31905	QVQLVQSGAEVKKPGSSVKVSCKASGGTFPSNA ISWVRQAPGQGLEWMGGIGFGTANYAQKFQGRV TITADESTSTAYMELSSLRSEDTAVYYCARGGA KYARTYGMDVWGQGTTVTVSSASTKGPSVFPLA PCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT KTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPA PEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFN STYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPS SIEKTISKAKGQPREPQVYTLPPSQEEMTKNQV SLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMH EALHNHYTQKSLSLSLGK
268	LC	31905	DIVMTQSPDSLAVSLGERATINCKSSKSVLYSN NNKNYLAWYQQKPGQPPKLLIYWASTRQSGVPD RFSGSGSGTDFTLTISSLQAEDVAVYYCQQYLL YPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLK SGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
269	HC	31901	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSLP ISWVRQAPGQGLEWMGGIGFGTANYAQKFQGRV TITADESTSTAYMELSSLRSEDTAVYYCARGGA KYAGRYGMDVWGQGTTVTVSSASTKGPSVFPLA PCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT KTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPA PEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFN STYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPS SIEKTISKAKGQPREPQVYTLPPSQEEMTKNQV SLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP

SEQ ID NO:	Region	Scheme/Clone	Sequence
			VLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMH EALHNHYTQKSLSLSLGK
270	LC	31901	GIVMTQSPDSLAVSLGERATINCKSSQSVLFSS NNKNYLAWYQQKPGQPPKLLIYWASTRASGVPD RFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYL YPLTFGGGTKVEIKRTVAAPSVFIFPPSDEQLK SGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDSTYSLSSTLTLSKADYEKHKVY ACEVTHQGLSSPVTKSFNRGEC
271	HC	31861	QVQLVQSGAEVKKPGSSVKVSCKASGGTFGSYG ISWVRQAPGQGLEWMGSIIPEFGIANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARE SGTYRDHRLDVWGQGTMVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
272	LC	31861	EIVMTQSPATLSVSPGERATLSCRASQSVGSNL AWYQQKPGQAPRLLIYGASTRATGIPARFSGSG SGTEFTLTISSLQSEDFAVYYCQQYLLWPLTFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC

SEQ ID NO:	Region	Scheme/Clone	Sequence
273	HC	31873	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSKYG ISWVRQAPGQGLEWMGSIIPEFGIANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARE SGGYRDHRLGVWGQGTMVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
274	LC	31873	EIVMTQSPATLSVSPGERATLSCRASQSVGSNL AWYQQKPGQAPRLLIYGASTRASGIPARFSGSG SGTEFTLTISSLQSEDFAVYYCQQYLLWPLTFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC
275	HC	31393	QVQLVQSGAEVKKPGSSVKVSCKASGGTFESYG ISWVRQAPGQGLEWMGSIIPEFGIANYAQKFQG RVTITADESTSTTYMELSSLRSEDTAVYYCARE SGGYRDHRLDVWGQGTMVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK

SEQ ID NO:	Region	Scheme/Clone	Sequence
276	LC	31393	EIVMTQSPATLSVSPGERATLSCRASQSVGSNL AWYQQKPGQAPRLLIYGASTRATGIPARFSGSG SGTEFTLTISSLQSEDFAVYYCQQYLLWPLTFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC
277	HC	27597	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYA ISWVRQAPGQGLEWMGSIIPIFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARE GRGYDSSRYYKFWFDPWGQGTLVTVSSASTKGP SVFPLAPCSRSTSESTAALGCLVKDYFPEPVTV SWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVP SSSLGTKTYTCNVDHKPSNTKVDKRVESKYGPP CPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPE VTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKP REEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVS NKGLPSSIEKTISKAKGQPREPQVYTLPPSQEE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTPPVLDSDGSFFLYSRLTVDKSRWQEGNVF SCSVMHEALHNHYTQKSLSLSLGK
278	LC	27597	EIVLTQSPATLSLSPGERATLSCRASQSVSSYL AWYQQKPGQAPRLLIYDASNRATGIPARFSGSG SGTDFTLTISSLEPEDFAVYYCQQFVLWPRTFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC
279	HC	27575	QVQLVQSGAEVKEPGSSVKVSCKASGGTFSSYA TSWVRQAPGQGLEWMGGIIPISGTANYAQEFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARD GGGYRHHYFDLWGRGTLVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP

SEQ ID NO:	Region	Scheme/Clone	Sequence
			PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
280	LC	27575	EIVLTQSPATLSLSPGERATLSCRASQSVSRYL AWYQQKPGQAPRLLIYDASNRATGIPARFSGSG SGTDFTLTISSLEPEDFAVYYCQQHVNFPLTFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC
281	HC	27568	QVQLVQSGAEVKKPGSSVKVPCKASGGTFSSYA ISWVRQAPEQGLEWMGSIIPIFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCAGE SGGYRDHKLDVWGQGTVVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
282	LC	27568	EIVLTQSPATLSLSPGERATLSCRASQSVSSYL AWYQQKPGQAPRLLIYDASNRATGIPARFSGSG SGTDFTLTISSLEPEDFAVYYCQQSVFWPITFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC

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283	HC	27577	QVQLVQSGAEVKKPGSSVKVSCKASGGAFSSYA IGWVRQAPGQGLEWMGGIIPTFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARD GGGYQHHYFDLWGRGTLVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
284	LC	27577	EIVMTQSPATLSVSPGERATLSCRASQSVGSNL AWYQQKPGQAPRLLIYGASTRATGIPARFSGSG SGTEFTLTISSLQSEDFAVYYCQQLTKWPLTFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC
285	HC	27587	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYA ISWVRQAPGQGLEWMGSIIPIFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARE SGGYRDHKLDVWGQGTMVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK

SEQ ID NO:	Region	Scheme/Clone	Sequence
286	LC	27587	EIVLTQSPATLSLSPGERATLSCRASQSVSSYL AWYQQKPGQAPRLLIYDASKRATGIPARFSGSG SGTDFTLTISSLEPEDFAVYYCQQDVLWPLTFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC
287	HC	27589	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYA ISWVRQAPGQGLEWMGGIIPIFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARD SGYHRHYSDYWGQGTLVTVSSASTKGPSVFPLA PCSRSTSESTAALGCLVKDYFPEPVTVSWNSGA LTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGT KTYTCNVDHKPSNTKVDKRVESKYGPPCPPCPA PEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFN STYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPS SIEKTISKAKGQPREPQVYTLPPSQEEMTKNQV SLTCLVKGFYPSDIAVEWESNGQPENNYKTTPP VLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMH EALHNHYTQKSLSLSLGK
288	LC	27589	DIQMTQSPSTLSASVGDRVTITCRASQSISSWL AWYQQKPGKAPKLLIYKASSLESGVPSRFSGSG SGTEFTLTISSLQPDDFATYYCQQYGLFPITFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC
289	HC	27596	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYA ISWVRQAPGQGLEWMGGIIPIFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARD PLGIRKHWFDPWGQGTLVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP

SEQ ID NO:	Region	Scheme/Clone	Sequence
			PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
290	LC	27596	EIVMTQSPATLSLSPGERATLSCRASQSVSSYL AWYQQKPGQAPRLLIYDASNRATGIPARFSGSG SGTDFTLTISSLEPEDFAVYYCQQHTVWPITFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC
291	HC	27535	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYA ISWVRQAPGQGLEWMGGIIPIFGTANYAQKFQG RVTITADESTSTAYMELSSLRSEDTAVYYCARD TPRWRYHYFDYWGQGTLVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
292	LC	27535	EIVLTQSPATLSLSPGERATLSCRASQSVSSYL AWYQQKPGQAPRLLIYDASKRATGIPARFSGSG SGTDFTLTISSLEPEDFAVYYCQQVLNYPLTFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC

SEQ ID NO:	Region	Scheme/Clone	Sequence
293	HC	27550	EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYS MNWVRQAPGKGLEWVSSISSSSSYIYYADSVKG RFTISRDNAKNSLYLQMNSLRAEDTAVYYCARE RRGSLALGMDVWGQGTLVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
294	LC	27550	DIQMTQSPSSLSASVGDRVTITCQASQDISNYL NWYQQKPGKAPKLLIYDASNLETGVPSRFSGSG SGTDFTFTISSLQPEDIATYYCQQSYFLPPTFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC
295	HC	27549	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYG MNWVRQAPGKGLEWVAVIWYDGSNKYYADSVKG RFTISRDNSKNTLYLQMNSLRAEDTAVYYCARD LGGYSYGEPYYYYYGMDVWGQGTTVTVSSASTK GPSVFPLAPCSRSTSESTAALGCLVKDYFPEPV TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVT VPSSSLGTKTYTCNVDHKPSNTKVDKRVESKYG PPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRT PEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKT KPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCK VSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQ EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTPPVLDSDGSFFLYSRLTVDKSRWQEGN VFSCSVMHEALHNHYTQKSLSLSLGK

SEQ ID NO:	Region	Scheme/Clone	Sequence
296	LC	27549	EIVLTQSPGTLSLSPGERATLSCRASQSVSSDY LAWYQQKPGQAPRLLIYGASSRATGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQAHSSPYTF GGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTAS VVCLLNNFYPREAKVQWKVDNALQSGNSQESVT EQDSKDSTYSLSSTLTLSKADYEKHKVYACEVT HQGLSSPVTKSFNRGEC
297	HC	31414	QVQLVQSGAEVKKPGASVKVSCKASGYTFKSYE MHWVRQAPGQGLEWMGRINPSVGSTWYAQKFQG RVTMTRDTSTSTVYMELSSLRSEDTAVYYCARG KREGGTEYLRNWGQGTLVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSG ALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLG TKTYTCNVDHKPSNTKVDKRVESKYGPPCPPCP APEFLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLP SSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTP PVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVM HEALHNHYTQKSLSLSLGK
298	LC	31414	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSY LAWYQQKPGQAPRLLIYGASSRATGIPDRFSGS GSGTDFTLTISRLEPEDFAVYYCQQYHSYITFG GGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASV VCLLNNFYPREAKVQWKVDNALQSGNSQESVTE QDSKDSTYSLSSTLTLSKADYEKHKVYACEVTH QGLSSPVTKSFNRGEC

Equivalents

[00465] The disclosure set forth above may encompass multiple distinct inventions with independent utility. Although each of these inventions has been disclosed in its preferred form(s), the specific embodiments thereof as disclosed and illustrated herein are not to be considered in a limiting sense, because numerous variations are possible. The subject matter of the inventions includes all novel and nonobvious combinations and subcombinations of the various elements, features, functions, and/or properties disclosed herein. The following claims particularly point

out certain combinations and subcombinations regarded as novel and nonobvious. Inventions embodied in other combinations and subcombinations of features, functions, elements, and/or properties may be claimed in this application, in applications claiming priority from this application, or in related applications. Such claims, whether directed to a different invention or to the same invention, and whether broader, narrower, equal, or different in scope in comparison to the original claims, also are regarded as included within the subject matter of the inventions of the present disclosure.

WHAT IS CLAIMED IS:

1. An antigen binding protein that binds specifically to a human CD39 (hCD39) and is capable of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or 18 of the following:
    a) inhibiting binding of CD39 to ATP;
    b) inhibiting conversion by CD39 of ATP to ADP and/or ADP to AMP;
    c) decreasing affinity of CD39 for ATP or ADP;
    d) inhibiting or impeding release of ADP or AMP from CD39;
    e) impeding or inhibiting CD39 processivity;
    f) inhibiting platelet aggregation;
    g) decreasing levels of phosphate, ADP, AMP, and/or adenosine and/or increasing levels of ATP;
    h) increasing T effector cell function;
    i) decreasing the number of regulatory T cells in tissues or in circulation;
    j) suppressing regulatory T cells or regulatory T cell activity;
    k) increasing B cell function;
    l) increasing antigen presenting cell function;
    m) inhibiting CD39 function on tumor cells;
    n) inhibiting processing of at least one of phospho-antigen from phosphorylated isoprenoid, phosphorylated vitamin B metabolite, and/or phosphorylated riboflavin;
    o) decreasing or preventing activation of phospho antigen specific T cells selected from MAIT cells and γδ T cells;
    p) inhibiting angiogenesis;
    q) increasing proliferation of stimulated $CD4^+$ and $CD8^+$ T cells;
    r) increasing stimulated PBMC Secretion of INF-γ, TNF-α, IL-2 and/or IL-1β.

2. The antigen binding protein of claim 1, wherein the antigen binding protein has 1, 2, 3, 4, 5, 6, or 7 of the following characteristics:
    a) is a monoclonal antibody;
    b) is a human antibody, a humanized antibody, or a chimeric antibody;

c) is a bispecific antibody, a multi-specific antibody, a diabody, or a multivalent antibody;

d) is of the IgG1, IgG2, IgG3, IgG4, or IgM type;

e) is an antigen-binding antibody fragment;

f) is a Fab fragment, a Fab' fragment, a F(ab')2 fragment, or an Fv fragment; and/or

g) is a single chain antibody, a single domain antibody, or a nanobody.

3. A pharmaceutical composition comprising an effective amount of an antibody which binds to hCD39 and has 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16 of the following of characteristics:

a) blocks or decreases hydrolysis of ATP to ADP and/or ADP to AMP as determined by at least one of: (i) a decreased phosphate release (Pi) , (ii) an increase in ATP levels, and (iii) a decrease of ADP, AMP, and/or adenosine levels,

b) increases T effector cell activity;

c) suppresses regulatory T cell or decreases a regulatory T cell activity;

d) decreases number of regulatory T cells in tissues or in circulation;

e) increases B cell function;

f) increases antigen presenting cell function;

g) inhibits CD39 function on tumor cells;

h) blocks or inhibits processing of at least one of phospho-antigen from a phosphorylated isoprenoid, phosphorylated vitamin B metabolite, and phosphorylated riboflavin;

i) decreases or prevents activation of phospho antigen specific T cells selected from MAIT cells and γδ T cells;

k) inhibits angiogenesis;

l) decreases affinity for ATP and/or ADP;

m) inhibits release of ADP or AMP from CD39;

n) impedes or inhibits CD39 processivity;

o) inhibits platelet aggregation;

p) increases proliferation of stimulated $CD4^+$ and $CD8^+$ T cells;

r) increases stimulated PBMC Secretion of INF-γ, TNF-α, IL-2, and/or IL-1β.

4. A pharmaceutical composition comprising the antigen-binding protein of claim 1 or claim 2.

5. The pharmaceutical composition of claim 4, further comprising an effective amount of at least one of the following

a) an anti-PD-1 antibody,

b) an anti-PD-L1 antibody,

c) an anti-CD73 antibody,

d) an anti-CD38 antibody,

e) an anti-A2A receptor antibody,

f) an anti-A2B receptor antibody,

g) an anti-A2A/A2B dual receptor antibody, or any combination thereof, or

h) a small molecule inhibitor,

or a combination thereof.

6. The pharmaceutical composition of claim 4 or claim 5, further comprising one or both of

a) an antibody to an inhibitory receptor or ligand and/or

b) an antibody to a costimulatory receptor or ligand,

or a combination thereof.

7. The pharmaceutical composition of claim 6, wherein

(i) the inhibitory receptor or ligand is at least one of CTLA-4, PD-L2, LAG-3, Tim3, neuritin, BTLA, CECAM-1, CECAM-5, VISTA, LAIR1, CD160, 2B4, TGF-R, HHLA2, ILT2, ILT3, ILT4, HLA-G, HLA-C, and/or a Killer-cell immunoglobulin-like receptor (KIR) and/or

(ii) the costimulatory receptor or ligand is at least one of OX40, CD2, CD27, CDS, ICAM-1, LFA-1, ICOS (CD278), 4-1BB (CD137), GITR, CD28, CD30, CD40, BAFFR, HVEM, CD7, LIGHT, NKG2C, SLAMF7, NKp80, CD160, B7-H3, and/or CD83.

8. The pharmaceutical composition of Claim 7, wherein the costimulatory receptor or ligand LFA-1 further comprises an LFA-1 β-chain CD18 and/or an LFA-1 α-chain CD11a.

9. The antigen binding protein of Claim 1, wherein the antigen binding protein has one or more of the following characteristics:

a) binds to a human CD39 polypeptide or a variant thereof with a KD of less than about 20 nM;

b) binds to a cyno CD39 polypeptide or a variant thereof with a KD of less than about 200 nM;

c) binds to a murine CD39 polypeptide or a variant thereof with a KD of less than about 200 nM; or

d) a combination of at least 2 of a), b), and c).

10. An antigen binding protein that competes or is capable of competing for binding to human CD39 with a reference antigen binding protein, wherein the reference antigen binding protein is the antigen binding protein of claim 1.

11. An antigen binding protein that binds to or is capable of competing for binding to human CD39 with a reference antigen binding protein, wherein the reference antigen binding protein binds to an epitope at positions 143-158 or 274-277 of SEQ ID NO: 249 on a human CD39 polypeptide, including, but not limited to, D150, E153, R154 or N99 alone or in combination with D150, E153, R154 or any combination thereof.

12. The antigen binding protein of claim 10 or claim 11, wherein the antigen binding protein and the reference antibody cross-compete or are capable of cross-competing for binding to a human CD39.

13. The antigen binding protein of claim 1, comprising a human heavy chain constant region or fragment or a variant thereof, wherein the constant region variant comprises up to 20 conservatively modified amino acid substitutions from any sequence set forth SEQ ID NOs: 179-218.

14. An isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain variable region (VH) and a light chain variable region (VL), VH and/or VL comprising 1, 2, 3, 4, 5, or 6 of:

a) a VHCDR1 having the sequence set forth in SEQ ID NOs: 1-45,

b) a VHCDR2 having the sequence set forth in SEQ ID NOs: 46-81,

c) a VHCDR3 having the sequence set forth in SEQ ID NOs: 82-109,

d) a VLCDR1 having the sequence set forth in SEQ ID NOs: 110-124,

e) a VLCDR2 having the sequence set forth in SEQ ID NOs: 125-140, and

f) a VLCDR3 having the sequence set forth in SEQ ID NOs: 141-166.

15. An isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain variable region (VH) and a light chain variable region (VL),

the VH comprising,

a) a VHCDR1 having a sequence set forth in SEQ ID NOs: 1-45,

b) a VHCDR2 having a sequence set forth in SEQ ID NOs: 46-81, and

c) a VHCDR3 having a sequence set forth in SEQ ID NOs: 82-109; and

the VL comprising,

a) a VLCDR1 having a sequence set forth in SEQ ID NO: 110-124,

b) a VLCDR2 having a sequence set forth in SEQ ID NO: 125-140, and

c) a VLCDR3 having a sequence set forth in SEQ ID NO: 141-166.

16. An isolated nucleic acid encoding an antigen binding protein according to claim 1, claim 14, or claim 15.

17. An expression vector comprising the nucleic acid according to claim 16.

18. A prokaryotic or eukaryotic host cell comprising the vector of claim 17.

19. An oncolytic virus encoding the nucleic acid of either of claims 16 or 17.

20. A method for the production of a recombinant protein comprising the steps of expressing a nucleic acid according to claim 16 in a prokaryotic or eukaryotic host cell and recovering the protein from the cell or the cell culture supernatant.

21. A method for treatment of a subject suffering from cancer, a chronic infection, or from an inflammatory disease, comprising the step of administering to the subject a

pharmaceutical composition comprising an effective amount of the antigen binding protein of claim 1 or the pharmaceutical composition of claim 3.

22. The method of claim 21, wherein the cancer is a solid cancer.

23. The method of claim 21, wherein the cancer is a hematological cancer.

24. A method for modulating immune system function in a subject in need thereof, comprising the step of contacting a population of immune cells of the subject with a pharmaceutical composition comprising an effective amount of the antigen binding protein of claim 1, under conditions such that the immune system is modulated.

25. A method for inducing or enhancing an immune response in a subject in need thereof, comprising the step of administering to the subject a pharmaceutical composition comprising an antigen binding protein, wherein the immune response is generated against a tumor antigen.

26. The method of Claim 24 or Claim 25, wherein the subject is a human subject.

27. The method of claim 25, wherein the antigen binding protein comprises a bispecific antibody or a complexing antigen binding protein.

28. The method of claim 27, wherein the antigen binding protein, the bispecific antibody, or the complexing antigen binding protein is administered in an amount sufficient to achieve 1, 2, 3, 4, 5, 6, or 7 of the following in the subject:

a) reduction of CD39 ATPase activity in a target cell population;

b) reduction of regulatory T cells suppression of activity of effector T cells;

c) reduction of levels of regulatory T cells;

d) activation of effector T cells;

e) induction or enhancement of effector T cell proliferation;

f) inhibition of tumor growth; and/or

g) induction of tumor regression.

29. The method of claim 28, wherein the target cell population comprises T cells, B cells, monocytes, macrophages, dendritic cells, myeloid-derived suppressor cells, and/or tumor cells.

30. The method of claim 25, wherein the method further comprises one or more of the following

a) administering chemotherapy;

b) administering radiation therapy; and/or

c) administering one or more additional therapeutic agents.

31. The method of claim 30, wherein the one or more additional therapeutic agents comprise one or more immunostimulatory agents.

32. The method of claim 31, wherein the one or more immunostimulatory agents comprise an antagonist to an inhibitory receptor of an immune cell.

33. The method of claim 32, wherein the inhibitory receptor is at least one of CTLA-4, PD-1, PD-L1, PD-L2, LAG-3, Tim3, neuritin, BTLA, CECAM-1, CECAM-5,

VISTA, LAIR1, CD160, 2B4, TGF-R, and/or a Killer-cell immunoglobulin-like receptor (KIR).

34. The method of claim 31, wherein the one or more immunostimulatory agents comprise an agonist of a co-stimulatory receptor of an immune cell.

35. The method of claim 34, wherein the co-stimulatory receptor is OX40, CD2, CD27, CDS, ICAM-1, LFA-1, ICOS (CD278), 4-1BB (CD137), GITR, CD28, CD30, CD40, BAFFR, HVEM, CD7, LIGHT, NKG2C, SLAMF7, NKp80, CD160, B7-H3, or a CD83 ligand.

36. The method of claim 35, wherein the costimulatory receptor or ligand LFA-1 further comprises an LFA-1 β-chains CD18 and/or an LFA-1 α-chain CD11a.

37. The method of claim 31, wherein the one or more immunostimulatory agents comprise a cytokine.

38. The method of claim 37, wherein the cytokine is at least one of IL-2, IL-5, IL-7, IL-12, IL-15, and/or IL-21.

39. The method of claim 31, wherein the one or more immunostimulatory agents comprise an oncolytic virus.

40. The method of claim 39, wherein the oncolytic virus is a Herpes simplex virus, a Vesicular stomatitis virus, an adenovirus, a Newcastle disease virus, a vaccinia virus, or a maraba virus.

41. The method of claim 31, wherein the one or more immunostimulatory agents comprise a chimeric antigen engineered T cell.

42. The method of claim 31, wherein the one or more immunostimulatory agents comprise a bi- or multispecific T cell directed antibody.

43. The method of claim 25, wherein the one or more additional therapeutic agents comprise at least one trap for an immune suppressive agent.

44. The method of Claim 43, wherein the at least one trap for an immune suppressive agent comprises at least one of an anti-TGF-beta antibody, a TGFb receptor trap, an anti-IL-10 antibody and/or anti-IL-10 receptor trap, and/or an anti-IL-35 antibody trap and/or an anti-IL-35 receptor trap.

45. The method of any one of any of claims 3-44, wherein administration of the pharmaceutical composition results in induction or enhancement of proliferation of a T-effector cell, or modulation of I-kappaB and/or NF- κB in the T cell, or modulation of CD39 activity in the T cell, or T cell receptor induced signaling in a T-effector cell, or a combination thereof.

46. A method of screening for a test compound comprising an antigen binding protein of claim 1 capable of inhibiting an activity of CD39, comprising the steps of:

contacting a test sample containing CD39 with a test compound;

comparing the activity of the test sample to a control sample;

whereby a decrease in the activity of CD39 in the test sample compared to the control sample identifies the compound as one that inhibits the activity of CD39.

47. The method of Claim 46, wherein the control sample comprises a sample not contacted with a test compound.

48. An isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain variable region (VH) and a light chain variable region (VL),

VH comprising at least one of:

a) a VHCDR1 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs: 1-45,

b) a VHCDR2 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs: 46-81, and

c) a VHCDR3 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs: 82-109; and

VL comprising at least one of:

a) a VLCDR1 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs: 110-124,

b) a VLCDR2 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs: 125-140, and

c) a VLCDR3 having an amino acid sequence that is at least 90% identical to the sequence set forth in SEQ ID NOs 141-166.

49. An isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain variable region (VH) and a light chain variable region (VL),

VH comprising at least one of:

a) a VHCDR1 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 1-45,

b) a VHCDR2 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 46-81, and

c) a VHCDR3 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 82-109; and

VL comprising at least one of:

a) a VLCDR1 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 110-124,

b) a VLCDR2 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 125-140, and

c) a VLCDR3 having an amino acid sequence that is homologous to the sequence set forth in SEQ ID NOs: 141-166.

50. An isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain and a light chain, the heavy chain comprising one or more molecules having a sequence consisting of one of SEQ ID NO: 255, SEQ ID NO: 257, SEQ ID NO: 259, SEQ ID NO: 261, SEQ ID NO: 263, SEQ ID NO: 265, SEQ ID NO: 267, SEQ ID NO: 269, SEQ ID NO: 271, SEQ ID NO: 273, SEQ ID NO: 275, SEQ ID NO: 277, SEQ ID NO: 279, SEQ ID NO: 281, SEQ ID NO: 283, SEQ ID NO: 285, SEQ ID NO: 287, SEQ ID NO: 289, SEQ ID NO: 291, SEQ ID NO: 293, or SEQ ID NO: 295 and the light chain comprising one or more molecules having a sequence consisting of one of SEQ ID NO: 256, SEQ ID NO: 258, SEQ ID NO: 260, SEQ ID NO: 262, SEQ ID NO: 264, SEQ ID NO: 266, SEQ ID NO: 268, SEQ ID NO: 270, SEQ ID NO: 272, SEQ ID NO: 274, SEQ ID NO: 276, SEQ ID NO: 278, SEQ ID NO: 280, SEQ ID NO: 282, SEQ ID NO: 284, SEQ ID NO: 286, SEQ ID NO: 288, SEQ ID NO: 290, SEQ ID NO: 292, SEQ ID NO: 294, or SEQ ID NO: 296.

51. An isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain and a light chain,

a) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 255 and the light chain comprising one or more, each molecule having a sequence consisting of SEQ ID NO: 256;

b) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 257 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 258;

c) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 259 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 260;

d) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 261 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 262;

e) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 263 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 264;

f) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 265 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 266;

g) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 267 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 268;

h) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 269 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 270;

i) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 271 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 272;

j) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 273 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 274;

k) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 275 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 276;

l) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 277 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 278

m) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 279 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 280;

n) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 281 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 282;

o) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 283 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 284;

p) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 285 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 286;

q) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 287 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 288;

r) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 289 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 290;

s) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 291 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 292;

t) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 293 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 294; or

u) the heavy chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 295 and the light chain comprising one or more molecules, each molecule having a sequence consisting of SEQ ID NO: 296.

52. An isolated nucleic acid encoding an antigen binding protein according to any one of claims 48-51.

53. An isolated antibody molecule capable of binding to human CD39 (hCD39), comprising a heavy chain variable region (VH) and a light chain variable region (VL), VH and/or VL comprising 1, 2, 3, 4, 5, or 6 of:

a) a VHCDR1 sequence comprising:

(i) a Kabat CDRH1 sequence defined by the consensus sequence S-Y-Δ_3-M-Δ_5 (SEQ ID NOS: 25-29 and 44-45), where Δ_3 is E, F, Q, or Y and Δ_5 is H or Y;

(ii) a Kabat CDR-H1 sequence defined by the consensus sequence θ_1-θ_2-θ_3-I-S (SEQ ID NOS: 30-37), where θ_1 is A, H, K, L, S, or W; θ_2 is L, M, N, or T; and θ_3 is A or P;

(iii) a Kabat CDR-H1 sequence defined by the consensus sequence η_1-Y-η_3-I-S SEQ ID NOS: 38-41), where η_1 is S, K, N, or R and η_3 is A or G;

(iv) a Chothia CDR-H1 sequence defined by the consensus sequence G-Y-T-F-Ω_5-S-Y (SEQ ID NOS: 1-2 and 4-6), where Ω_5 is T, K, Q, F, or V;

(v) a Chothia CDR-H1 sequence defined by the consensus sequence G-G-T-F-ν_5- ν_6-Y (SEQ ID NOS: 17-22 and 24), where ν_5 is S, G, or E and ν_6 is S, K, R, or S; or

(vi) a Chothia CDR-H1 consensus sequence defined by the consensus sequence G-G-T-F-κ_5-κ_6-κ_7 (SEQ ID NOS: 7-16), where κ_5 is S, Q, P, or A; κ_6 is S, K, H, L, A, or W; and κ_7 is Y, L, T, N, or M,

b) a VHCDR2 sequence comprising:

(i) a Kabat CDR-H2 sequence defined by the consensus sequence ε_1-I-N-P-ε_5-ε_6-G-S-T-ε_{10}-Y-A-Q-K-F-Q-G (SEQ ID NOS: 63-66 and 68), where ε_1 is K, S, R, or V; ε_5 is L, R, or S; ε_6 is G or V; and ε_{10} is S or W;

(ii) a Kabat CDR-H2 sequence defined by the consensus sequence G-I-α_3-α_4-α_5-α_6-G-T-A-N-Y-A-Q-K-F-Q-G (SEQ ID NOS: 69-72), where α_3 is I or L or is absent; α_4 is P or is absent; and α_5 is I, G, or R; and α_6 is A, F, or G;

(iii) a Kabat CDR-H2 sequence defined by the consensus sequence β_1-I-I-P-β_5-β_6-G-β_8-A-N-Y-A-Q-K-F-G-Q (SEQ ID NOS: 74 and 76-79), where β_1 is S or G; β_5 is I, E, S, or T; β_6 is F, I, or S; and β_8 is I or T;

(iv) a Chothia CDR-H2 sequence defined by the consensus sequence N-P-ε_5-ε_6-G-S-T (SEQ ID NOS: 46-48), where ε_5 is L, R, or S and ε_6 is G or V;

(v) a Chothia CDR-H2 sequence defined by the consensus sequence α_3-α_4-α_5-α_6-G-T-A (SEQ ID NOS: 51-54), where α_3 is I or L or is absent; α_4 is P or is absent; and α_5 is I, G, or R; and α_6 is A, F, or G; or

(vi) a Chothia CDR-H2 sequence defined by the consensus sequence I-P-β_5-β_6-G-β_8-A (SEQ ID NOS: 56-60), where β_5 is I, E, S, or T; β_6 is F, I, or S; and β_8 is I or T,

c) a VHCDR3 sequence comprising:

(i) a CDR-H3 sequence defined by the consensus sequence G-K-R-E-G-G-T-E-Y-L-R-$У_{12}$ (SEQ ID NOS: 82-86), where $У_{12}$ is H, K, S, N, or V;

(ii) a CDR-H3 sequence defined by the consensus sequence E-S-G-Φ_4-Y-R-D-H-R-L-Φ_{11}-V (SEQ ID NOS: 94-96), where Φ_4 is G or T and Φ_{11} is D or

G; or

(iii) a CDR-H3 sequence defined by the consensus sequence G-G-A-K-Y-A-Э$_7$-Э$_8$-Э$_9$-G-M-D-V (SEQ ID NOS: 87-93), where Э$_7$ is S, V, G, or R; Э$_8$ is T, Q, K, G, or R; and Э$_9$ is Y, H, L, or W,

d) a VLCDR1 sequence comprising:

(i) a CDR-L1 sequence defined by the consensus sequence ϕ_1-A-S-ϕ_4-ϕ_5-V-ϕ_7-ϕ_8-ϕ_9-Y-L-A (SEQ ID NOS: 1101-114), where ϕ_1 is E, K, or R; ϕ_4 is Q or E; ϕ_5 is S or Y; ϕ_7 is S or A; ϕ_8 is S or Y; and ϕ_9 is D or S;

(ii) a CDR-L1 sequence defined by the consensus sequence Б$_1$-A-S-Q-Б$_5$-Б$_6$-Б$_7$-Б$_8$-Б$_9$-L-Б$_{11}$ (SEQ ID NOS: 118 and 120-123), where Б$_1$ is Q or Rl; Б$_5$ is D or S; Б$_6$ is I or V; Б$_7$ is G or S; Б$_8$ is N, R, or S; Б$_9$ is N, Y, or W; and Б$_{11}$ is A or N; or

(iii) a CDR-L1 sequence defined by the consensus sequence K-S-S-Г$_4$-S-V-L- Г$_8$-S- Г$_{10}$-N-N-K-N-Y-L-A (SEQ ID NOS: 115-117), where Г$_4$ is Q, R or K; Г$_8$ is F or Y; and Г$_{10}$ is S or N,

e) a VLCDR2 sequence comprising:

(i) a CDR-L2 sequence defined by the consensus sequence ψ_1-A-S-ψ_4-R-ψ_6-ψ_7 (SEQ ID NOS: 125-136), where ψ_1 is G or Y, ψ_4 is S or N; ψ_6 is A or H; and ψ_7 is T, Y, or N;

(ii) a CDR-L2 sequence defined by the consensus sequence D-A-S- χ_4-R-A-T (SEQ ID NOS: 138 and 139), where £$_4$ is N or K; or

(iii) a CDR-L2 sequence defined by the consensus sequence W-A-S-T-R-σ_6-S (SEQ ID NOS: 131 and 133-134), where σ_6 is A, E, or Q, and

f) a VLCDR3 sequence comprising:

(i) a CDR-L3 sequence defined by the consensus sequence Q-Q-Y-π_4- π_5-π_6-π_7-T (SEQ ID NOS: 141-147), where π_4 is G, H, or Y; π_5 is S, N, F, G, or R; π_6 is S, Y, A, G, or R; and π_7 is P, I, or L;

(ii) a CDR-L3 sequence defined by consensus sequence Q-Q-λ_3-λ_4-λ_5-λ_6-P-T (SEQ ID NOS: 148-150), where λ_3 is R, F, H, S, L, D, Y, or V; λ_4 is S, V, T,

G, L, Y, or N; λ_5 is N, L, F, K, or V; and λ_6 is W, F, Y, or L;

(iii) a CDR-L3 sequence defined by the consensus sequence Q-Q-Y-ρ_3-ρ_4-W-P-L-T (SEQ ID NOS: 151 and 152), where ρ_3 is N or L and ρ_4 is N or L; or

(iv) a CDR-L3 sequence defined by the consensus sequence Q-Q-ω_3-ω_4-ω_5-ω_6-P- ω_8-T (SEQ ID NOS: 153-156), where ω_3 is Y or F; ω_4 is Y or W; ω_5 is S, L, T, or F; ω_6 is T, Y, or F; and ω_8 is L or P.

FIG. 1

Clone ID	K_D (M)	kon ($M^{-1}s^{-1}$)	koff (s^{-1})	Clone ID	K_D (M)	kon ($M^{-1}s^{-1}$)	koff (s^{-1})
27535	PF	PF	PF	29872	1.13E-08	1.75E+05	2.02E-03
27536	1.14E-07	6.59E+04	7.51E-03	31393	6.72E-10	2.98E+05	2.00E-04
27549	4.05E-08	1.93E+04	7.82E-04	31414	1.01E-08	4.31E+05	4.37E-03
27550	1.43E-07	4.44E+05	6.33E-02	31415	1.63E-08	2.27E+05	3.71E-03
27568	1.73E-07	2.72E+05	4.70E-02	31418	1.30E-08	3.14E+05	4.06E-03
27571	1.64E-08	6.39E+05	1.05E-02	31421	1.88E-08	2.81E+05	5.26E-03
27575	PF	PF	PF	31429	2.39E-08	4.73E+05	1.13E-02
27577	4.09E-07	8.93E+05	3.65E-01	31430	1.01E-08	3.26E+05	3.28E-03
27579	1.67E-07	9.55E+05	1.60E-01	31431	1.60E-08	1.73E+05	2.76E-03
27587	3.37E-08	2.11E+05	7.11E-03	31432	1.07E-09	2.68E+05	2.86E-04
27588	5.49E-08	1.17E+05	6.44E-03	31436	9.24E-10	2.63E+05	2.43E-04
27589	1.91E-07	2.02E+05	3.85E-02	31437	5.58E-10	3.82E+05	2.13E-04
27590	1.31E-07	1.76E+05	2.30E-02	31861	1.16E-09	2.46E+05	2.86E-04
27596	3.11E-08	1.72E+06	5.33E-02	31873	9.22E-10	3.11E+05	2.86E-04
27597	3.35E-07	2.73E+05	9.14E-02	31891	1.34E-09	4.53E+05	6.09E-04
28337	1.27E-08	1.43E+05	1.80E-03	31895	1.81E-09	4.63E+05	8.39E-04
28347	9.05E-09	9.01E+05	8.15E-03	31896	9.05E-09	9.01E+05	8.15E-03
29851	1.23E-09	3.13E+05	3.85E-04	31901	1.28E-10	1.03E+06	1.32E-04
29852	2.66E-10	5.03E+05	1.34E-04	31905	7.31E-11	1.52E+06	1.11E-04
29857	7.60E-10	3.02E+05	2.29E-04	31915	8.11E-10	3.53E+05	2.86E-04
29871	2.44E-07	2.73E+05	6.66E-02	A1	1.92E-09	1.66E+05	3.18E-04

FIGS. 2 A-B

A.

Clone Name	Human CD39 Inhibition Assay Cell Titer Glo Average Response (RLU)
27536	7489
27549	16867
27550	5574
27568	5727
27571	6823
27575	2598
27577	3596
27579	6471
27587	8733
27588	11166
27589	6580
27590	5680
27596	3929
27597	8889
Isotype Control	375

B.

Clone Name	Human CD39 Inhibition Assay Cell Titer Glo Average Response (RLU)
28337	9399
28347	9083
27535	4890
Isotype Control	857

FIGS. 2 C-E

C.

Clone Name	Human CD39 Inhibition Assay Cell Titer Glo Average Response (RLU)
28337	11768
27549	15648
28347	11182
29851	11554
29852	11980
29857	11637
27571	8543
27579	8878
29871	8708
29872	8372
BY40va	415
no IgG	979

D.

Clone Name	Human CD39 Inhibition Assay Cell Titer Glo Average Response (RLU)
27571	10885
31393	12105
27579	8035
29872	8368
31414	10254
31415	10289
31418	9447
31421	7263
31429	11441
31430	8380
31431	9993
28347	13306
31436	14157
31437	13509
31393	12105
Isotype Control	38

E.

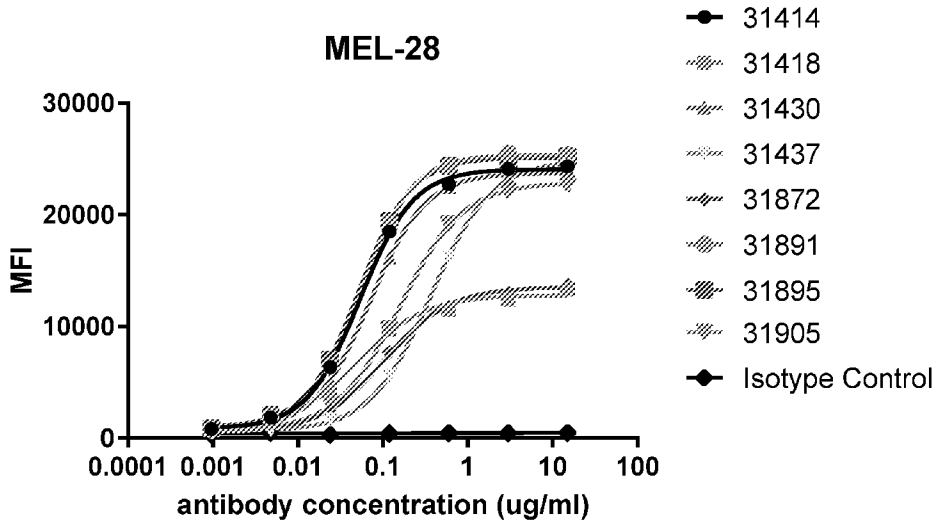
Clone Name	Human CD39 Inhibition Assay Cell Titer Glo Average Response (RLU)
27571	14303
31861	17866
31873	16645
27579	6575
31414	11375
31891	13470
31895	12828
28347	18736
31432	18610
31896	11911
31901	14798
31905	20329
31915	15694
Isotype Control	44
BY40va	11

FIG. 2F

Clone Number	Cell Binding (FOB)		Clone Number	Cell Binding (FOB)	
	hCD39-CHO	cCD39-CHO		hCD39-CHO	cCD39-CHO
27535	301	738	31393	1064	2955
27536	89	113	31414	1236	3568
27549	822	566	31415	1168	3365
27550	2,033	2870	31418	1077	3183
27568	267	260	31421	1075	3053
27571	1,405	1607	31429	1291	3800
27575	2	128	31430	1222	3573
27577	390	339	31431	1235	3533
27579	1,953	2667	31432	1167	5697
27587	1,450	1403	31436	1317	3568
27588	10	14	31437	1292	3643
27589	311	531	31861	1432	5477
27590	33	44	31873	1321	5083
27596	252	257	31891	1026	4651
27597	799	908	31895	1042	4493
28337	4	17	31896	1042	4539
28347	1,020	1340	31901	1113	4662
29851	129	398	31905	1077	4937
29852	337	1418	31915	1087	4578
29857	224	1145	A1	796-2191	2426-3054
29871	451	3350	BY40va	1292	3867
29872	1454	4191	*Isotype Control*	1	1

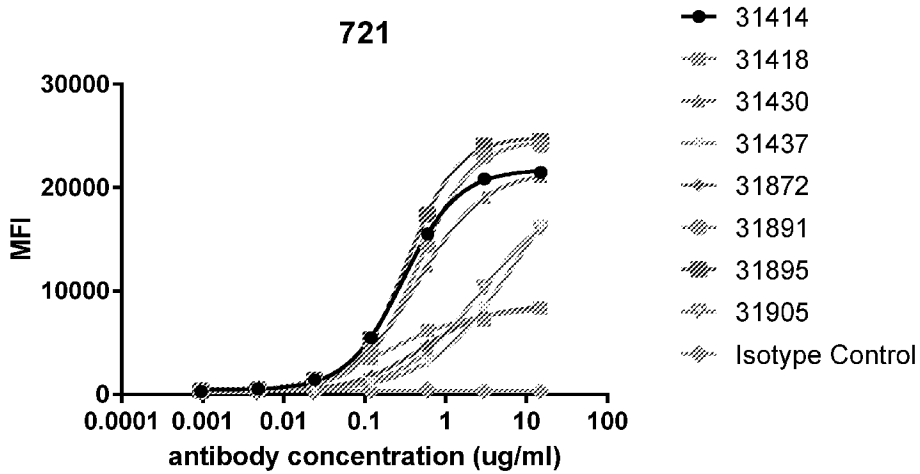
FIG. 3

A.



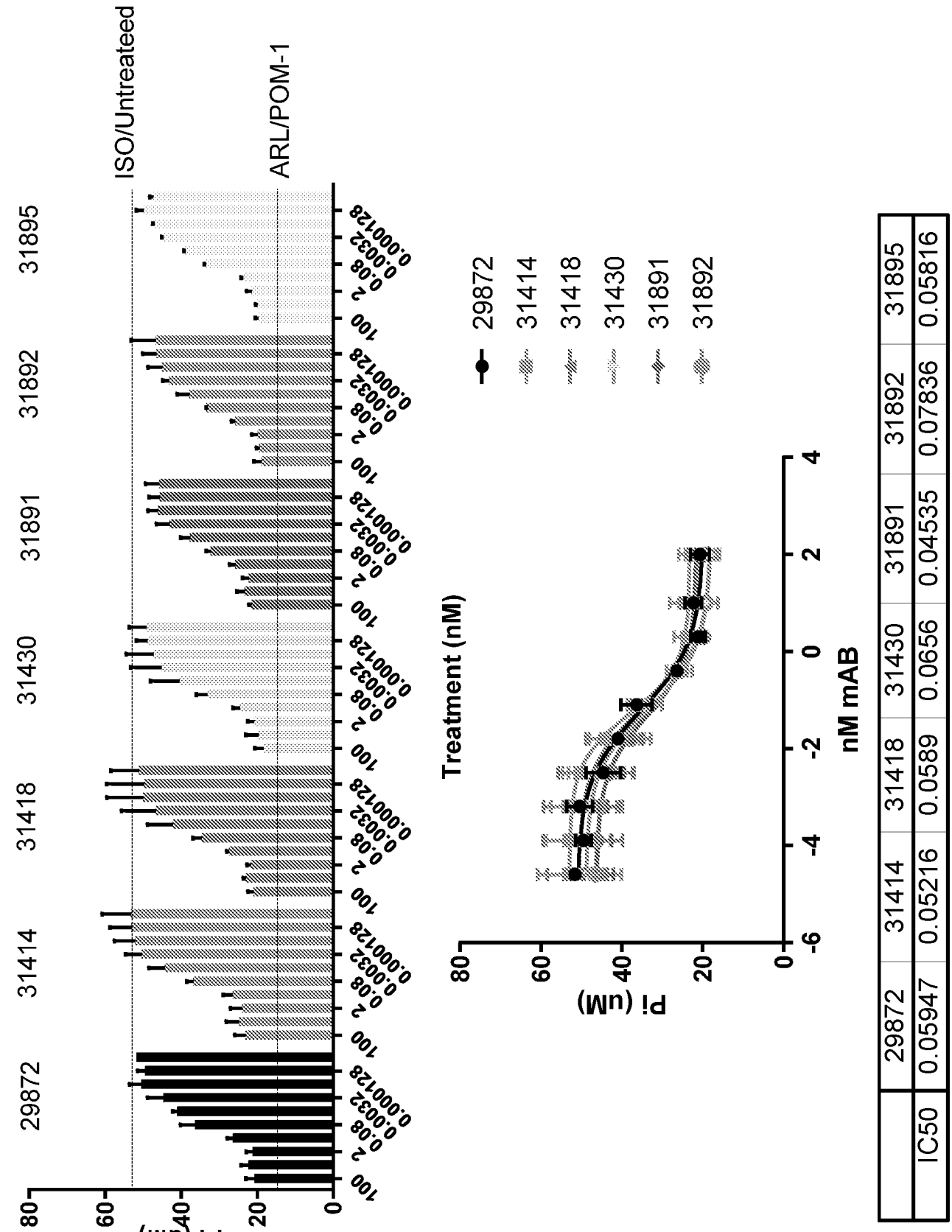
	31414	31418	31430	31437	29872	31891	31894	31895	31901	31905
EC50	0.0542	0.04756	0.07094	0.3682	0.1047	0.05622	0.06163	0.05181	0.1023	0.159

B.



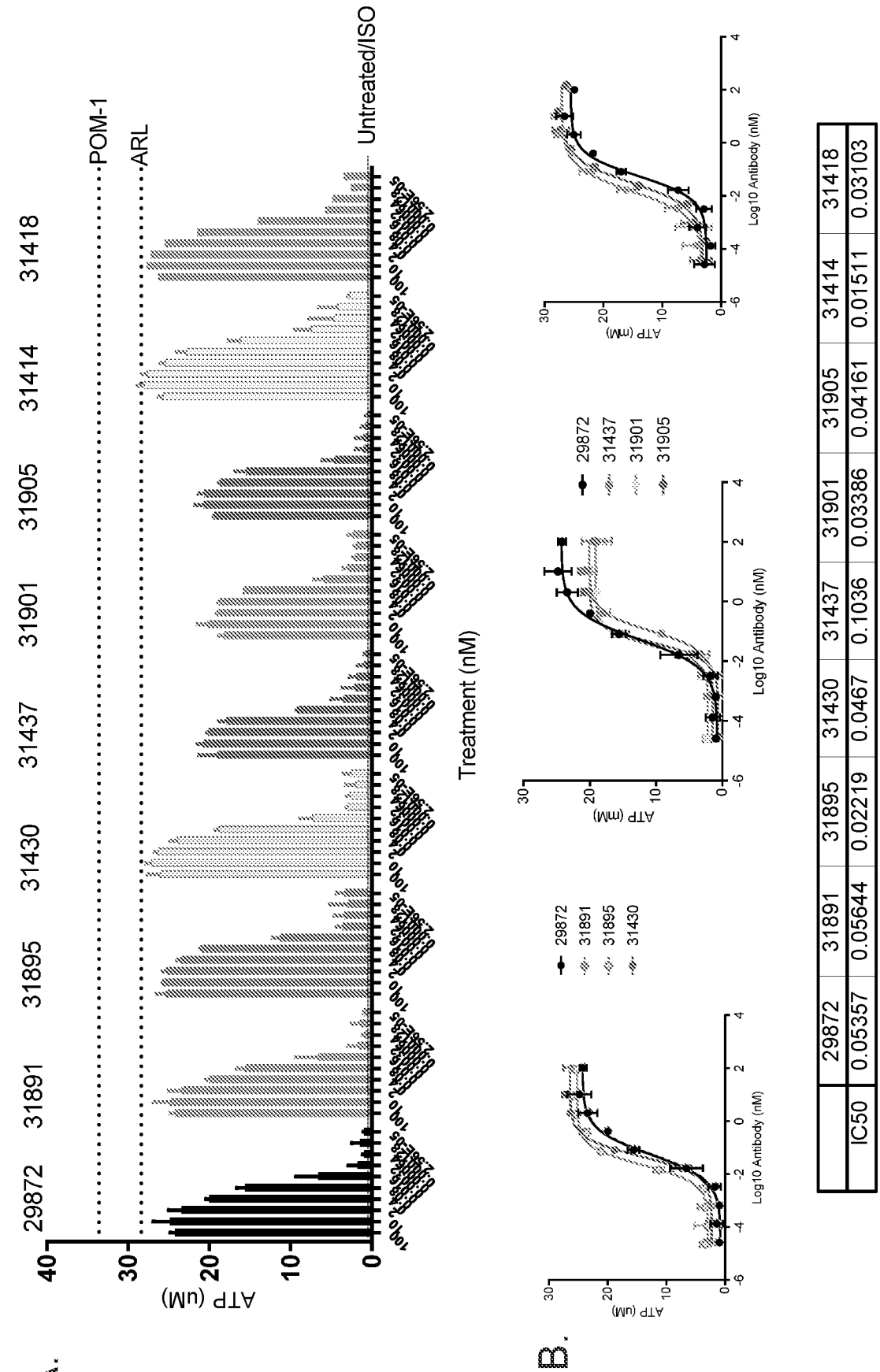
	43114	31418	31430	31437	29872	31891	31894	31895	31901	31905
EC50	0.2976	0.192	0.4626	7.461	0.514	0.4619	0.425	0.3301	0.851	2.626

FIG. 4



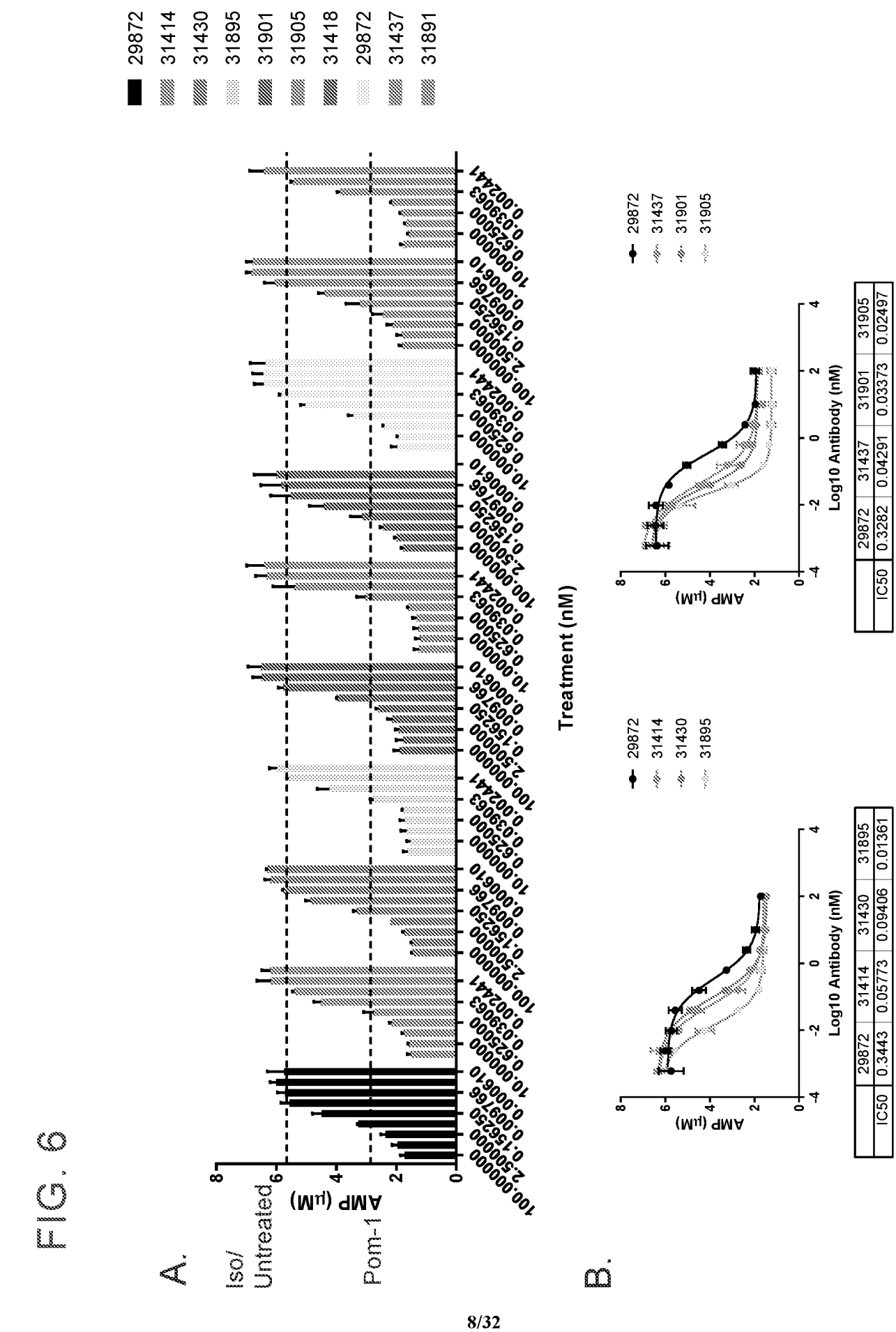
	29872	31414	31418	31430	31891	31892	31895
IC50	0.05947	0.05216	0.0589	0.0656	0.04535	0.07836	0.05816

FIG. 5



	29872	31891	31895	31430	31437	31901	31905	31414	31418
IC50	0.05357	0.05644	0.02219	0.0467	0.1036	0.03386	0.04161	0.01511	0.03103

FIG. 6

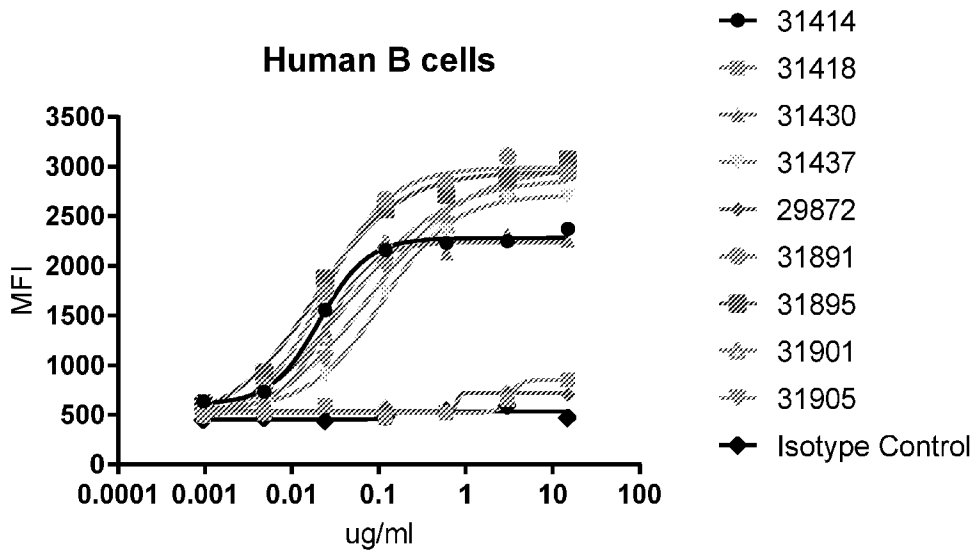


	29872	31414	31430	31895
IC50	0.3443	0.05773	0.09406	0.01361

	29872	31437	31901	31905
IC50	0.3282	0.04291	0.03373	0.02497

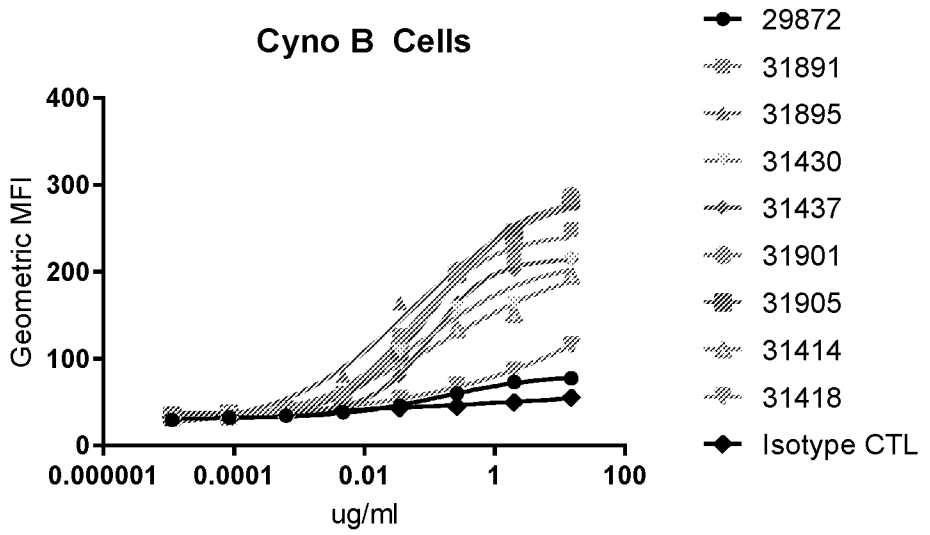
FIG. 7

A.



	31414	31418	31430	31437	29872	31891	31894	31895	31901	31905
EC50	0.02073	~ 3.188	0.025	0.1088	~ 0.7951	0.02379	0.02078	0.01882	0.04379	0.08046

B.



	29872	31891	31895	31430	31437	31901	31905	31414	31418	Isotype CTL
EC50	0.1552	0.0529	0.05547	0.08159	0.1081	0.1237	0.124	0.174	~ 4341417	~ 1.479e+043

FIG. 8

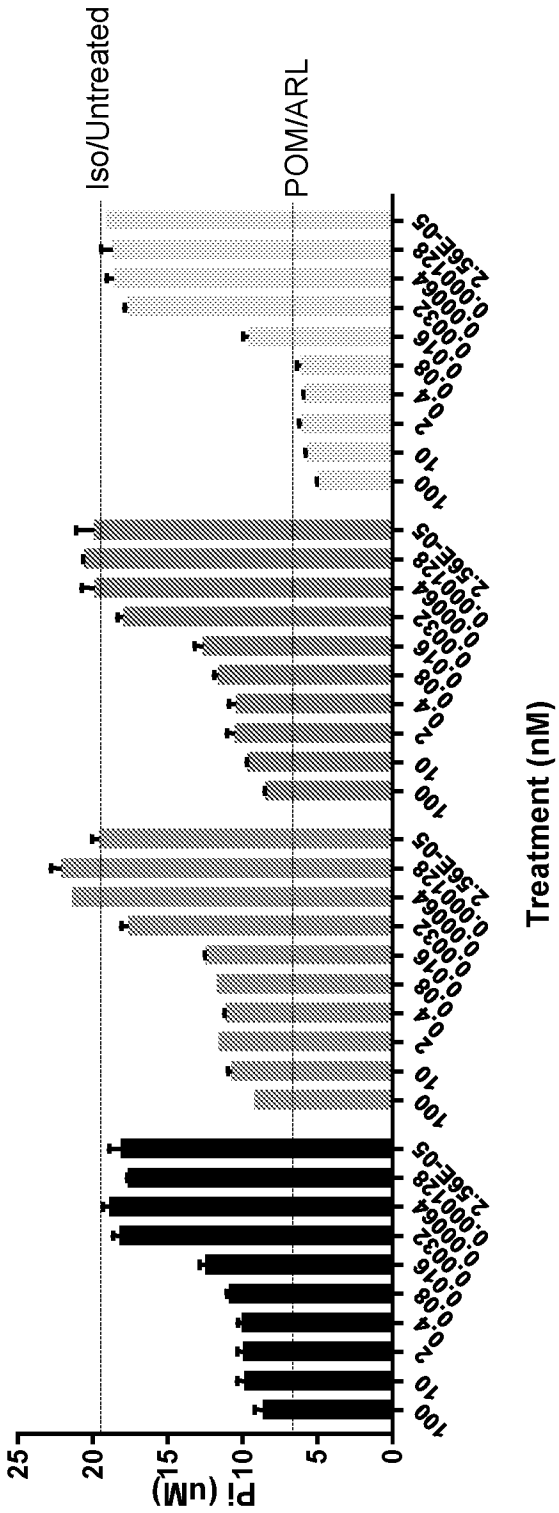

Iso/Untreated
POM/ARL
29872
31414
31895
31905
Pi (uM)
0
5
10
15
20
25
100
10
2
0.4
0.08
0.016
0.0032
0.00064
0.000128
2.56E-05
Treatment (nM)

FIG. 9

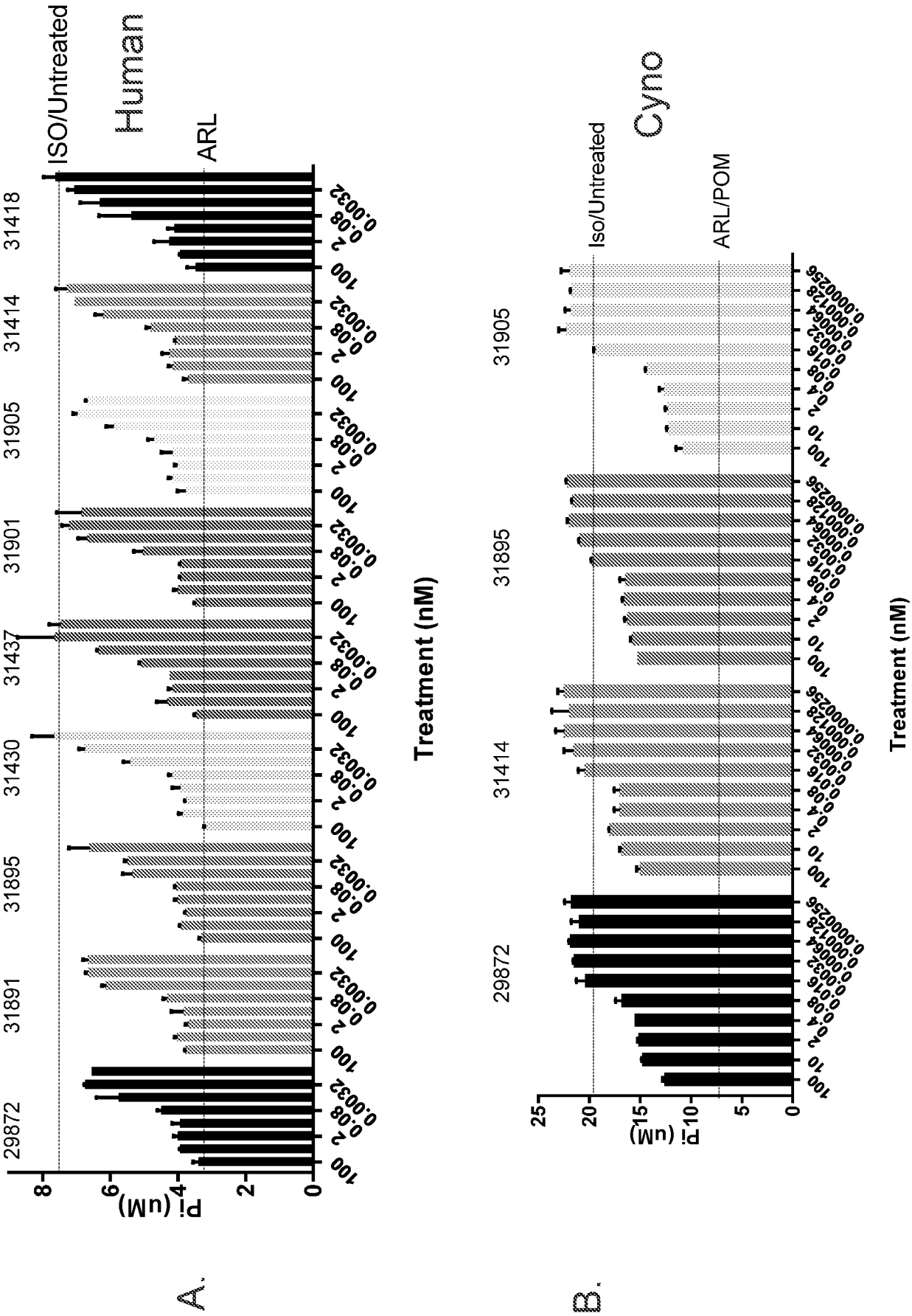
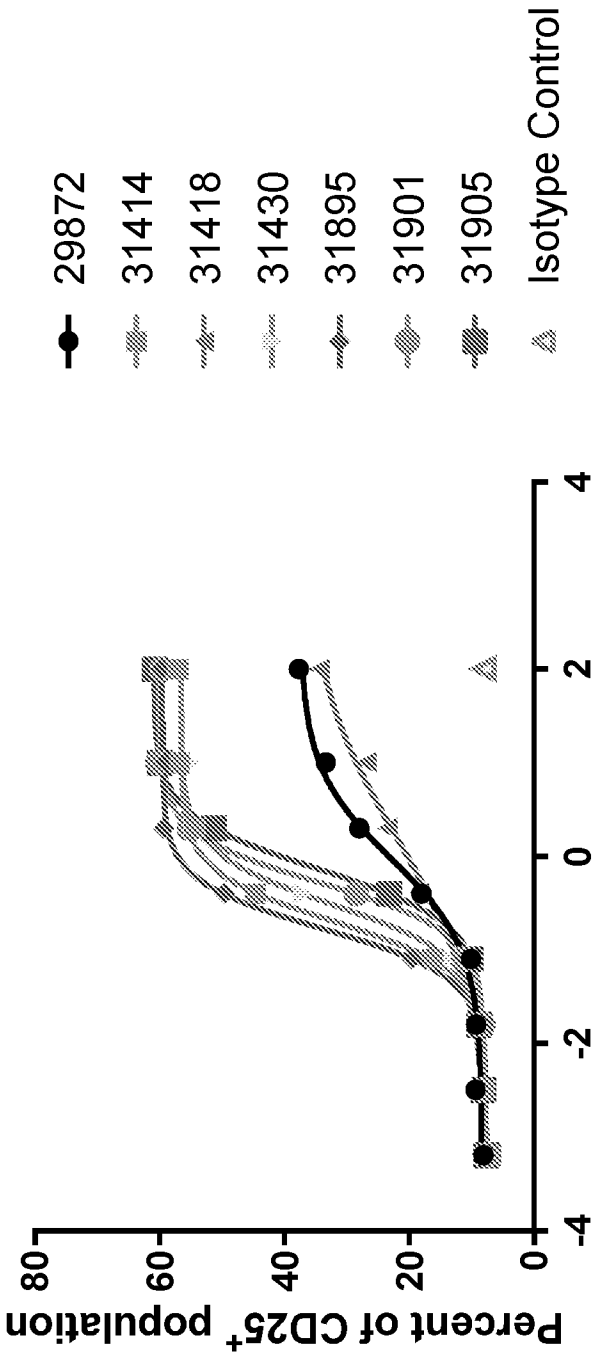

A.
Human
ISO/Untreated
ARL
Pi (uM)
Treatment (nM)
29872
31891
31895
31430
31437
31901
31905
31414
31418
B.
Cyno
Iso/Untreated
ARL/POM
Pi (uM)
Treatment (nM)
29872
31414
31895
31905

FIG. 10



	29872	31414	31418	31430	31895	31901	31905
EC50	0.9501	0.2025	1.607	0.3065	0.1685	0.5192	0.7349

FIG. 11

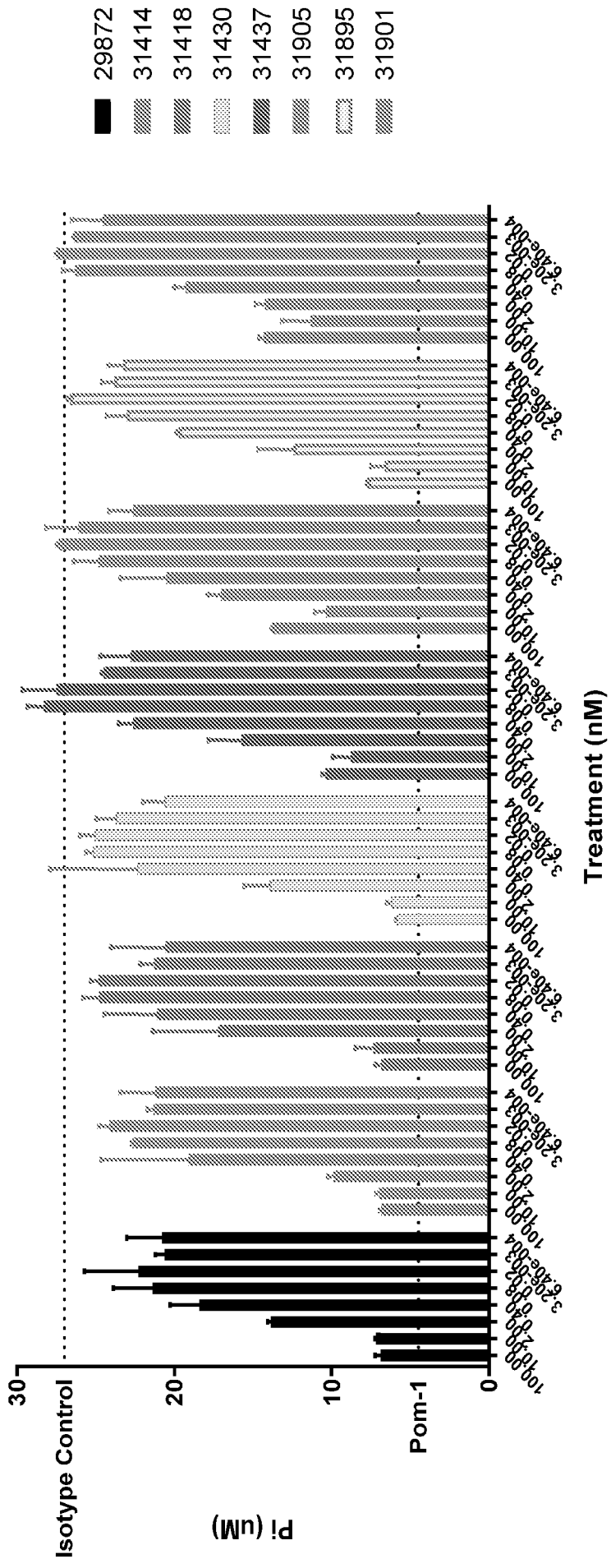

29872
31414
31418
31430
31437
31905
31895
31901
Isotype Control
Pom-1
30
20
10
0
Pi (uM)
Treatment (nM)

FIG. 12

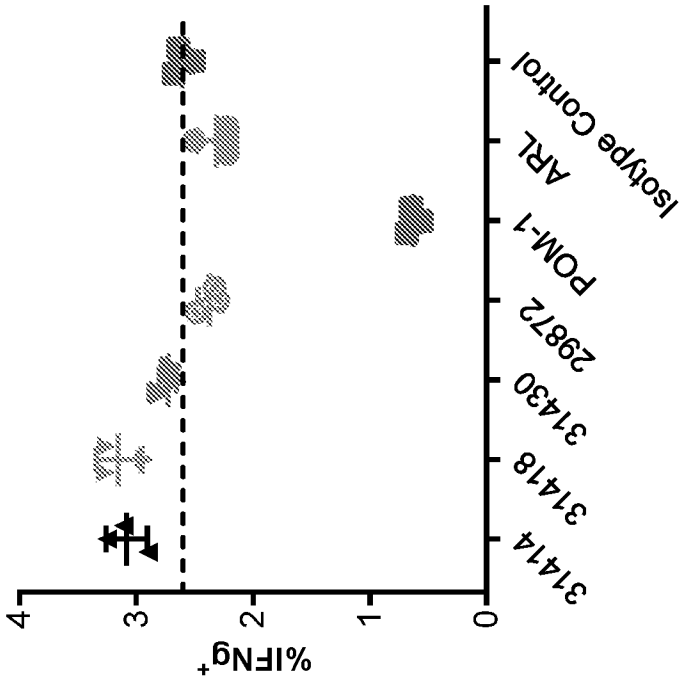

CD8+ T cells
%IFNg+
0
1
2
3
4
31414
31418
31430
29872
POM-1
ARL
Isotype Control

FIG. 13

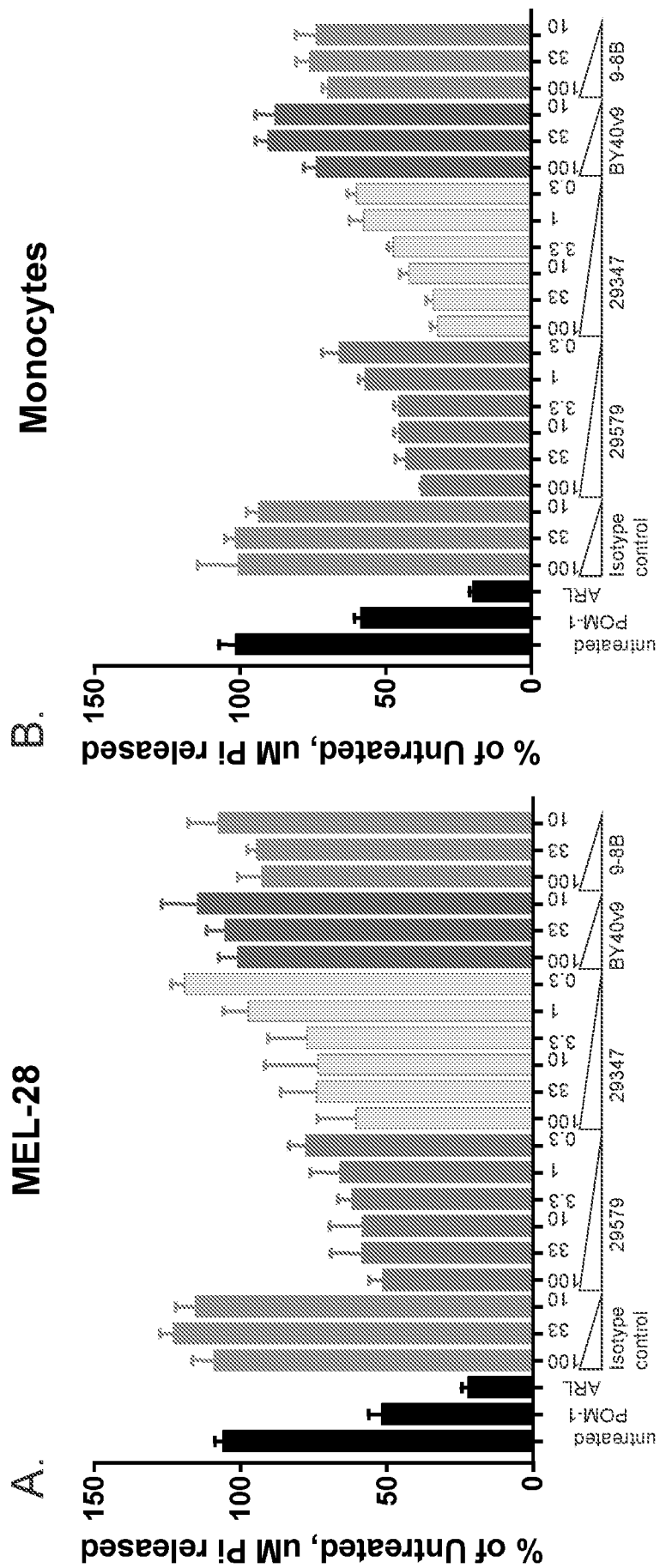

A.
MEL-28
% of Untreated, uM Pi released
150
100
50
0
untreated
POM-1
ARL
Isotype control
29579
29347
BY40v9
9-8B
100
33
10
3.3
1
0.3
B.
Monocytes

FIG. 14A

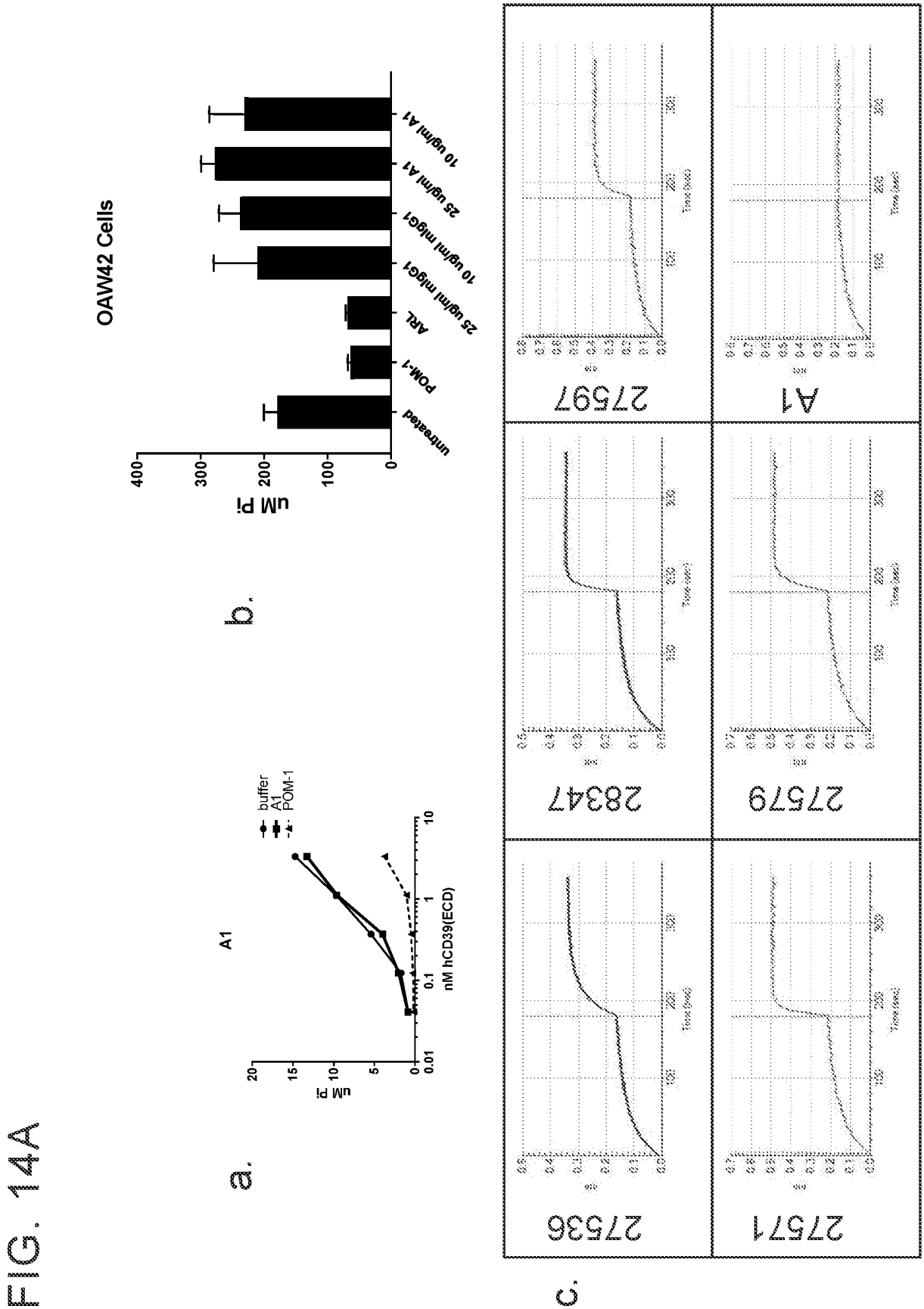

a.
A1
buffer
A1
POM-1
uM Pi
nM hCD39(ECD)
b.
OAW42 Cells
uM Pi
untreated
POM-1
ARL
25 ug/ml mIgG1
10 ug/ml mIgG1
25 ug/ml A1
10 ug/ml A1
c.
27536
27571
28347
27579
27597
A1

FIG. 14B

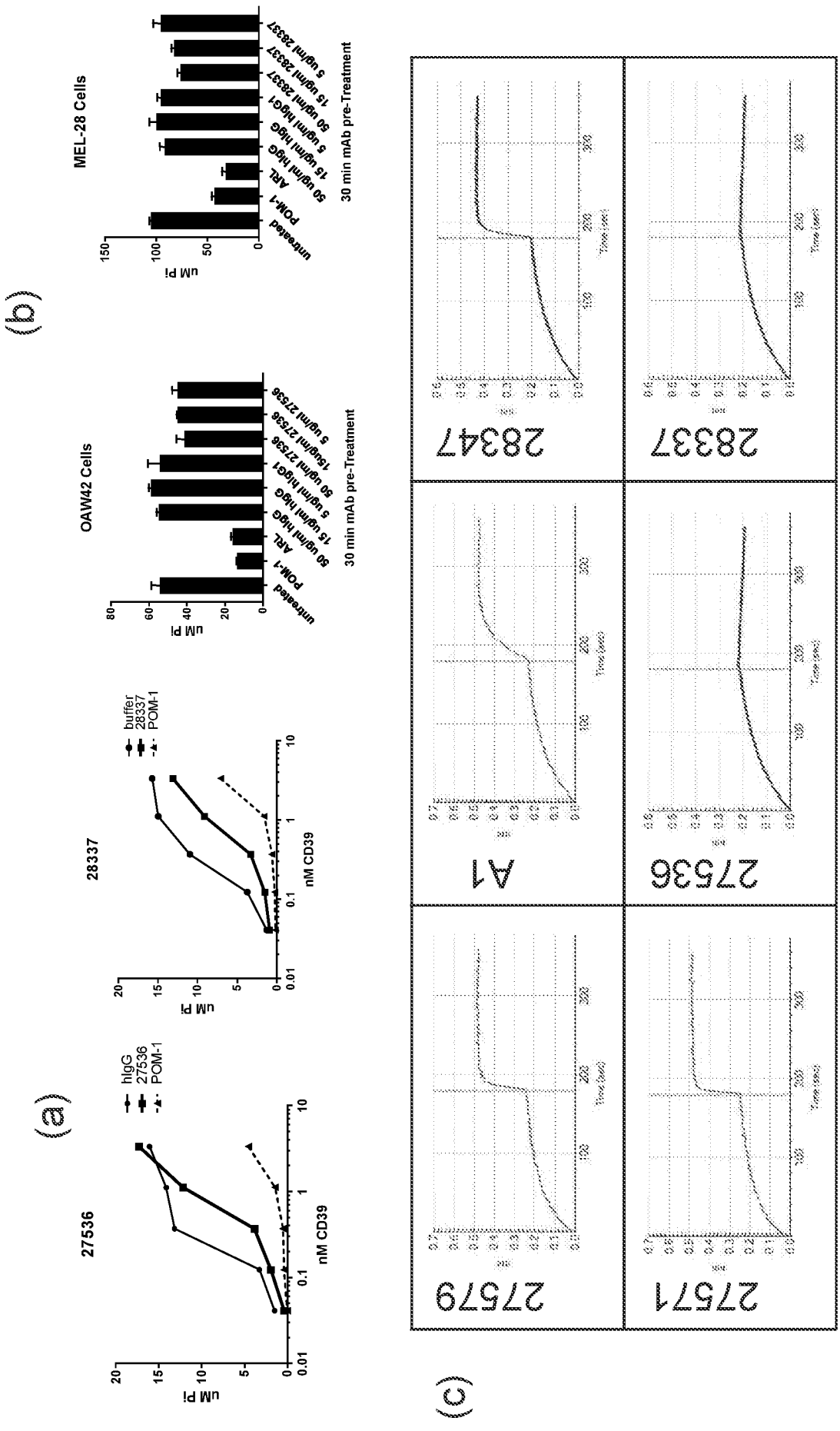

(a)
27536
28337
hIgG
27536
POM-1
buffer
28337
POM-1
uM PI
nM CD39
(b)
OAW42 Cells
MEL-28 Cells
untreated
POM-1
ARL
50 ug/ml hIgG
15 ug/ml hIgG
5 ug/ml hIgG
50 ug/ml hIgG1
15ug/ml 27536
5 ug/ml 27536
15 ug/ml 28337
5 ug/ml 28337
30 min mAb pre-Treatment
(c)
27579
A1
27536
28337
27571
28347

FIG. 14C

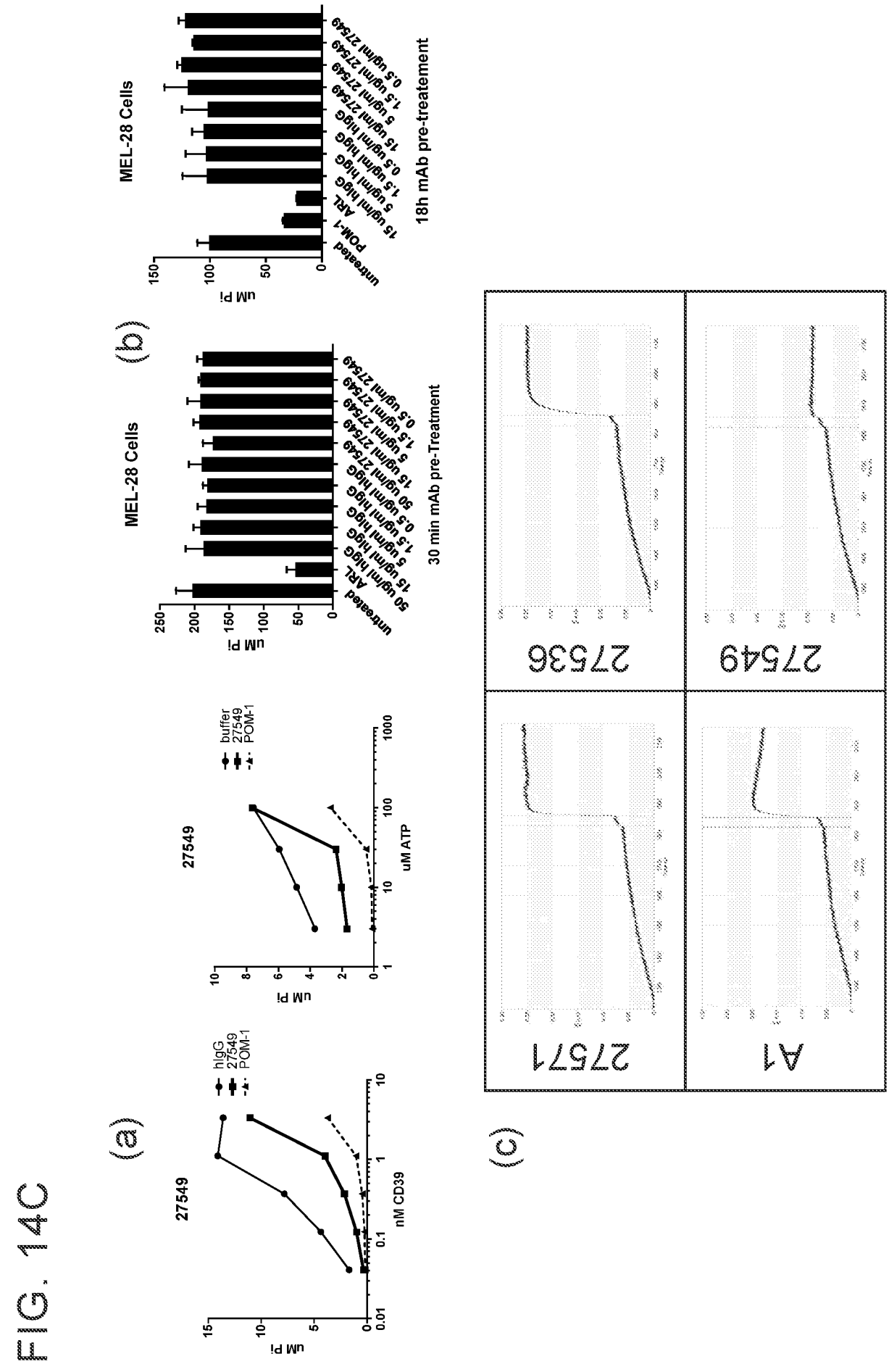

(a)
27549
hIgG
27549
POM-1
uM PI
nM CD39
0.01
0.1
1
10
(b)
MEL-28 Cells
uM PI
untreated
POM-1
ARL
15 ug/ml hIgG
5 ug/ml hIgG
1.5 ug/ml hIgG
0.5 ug/ml hIgG
15 ug/ml 27549
5 ug/ml 27549
1.5 ug/ml 27549
0.5 ug/ml 27549
18h mAb pre-treatement
50 ug/ml hIgG
50 ug/ml 27549
30 min mAb pre-Treatment
(c)
27571
27536
27549
A1

FIG. 14D

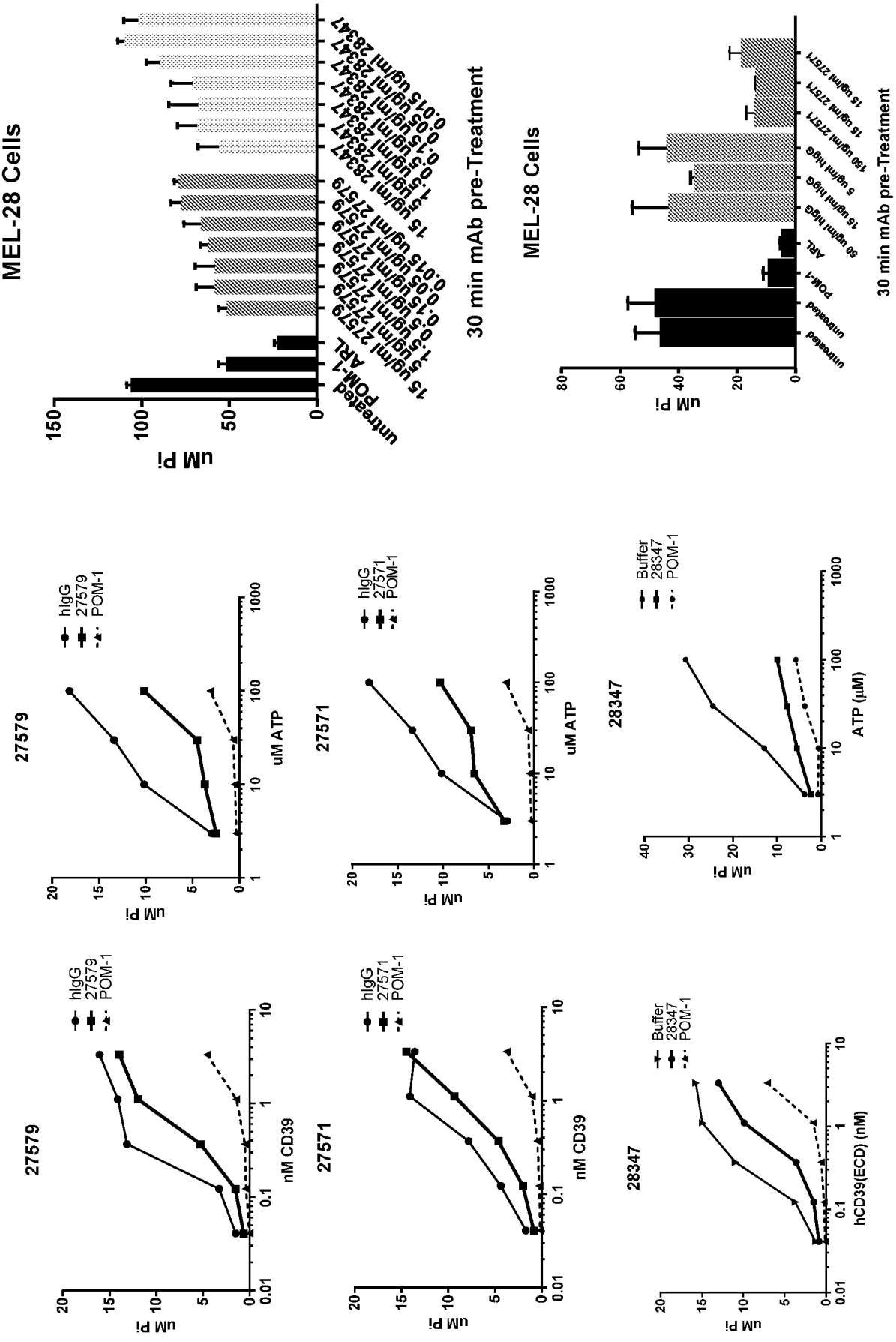

MEL-28 Cells
30 min mAb pre-Treatment
uM PI
untreated
POM-1
ARL
15 ug/ml 27579
1.5 ug/ml 27579
0.15 ug/ml 27579
0.015 ug/ml 27579
15 ug/ml 28347
1.5 ug/ml 28347
0.15 ug/ml 28347
0.015 ug/ml 28347
50 ug/ml hIgG
15 ug/ml hIgG
5 ug/ml hIgG
150 ug/ml 27571
15 ug/ml 27571
15 ug/ml 27571
27579
27571
28347
hIgG
POM-1
Buffer
nM CD39
uM ATP
ATP (µM)
hCD39(ECD) (nM)

FIG.14E

Table 1.

Chimera #	FASTA Residue Number from Species of Origin in Chimera			Mouse amino acid sequence[4]	mAb binding to human-mouse CD39 chimeras					
	Human[1]	Mouse[2]	Human[3]		31895 31414 31418	31873	31901 31905	BY40v9	9-8B	A1 498403#
1	M1-E110	L111-Q123	T124-V510	L_{111}STELIPTSKHHQ	yes	yes	yes	yes	yes	yes
2	M1-E142	Q143-S158	Y159-V510	Q_{143}SADEVLAAVSTSLKS	NO	NO	NO	yes	yes	yes
3	M1-G187	R188-K204	Q206-V510	R_{188}FTQEQSWLSLISDSQK	yes	yes	yes	yes	yes	yes
4	M1-S274	G274-V277	L278-V510	G_{278}GV	yes	yes	yes	yes	yes	NO
5	M1-E306	K306-E322	Q324-V510	K_{306}KLPFDQFRIQGTGDYE	yes	yes	yes	yes	yes	yes
6	M1-M367	D367-I378	S378-V510	D_{367}FFKKVAKNSVI	yes	yes	yes	yes	yes	yes
7	M1-C390	S392-S404	V404-V510	S_{392}KSWEETKTSYPS	yes	yes	yes	yes	yes	yes
8	M1-H428	N428-N447	A448-V510	N_{428}FTDSSWEQIHFMGKIK DSN	yes	yes	yes	yes	yes	yes

WO 2019/027935 PCT/US2018/044449

FIG.14E

Table 2.

Chimera #	FASTA Residue Number from Species of Origin in Chimera			Mouse and Human amino acid sequences*	mAb binding to human-mouse CD39 chimeras				
	Human	Mouse	Human		31895 31414 31418	3187 3	3190 1 3190 5	BY40v9	9-8B
2	M1-E142	Q143-S158	Y159-V510	Q_{143}SADEVLAAVSTSLKS	NO	NO	NO	yes	yes
9	M1-E142 Y159-V510	Q143-L149 A151-S158	**D150**	Q_{143}SADEVL**D**AVSTSLKS	**YES**	NO	NO	yes	yes
10	M1-E142 Y159-V510	Q143-V152 R154-S158	**E153**	Q_{143}SADEVLAAV**E**TSLKS	**YES**	NO	NO	yes	yes
WT	M1-V510			V_{95}QKVNEIGI E_{143}LADRVLDVVERSKSN	yes	yes	yes	yes	yes
11	M1-V98 E100-V510	**D99**		V_{95}QKV**D**EIGI	yes	yes	yes	yes	yes
12	M1-E153 S155-V510	**T154**		E_{143}LADRVLDVVE**T**SKSN	yes	yes	yes	yes	yes
13	M1-V98 E100-E153 S155-V510	**D99 T154**		V_{95}QKV**D**EIGI E_{143}LADRVLDVVE**T**SKSN	yes	**NO**	**NO**	yes	yes
14	M1-V152 S155-V510	**S153 T154**		E_{143}LADRVLDVV**ST**SKSN	yes	**NO**	**NO**	yes	yes

FIG. 14F

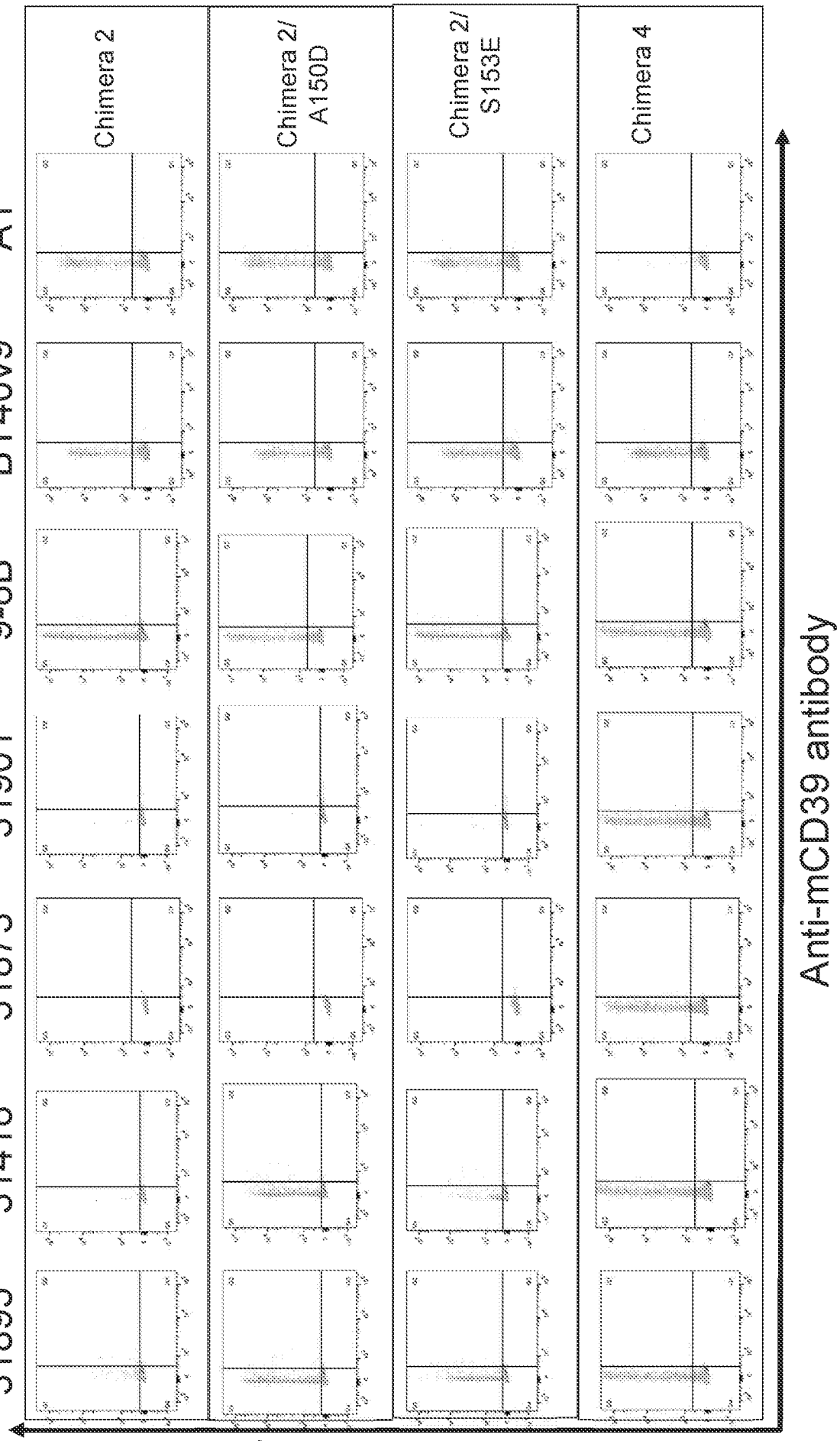
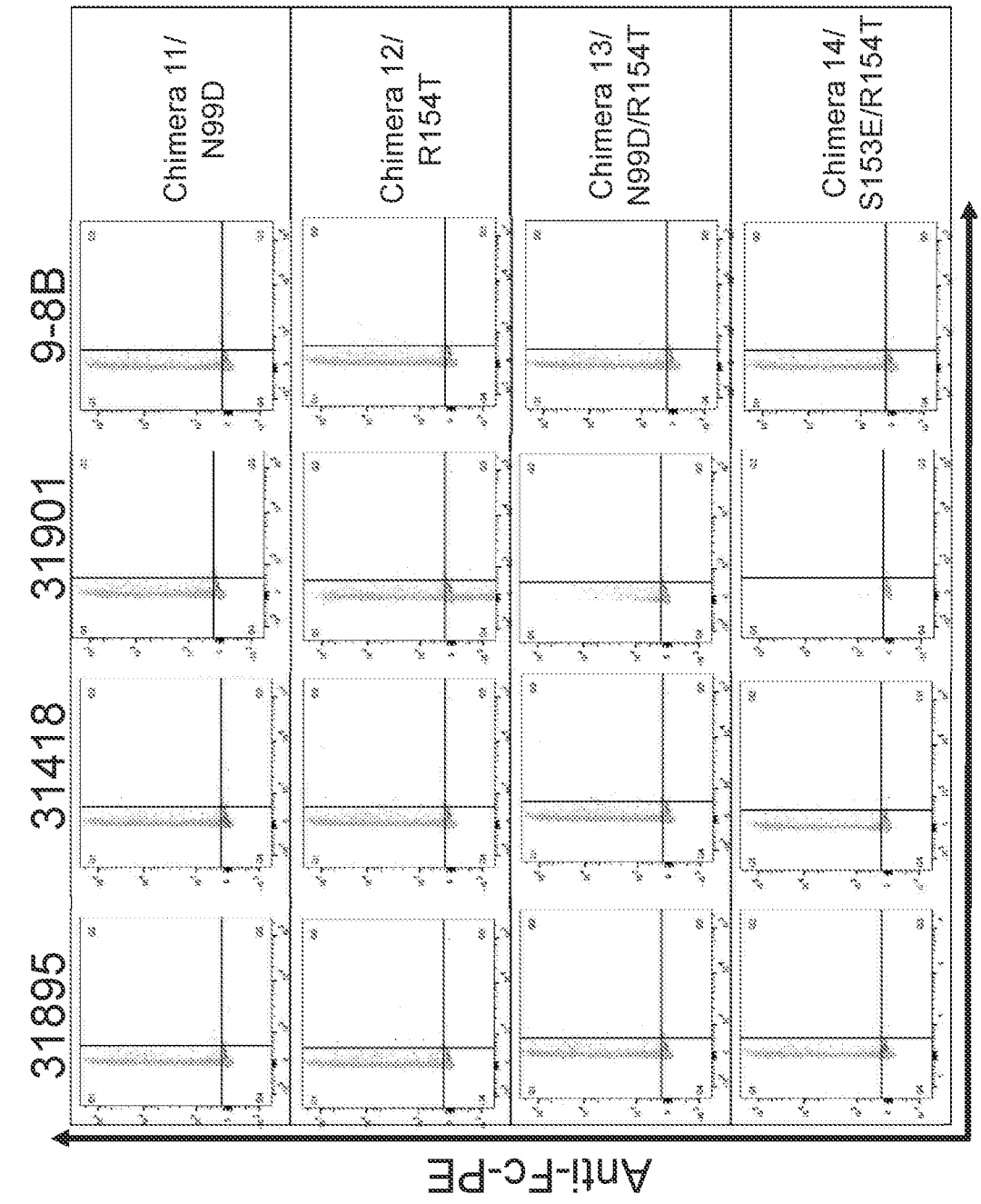

31895
31418
31873
31901
9-8B
BY40v9
A1
Chimera 2
Chimera 2/ A150D
Chimera 2/ S153E
Chimera 4
Anti-hCD39 antibody
Anti-mCD39 antibody

FIG. 14G


Chimera 11/ N99D
Chimera 12/ R154T
Chimera 13/ N99D/R154T
Chimera 14/ S153E/R154T
9-8B
31901
31418
31895
Anti-FC-PE
Anti-mCD39-APC

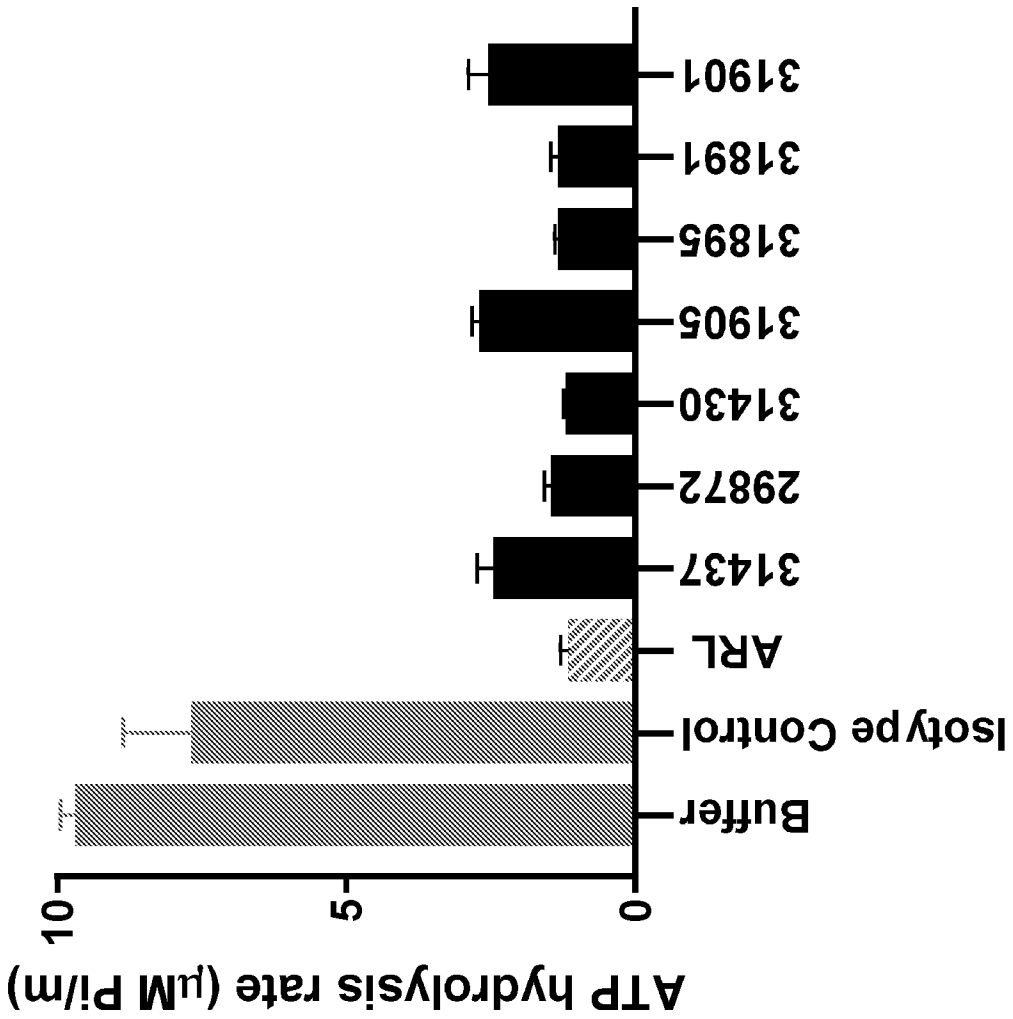

ATP hydrolysis rate (μM Pi/m)
10
5
0
Buffer
Isotype Control
ARL
31437
29872
31430
31905
31895
31891
31901

FIG. 15

FIG. 16A

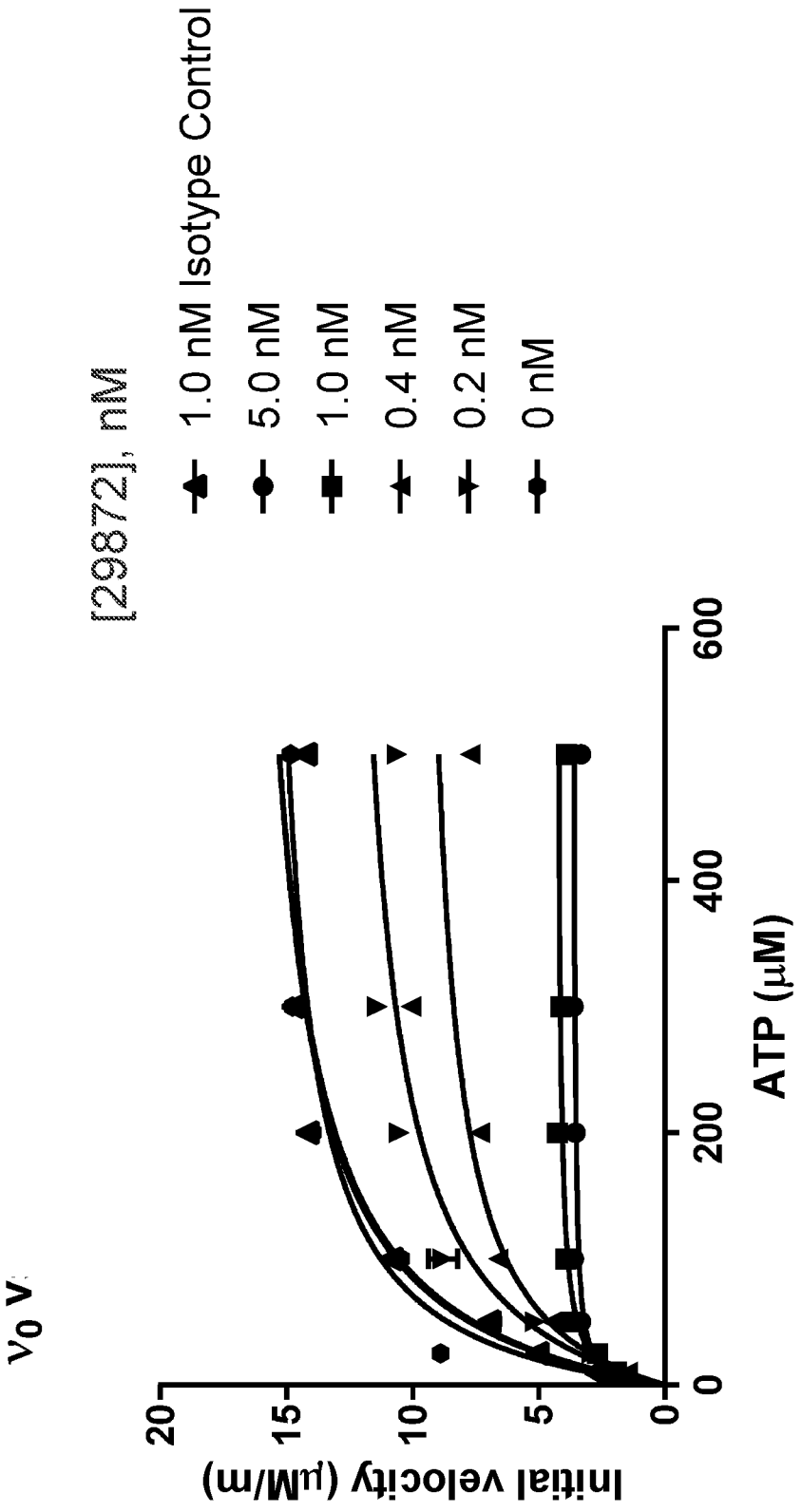
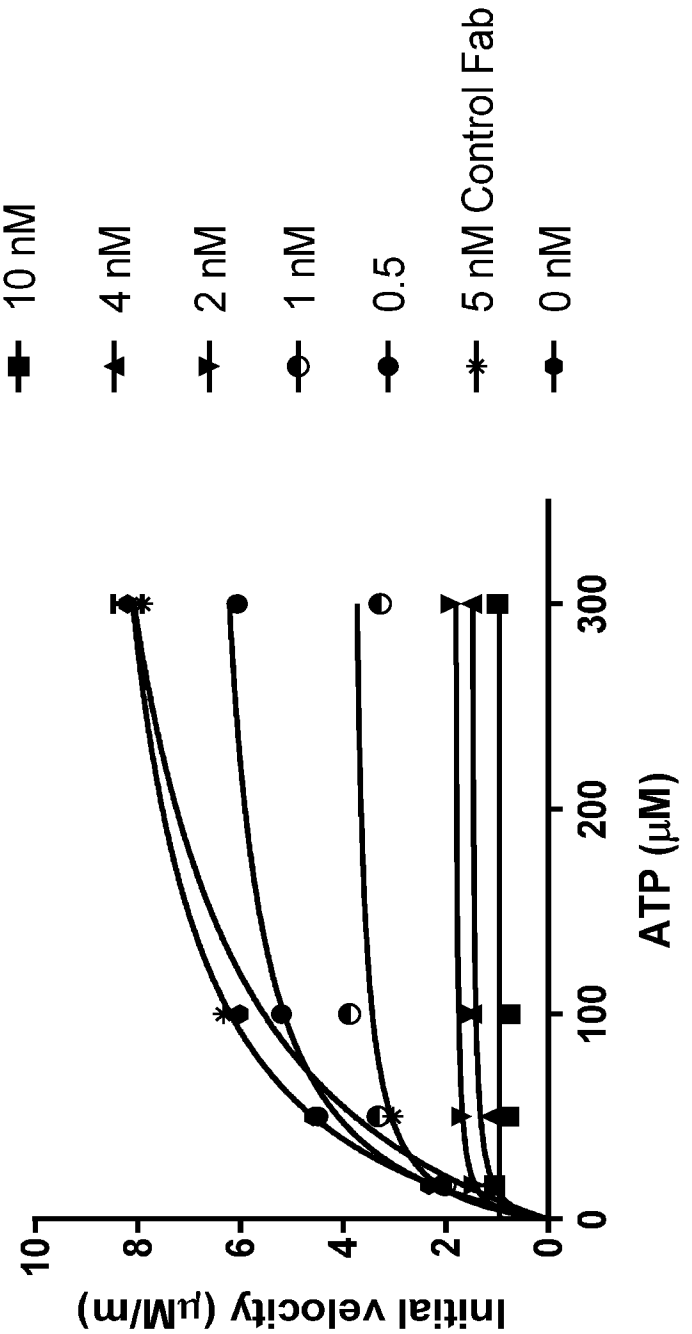

v_0 v
[29872], nM
1.0 nM Isotype Control
5.0 nM
1.0 nM
0.4 nM
0.2 nM
0 nM
Initial velocity (μM/m)
0
5
10
15
20
0
200
400
600
ATP (μM)

FIG. 16B


[29872 Fab]
10 nM
4 nM
2 nM
1 nM
0.5
5 nM Control Fab
0 nM
Initial velocity (μM/m)
0
2
4
6
8
10
0
100
200
300
ATP (μM)

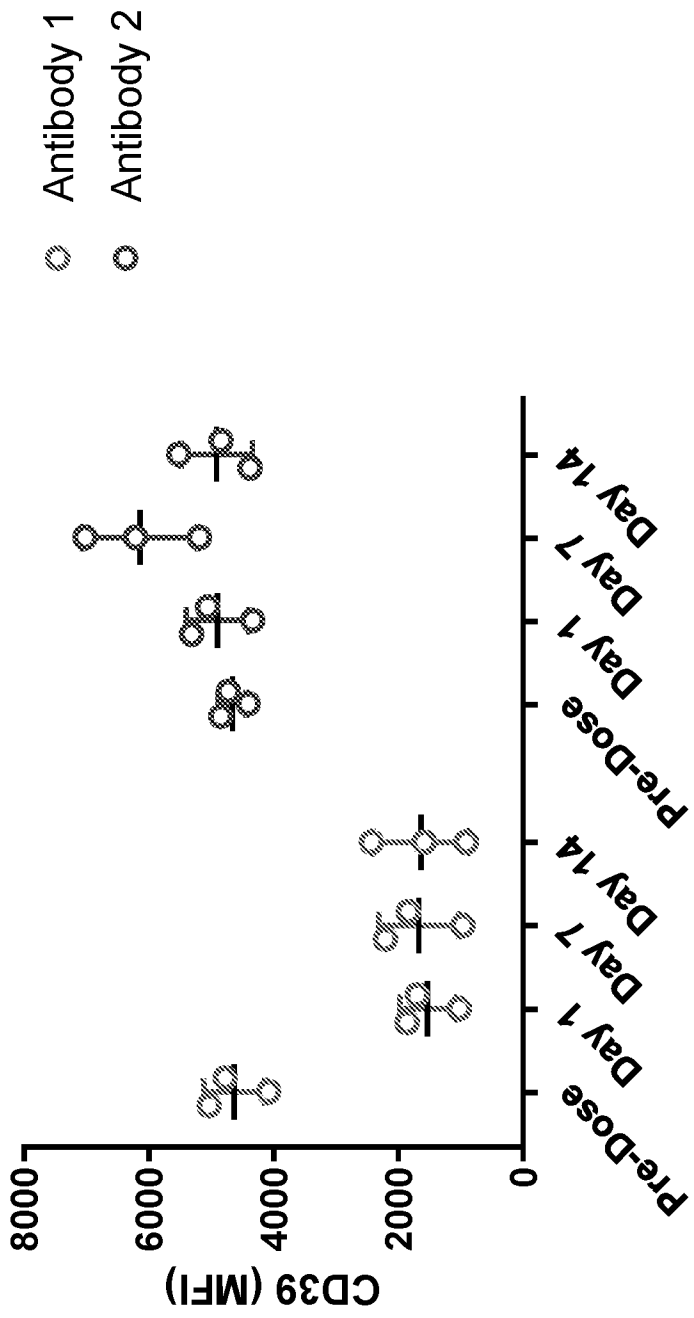

Antibody 1
Antibody 2
CD39 (MFI)
8000
6000
4000
2000
0
Pre-Dose
Day 1
Day 7
Day 14
Pre-Dose
Day 1
Day 7
Day 14

FIG. 17

FIG. 18

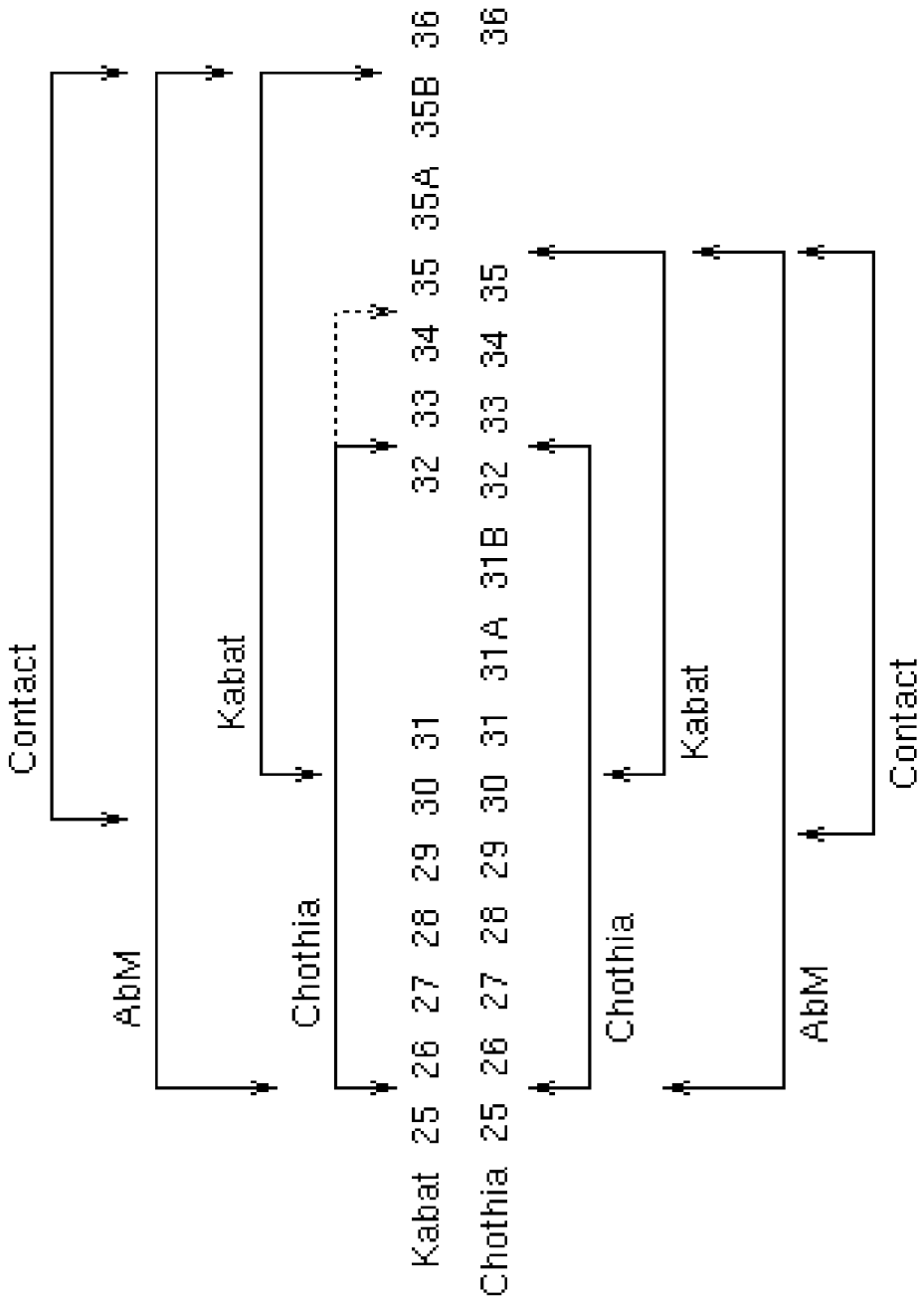
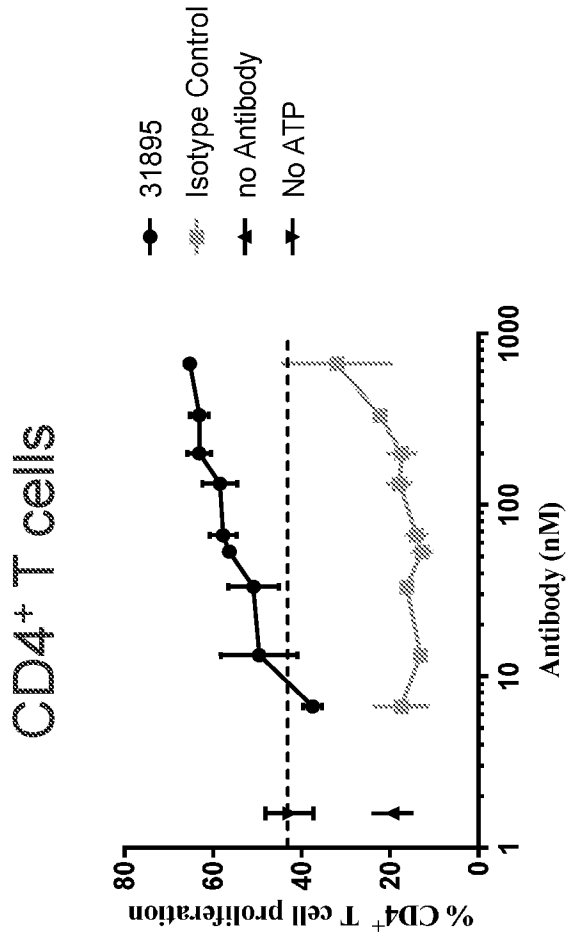

Kabat
Chothia
25
26
27
28
29
30
31
31A
31B
32
33
34
35
35A
35B
36
Contact
AbM
Chothia
Kabat
Contact
AbM
Chothia
Kabat

FIG. 19


CD4+ T cells
31895
Isotype Control
no Antibody
No ATP
% CD4+ T cell proliferation
0
20
40
60
80
1
10
100
1000
Antibody (nM)

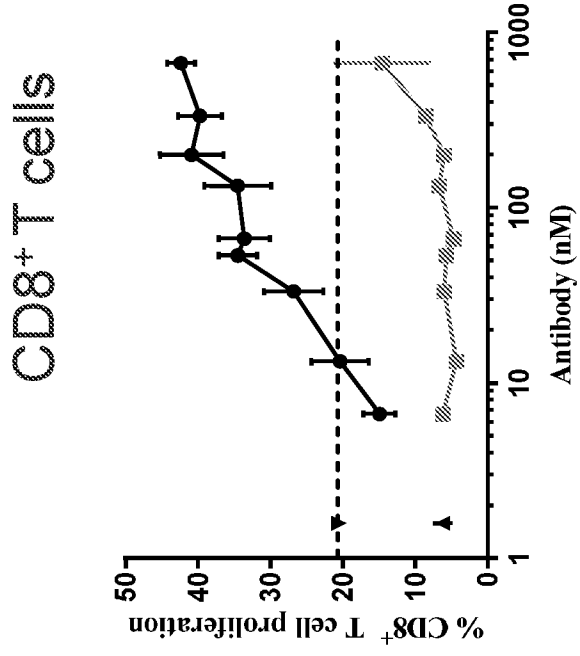

CD8+ T cells
% CD8+ T cell proliferation
0
10
20
30
40
50
1
10
100
1000
Antibody (nM)

FIG. 20

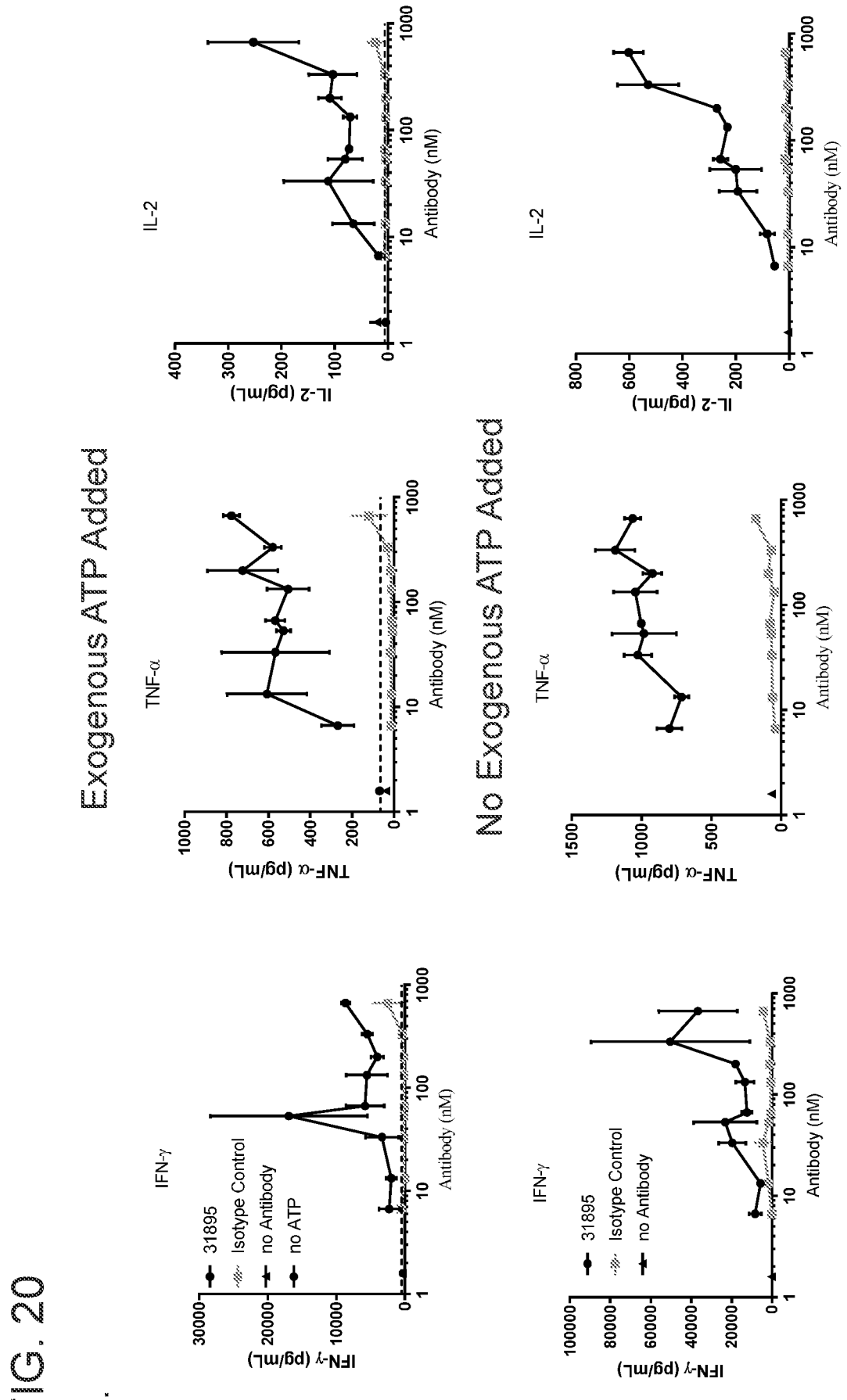
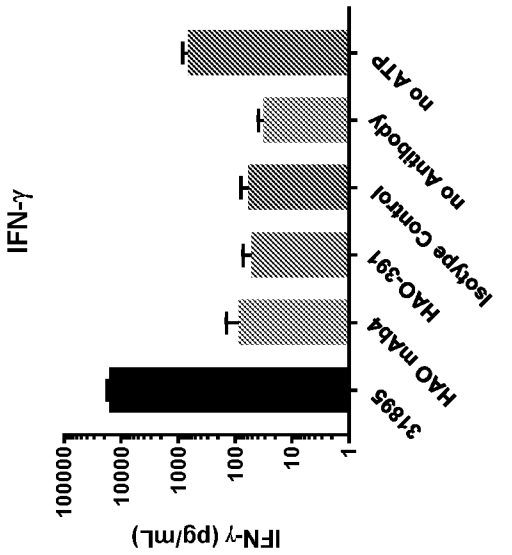
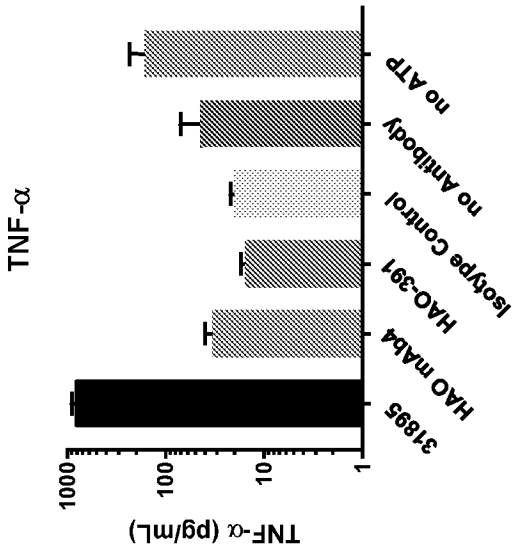
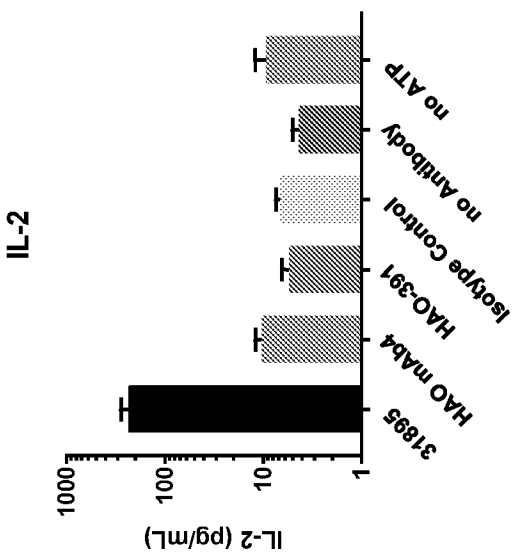

A.
Exogenous ATP Added
IFN-γ
TNF-α
IL-2
31895
Isotype Control
no Antibody
no ATP
IFN-γ (pg/mL)
TNF-α (pg/mL)
IL-2 (pg/mL)
Antibody (nM)
B.
No Exogenous ATP Added
IFN-γ
TNF-α
IL-2
31895
Isotype Control
no Antibody
IFN-γ (pg/mL)
TNF-α (pg/mL)
IL-2 (pg/mL)
Antibody (nM)

FIG. 21


IFN-γ
IFN-γ (pg/mL)
100000
10000
1000
100
10
1
3189S
HAO mAb4
HAO-391
Isotype Control
no Antibody
no ATP


TNF-α
TNF-α (pg/mL)
1000
100
10
1
3189S
HAO mAb4
HAO-391
Isotype Control
no Antibody
no ATP


IL-2
IL-2 (pg/mL)
1000
100
10
1
3189S
HAO mAb4
HAO-391
Isotype Control
no Antibody
no ATP

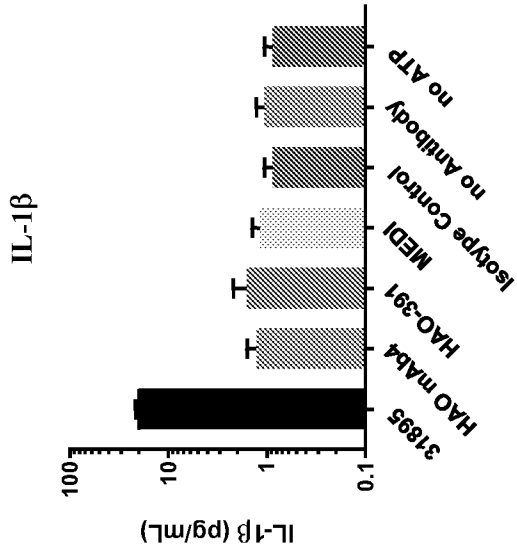
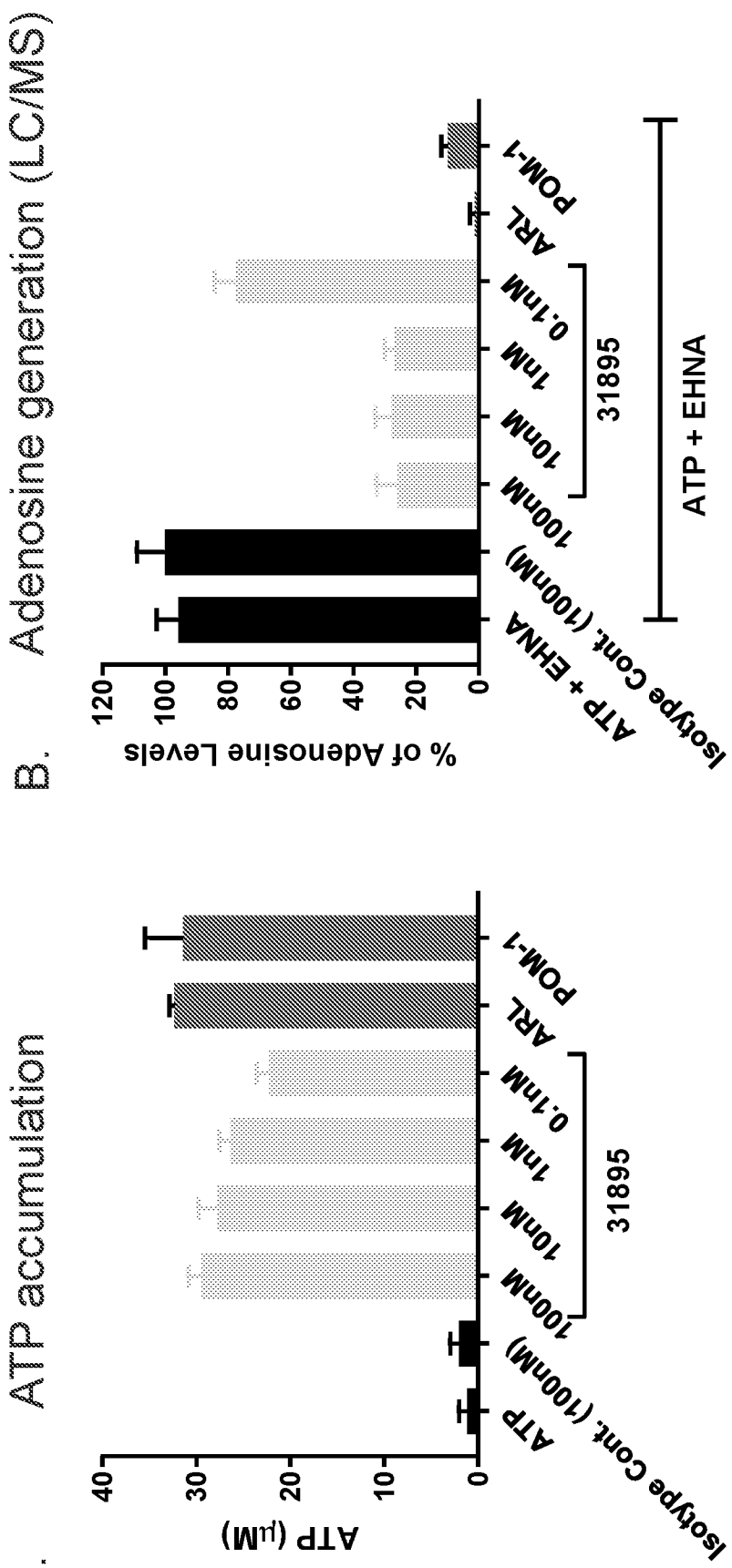

IL-1β
IL-1β (pg/mL)
100
10
1
0.1
3189S
HAO mAb4
HAO-391
MEDI
Isotype Control
no Antibody
no ATP

FIG. 22


A.
ATP accumulation
ATP (μM)
40
30
20
10
0
ATP
Isotype Cont. (100nM)
100nM
10nM
1nM
0.1nM
ARL
POM-1
31895
B.
Adenosine generation (LC/MS)
% of Adenosine Levels
120
100
80
60
40
20
0
ATP + EHNA
Isotype Cont. (100nM)
100nM
10nM
1nM
0.1nM
ARL
POM-1
31895
ATP + EHNA

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 18/44449

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - C07K 16/28, C07K 16/30, G01N 33/574 (2018.01)
CPC - C07K 16/2896, C07K 16/30, C07K 16/3061, C07K 16/40, G01N 33/57492, A61K 2039/505, C07K 2317/92

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History Document

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

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y -- A	WO 2016/073845 A1 (IGENICA BIOTHERAPEUTICS, INC.) 12 May 2016 (12.05.2016) Claim 1, Claim 7, para [0008], [0013], [0014], [00114], [00131], [00175], [00375], [00406], [00409], [00410], Table 10	1-5, 9, 10, 12/10, (16-18)/1 ---- 11, 12/11 ---- 13, 15, (16-18)/15, 48-52
X -- A	US 2011/0318339 A1 (SMIDER et al.) 29 December 2011 (29.12.2011) claim 136, para [0318], [0399], SEQ ID NO: 176	14, (16-18)/14, 53 ---- 13, 15, (16-18)/15, 48-52
Y	UniProt KB accession number P49961 "Ectonucleoside triphosphate diphosphohydrolase 1", 07 June 2017, [online]. [Retrieved 18 November 2018]. Retrieved from the internet <URL: https://www.uniprot.org/uniprot/P49961.txt?version=169 > whole doc.	11, 12/11
Y	WO 2017/089334 A1 (INNATE PHARMA) 01 June 2017 (01.06.2017) abstract, pg 64, ln 24-28	11, 12/11
A	US 2011/0020329 A1 (KING et al.) 27 January 2011 (27.01.2011) abstract, SEQ ID NO: 15	13, 15, (16-18)/15, 48-52
A	US 2017/0165366 A1 (POTENZA THERAPEUTICS, INC.) 15 June 2017 (15.06.2017) abstract, SEQ ID NO: 112	13, 15, (16-18)/15, 48-52
A	US 2011/0229476 A1 (LIU et al.) 22 September 2011 (22.09.2011) SEQ ID NO: 79	13, 15, (16-18)/15, 48-52

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

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 November 2018	04 DEC 2018
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (January 2015)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 18/44449

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

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

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

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

3. ☒ Claims Nos.: 6-8, 19, 45
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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

This International Searching Authority found multiple inventions in this international application, as follows:

- see extra sheet for Box No. III Observations where unity of invention is lacking -

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

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

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

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-5, 9-18, 48-53 limited to SEQ ID NOs: 1, 46, 82, 110, 125, 141, 179, 255, 256

Remark on Protest

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

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

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 18/44449

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

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

Group I+: Claims 1-5, 9-18, 48-53, drawn to an antigen binding protein that binds specifically to a human CD39 (hCD39). The composition will be searched to the extent that the anti-hCD39 antibody encompasses VHCDR-1, -2, -3 of SEQ ID NOs: 1, 46, 82, respectively; VLCDR-1, -2, -3 of SEQ ID NOs: 110, 125, 141, respectively; heavy chain SEQ ID NO: 255; light chain SEQ ID NO: 256; and a heavy chain constant region of SEQ ID NO: 179. It is believed that claims 1-5, 9-18, 48-53 encompass this first named invention, and thus these claims will be searched without fee to the extent that they encompass SEQ ID NOs: 1, 46, 82, 110, 125, 141, 179, 255, 256. Additional anti-hCD39 antibodies will be searched upon the payment of additional fees. Applicants must specify the claims that encompass any additionally elected anti-hCD39 antibodies. Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched. An exemplary election would be an anti-hCD39 antibody comprising VHCDR-1, -2, -3 of SEQ ID NOs: 2, 47, 83, respectively; VLCDR-1, -2, -3 of SEQ ID NOs: 111, 126, 142, respectively; heavy chain SEQ ID NO: 257; light chain SEQ ID NO: 258; and a heavy chain constant region of SEQ ID NO: 180 (Claims 1-5, 9-18, 48-53).

Group II: claims 20-44, 46-47, drawn to a method for the production of a recombinant protein, a method for the treatment of a subject suffering from a disorder, or a method of screening for a test compound.

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

No technical features are shared between the amino acid sequences of anti-hCD39 antibodies of Groups I+ and, accordingly, these groups lack unity a priori.
Additionally, even if Groups I+ were considered to share the technical features of an antigen binding protein that binds specifically to a human CD39 (hCD39); and the inventions of Groups I+ and II share the technical feature of claims 1 and 16; these shared technical features are previously disclosed by WO 2016/073845 A1 to Igenica Biotherapeutics, Inc. (hereinafter 'Igenica').

Igenica teaches (instant claim 1) an antigen binding protein that binds specifically to a human CD39 (hCD39) (Claim 1, An isolated antibody that binds to CD39.; para [00406], Affinity measurements of thirty-five purified anti-CD39 antibodies....association and dissociation of recombinant human CD39 (R&D Systems) was monitored.) and is capable of the following:
b) inhibiting conversion by CD39 of ATP to ADP (para [00409], Using a highly sensitive radioactive CD39-based assay, ATPase activity in cell suspension aliquots was measured by detecting 33Pi formed due to enzymatic cleavage of [gamma-33P]-ATP. Uncleaved [gamma-33P]-ATP was precipitated with charcoal suspension, and 33Pi was determined by liquid scintillation counting of supernatants. Table 10 "Inhibition of ATPase Activity in ARH-77 cells" shows antibody 9-8B inhibits ATPase activity 36.5%.);
f) inhibiting platelet aggregation (para [00410], Anti-CD39 antibodies were also tested for their ability to modulate (e.g., inhibit) ATPase activity of CD39 with a flow-based platelet aggregation assay.....ADP-mediated platelet aggregation was induced by addition of ATP to enzymatically-active recombinant human CD39. ADP-induced platelet aggregation was increased 1.6 fold compared with untreated cells, but significantly inhibited by 67% in the presence of 4mM 9-8B ($p<0.001$).).

Igenica teaches (instant claim 3) a pharmaceutical composition (para [0013], Also provided herein are pharmaceutical compositions comprising an anti-CD39 antibody.) comprising an effective amount of an antibody which binds to hCD39 (Claim 1, para [00406]) and has one of the following of characteristics:
a) blocks or decreases hydrolysis of ATP to ADP and/or ADP to AMP as determined by (i) a decreased phosphate release (Pi) (para [00409], Using a highly sensitive radioactive CD39-based assay, ATPase activity in cell suspension aliquots was measured by detecting 33Pi formed due to enzymatic cleavage of [gamma-33P]-ATP. Uncleaved [gamma-33P]-ATP was precipitated with charcoal suspension, and 33Pi was determined by liquid scintillation counting of supernatants. Table 10 "Inhibition of ATPase Activity in ARH-77 cells" shows antibody 9-8B inhibits ATPase activity 36.5%.).

Igenica teaches (instant claim 10) an antigen binding protein that competes or is capable of competing for binding to human CD39 with a reference antigen binding protein, wherein the reference antigen binding protein is the antigen binding protein of claim 1 (Claim 7, An isolated antibody that binds to a CD39 epitope, wherein the binding to the epitope competitively blocks the binding of the antibody of any one of claims 1 to 6.).

Igenica teaches (instant claim 11) an antigen binding protein that binds to or is capable of competing for binding to human CD39 with a reference antigen binding protein (Claim 7), wherein the reference antigen binding protein binds to an epitope on a human CD39 polypeptide (para [0010], a humanized monoclonal antibody, or antigen binding fragment thereof, that binds to CD39, including a CD39 polypeptide, a CD39 fragment, or a CD39 epitope.).

Igenica teaches (instant claim 14) an isolated antibody molecule capable of binding to human CD39 (hCD39) (Claim 1, para [00406]), comprising a heavy chain variable region (VH) and a light chain variable region (VL), VH and/or VL comprising a VHCDR1, a VHCDR2, a VHCDR3, a VLCDR1 , a VLCDR2, and a VLCDR3 (Claim 1, An isolated antibody that binds to CD39, wherein the antibody comprises: (a) a heavy chain variable (VH) region comprising a VH CDR1 , a VH CDR2, and a VH CDR3 amino acid sequence depicted in Tables 1 -4; and/or (b) a light chain variable (VL) region comprising a VL CDR1 , a VL CDR2, and a VL CDR3 amino acid sequence depicted in Tables 1 -4.).

Igenica teaches (instant claims 16-18) an isolated nucleic acid encoding an antigen binding protein (para [0014], The present disclosure also provides isolated nucleic acid molecules.); an expression vector, a prokaryotic or eukaryotic host cell comprising the vector (para [0014], Also provided herein are vectors and host cells comprising the nucleic acid molecules encoding an anti-CD39 antibody.).

As said technical features were known in the art at the time of the invention, these cannot be considered special technical features that would otherwise unify the groups.
Groups I+ and II therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.