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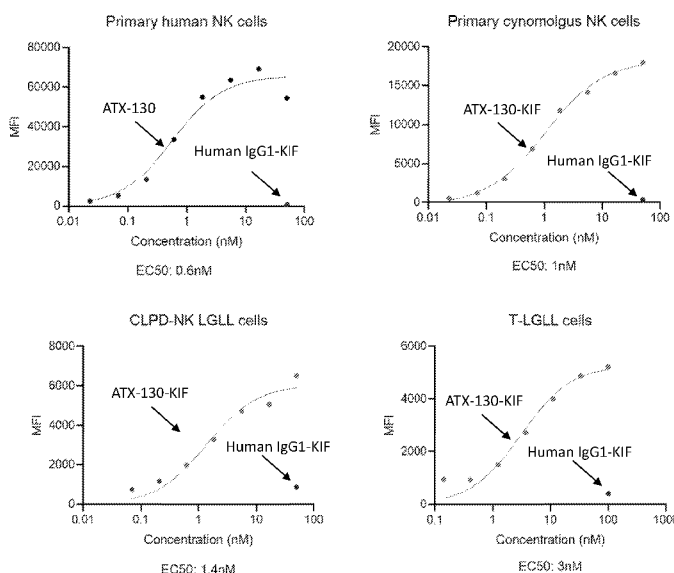


FIG. 12

(57) **Abstract:** The present disclosure relates to antibodies that bind to human CD94, as well as methods, uses, polynucleotides, vectors, host cells, and pharmaceutical compositions related thereto. In some embodiments, the antibodies are human or humanized antibodies that bind to human CD94 and do not block binding between CD94 and HLA-E. In some embodiments, the antibodies cross-react with cynomolgus CD94. In some embodiments, the antibodies do not promote internalization of surface-expressed CD94 to the extent of existing antibodies. In some embodiments, the antibodies promote ADCC targeting cells that express human CD94, e.g., on the cell surface.



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ANTI-CD94 ANTIBODIES AND METHODS OF USE THEREOF**CROSS-REFERENCE TO RELATED APPLICATIONS**

[0001] This application claims priority to U.S. Provisional Application Serial Nos. 63/085,932, filed September 30, 2020, and 63/088,926, filed October 7, 2020, the disclosures of each of which are incorporated herein by reference in their entirety.

SUBMISSION OF SEQUENCE LISTING ON ASCII TEXT FILE

[0002] The content of the following submission on ASCII text file is incorporated herein by reference in its entirety: a computer readable form (CRF) of the Sequence Listing (file name: 186542000340SEQLIST.TXT, date recorded: September 28, 2021, size: 52,165 bytes).

FIELD OF THE INVENTION

[0003] The present disclosure relates to antibodies that bind to CD94 and to uses thereof for treating diseases and disorders associated with NK cells and/or T cells.

BACKGROUND OF THE INVENTION

[0004] Natural Killer (NK)/T cell lymphomas and leukemias are characterized by a clonal expansion of NK and/or CD8+ and CD4+ T cells. NK/T cell lymphomas represent a small percentage of non-Hodgkin's lymphomas (NHL), and have a 5-year survival rate of less than 50% (Kwong, 2012). There are approximately 4,000-7,000 new patients each year in the United States alone, with higher frequencies in Asian populations (Bajaj, A. (2019) *Int. J. Hematol. Ther* 5:1-7). NK/T cell lymphoma can occur at any age, and more than half of NHL patients are 65 or older (Bajaj, 2019). There are also NK and T cell-based leukemias such as LGL and aggressive NK leukemia. Other examples of diseases and disorders in which NK cells play a role include LGL leukemia (*e.g.*, T-cell LGL leukemia), chronic lymphoproliferative disorders of NK cells (CLPD-NK, formerly NK-LGL), Rheumatoid arthritis, Felty's syndrome, aggressive NK leukemia (*e.g.*, aggressive natural killer leukemia (ANKL) and extranodal NK/T cell nasal type (ENKT)), IBM, and IBD.

[0005] There are thirteen distinct diseases involving NK/T cell lymphoma: extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL (not otherwise specified), angioimmunoblastic TCL, adult TCL, monomorphic epitheliotropic intestinal TCL, epidermotropic CD8+ cutaneous TCL, primary cutaneous gamma/delta TCL, and subcutaneous panniculitis TCL (Bajaj, 2019). The major subtypes of NK/T cell lymphoma, which are mostly cytotoxic cell-driven (NK/CD8+ T cells), include extranodal NK/T cell lymphoma, hepatosplenic TCL, enteropathy-associated TCL, monomorphic epitheliotropic intestinal TCL, epidermotropic CD8+ cutaneous TCL, primary cutaneous gamma/delta TCL, and subcutaneous panniculitis TCL. NK/T cell

lymphoma affects various organs, such as skin, gastrointestinal (GI) tract, liver, spleen, and bone marrow. Symptoms include enlarged lymph nodes of the neck. Most NK/T cell lymphoma subtypes are driven by Epstein bar viral infections.

[0006] Current treatments include chemotherapy (cyclophosphamide, doxorubicin, vincristine, prednisone), followed by stem cell transplant; but progression-free survival remains at 40-50%. Current treatments under investigation include Alemtuzumab, Carfilzomib (proteasome inhibitor), Romidepsin (HDAC inhibitor), Bevacizumab, Brentuximab vedotin (antibody-drug conjugate), Bortezomib (proteasome inhibitor), Belinostat (HDAC inhibitor), Pralatrexate, Vorinostat (HDAC inhibitor), and Avelumab. Despite the variety of drugs in development, many of them are often used off-label and have yielded mixed results.

[0007] There are currently no effective therapies for the treatment of NK/T cell lymphoma, and no therapy that selectively targets NK/T cell lymphoma has been developed. Current therapies for NK/T cell lymphoma may have off-target effects and are not entirely effective. The high disease mortality combined with the lack of effective treatments emphasize the need for therapeutic advancements in NK/T cell lymphoma.

[0008] Accordingly, there is a need in the art to develop safe and effective therapies for treating diseases mediated by NK cells and/or T cells that express CD94, such as NK/T cell lymphoma.

SUMMARY OF THE DISCLOSURE

[0009] To meet these and other needs, the present disclosure provides, *inter alia*, antibodies that bind specifically to CD94 (*e.g.*, human CD94), methods of treating diseases or injuries associated with NK cells and/or T cells that express CD94, *e.g.*, NK/T cell lymphomas and leukemias (*e.g.*, LGL leukemia), and methods of depleting or reducing the numbers of NK cells and/or T cells that express CD94 in a subject upon administration of an antibody that specifically binds to CD94. These antibodies of the present disclosure may have one or more of the following characteristics: high affinity binding to human CD94 (*e.g.*, cells expressing human CD94 on their surface), cross-reactivity to cynomolgus monkey CD94 (useful for preclinical studies), ability to bind human CD94 without blocking its interaction with HLA-E, minimal internalization following binding to CD94, and/or induction of ADCC against cells expressing CD94, such as leukemic cells. These characteristics are thought to be advantageous, *e.g.*, for testing, development, and use in treating NK/T cell-based diseases, such as lymphomas and leukemias. For example, without wishing to be bound to theory, it is thought that targeting CD94 on NK cells for ADCC may induce cancer cells (*e.g.*, LGL leukemic or lymphoma cells) to kill other cancer cells.

[0010] In some aspects, provided herein are human or humanized antibodies that bind to human CD94, wherein binding of the antibody to human CD94 does not block binding between human CD94 and human HLA-E. In some embodiments, the antibody binds human CD94 expressed on the surface of a cell (*e.g.*, a human natural killer (NK) cell). In some embodiments, the antibody binds an extracellular domain of human CD94. In some embodiments, the antibody binds cynomolgus CD94 expressed on the surface of a cell. In some embodiments, binding of the antibody to cells expressing human CD94 blocks less than

20% of HLA-E binding to the human CD94. In other aspects, provided herein are human or humanized antibodies that bind to human CD94 and cynomolgus CD94 (*e.g.*, that are capable of binding to human CD94 and cynomolgus CD94 separately). In some embodiments, the antibody binds human CD94 expressed on the surface of a cell (*e.g.*, a human natural killer (NK) cell). In some embodiments, the antibody binds cynomolgus CD94 expressed on the surface of a cell (*e.g.*, a cynomolgus NK cell, or a cell such as a human cell that overexpresses cynomolgus CD94). In some embodiments, binding of the antibody to human CD94 does not block binding between human CD94 and human HLA-E. In some embodiments, incubating the antibody with a cell expressing human CD94 on its surface for 24 hours at 37°C results in a decrease in surface antibody staining of less than 50% due to internalization.

[0011] In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:6. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6. In some embodiments, the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:19, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:20. In some embodiments, the VH domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:19, and the VL domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:20. In some embodiments, the VH domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:19, and the VL domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:20. In some embodiments, the VH domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:19, and the VL domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:20. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:19, and the VL domain comprises the

amino acid sequence of SEQ ID NO:20. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:7, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:8, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:9; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:10, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:11, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:12. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:7, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:8, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:9; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:10, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:11, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:12. In some embodiments, the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:21, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:22. In some embodiments, the VH domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:21, and the VL domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:22. In some embodiments, the VH domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:21, and the VL domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:22. In some embodiments, the VH domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:21, and the VL domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:22. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:21, and the VL domain comprises the amino acid sequence of SEQ ID NO:22. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID

NO:17, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:18. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18. In some embodiments, the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:23, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:24. In some embodiments, the VH domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:23, and the VL domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:24. In some embodiments, the VH domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:23, and the VL domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:24. In some embodiments, the VH domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:23, and the VL domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:24. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:23, and the VL domain comprises the amino acid sequence of SEQ ID NO:24. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein: (a) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:30, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:31, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:32; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:35; (b) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:37, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:38; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID

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sequence of SEQ ID NO:58, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:59; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:60, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:61; (h) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:83, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:84, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:85; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:86, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:61; or (i) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:62; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:63, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:64. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein: (a) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:88, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:89; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:35; (b) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:92, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:93; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence

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amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:101, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:102, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:103; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:104, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:61; (h) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:105, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:106, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:107; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:108, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:61; or (i) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:109, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:110, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:111; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:112, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:113, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:64. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein: (a) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:30, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:31, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:32; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35; (b) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:37, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:38; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35; (c) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:39, and a CDR-H3 comprising the amino acid

sequence of SEQ ID NO:40; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35; (d) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:41, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:42, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:43; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:44, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:46; (e) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:49; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:51, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:52; (f) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:54, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:55; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:56; (g) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:57, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:58, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:59; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:60, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61; (h) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:83, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:84, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:85; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:86, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61; or (i) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:62; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:63, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:64. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein: (a) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:88, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:89; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35; (b) the VH domain comprises a CDR-

H1 comprising the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:92, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:93; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:350; (c) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:92, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:94; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35; (d) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:95, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:96, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:97; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:98, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:99, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:100; (e) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:109, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:110, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:114; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:115, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:99, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:52; (f) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:116, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:117, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:118; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:115, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:99, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:56; (g) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:101, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:102, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:103; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:104, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61; (h) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:105, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:106, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:107; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:108, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61; or (i) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:109, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:110, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:111; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:112, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:113, and a CDR-L3 comprising

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sequence identity to the amino acid sequence of SEQ ID NO:72; (e) the VH domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:73, and the VL domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:74; (f) the VH domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:75, and the VL domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:76; (g) the VH domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:77, and the VL domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:78; (h) the VH domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:79, and the VL domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:80; or (i) the VH domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:81, and the VL domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:82. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein: (a) the VH domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:65, and the VL domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:66; (b) the VH domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:67, and the VL domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:68; (c) the VH domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:69, and the VL domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:70; (d) the VH domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:71, and the VL domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:72; (e) the VH domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:73, and the VL domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:74; (f) the VH domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:75, and the VL domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:76; (g) the VH domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:77, and the VL domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:78; (h) the VH domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:79, and the VL domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:80; or (i) the VH domain comprises an amino acid

sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:81, and the VL domain comprises an amino acid sequence with at least 95% sequence identity to the amino acid sequence of SEQ ID NO:82. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein: (a) the VH domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:65, and the VL domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:66; (b) the VH domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:67, and the VL domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:68; (c) the VH domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:69, and the VL domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:70; (d) the VH domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:71, and the VL domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:72; (e) the VH domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:73, and the VL domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:74; (f) the VH domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:75, and the VL domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:76; (g) the VH domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:77, and the VL domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:78; (h) the VH domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:79, and the VL domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:80; or (i) the VH domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:81, and the VL domain comprises an amino acid sequence with at least 99% sequence identity to the amino acid sequence of SEQ ID NO:82. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein: (a) the VH domain comprises the amino acid sequence of SEQ ID NO:65, and the VL domain comprises the amino acid sequence of SEQ ID NO:66; (b) the VH domain comprises the amino acid sequence of SEQ ID NO:67, and the VL domain comprises the amino acid sequence of SEQ ID NO:68; (c) the VH domain comprises the amino acid sequence of SEQ ID NO:69, and the VL domain comprises the amino acid sequence of SEQ ID NO:70; (d) the VH domain comprises the amino acid sequence of SEQ ID NO:71, and the VL domain comprises the amino acid sequence of SEQ ID NO:72; (e) the VH domain comprises the amino acid sequence of SEQ ID NO:73, and the VL domain comprises the amino acid sequence of SEQ ID NO:74; (f) the VH domain comprises the amino acid sequence of SEQ ID NO:75, and the VL domain comprises

the amino acid sequence of SEQ ID NO:76; (g) the VH domain comprises the amino acid sequence of SEQ ID NO:77, and the VL domain comprises the amino acid sequence of SEQ ID NO:78; (h) the VH domain comprises the amino acid sequence of SEQ ID NO:79, and the VL domain comprises the amino acid sequence of SEQ ID NO:80; or (i) the VH domain comprises the amino acid sequence of SEQ ID NO:81, and the VL domain comprises the amino acid sequence of SEQ ID NO:82.

[0012] In some aspects, provided herein are antibodies that bind to human CD94. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:6. In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6. In some embodiments, the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:19, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:20. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:19, and the VL domain comprises the amino acid sequence of SEQ ID NO:20. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:7, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:8, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:9; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:10, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:11, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:12. In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:7, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:8, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:9; and wherein the VL domain comprises a CDR-

L1 comprising the amino acid sequence of SEQ ID NO:10, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:11, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:12. In some embodiments, the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:21, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:22. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:21, and the VL domain comprises the amino acid sequence of SEQ ID NO:22. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:18. In some embodiments, the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18. In some embodiments, the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:23, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:24. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO:23, and the VL domain comprises the amino acid sequence of SEQ ID NO:24. In some embodiments, the antibody is a human antibody.

[0013] In some aspects, provided herein are antibodies that bind to human CD94. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein: (a) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:30, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:31, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:32; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the

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sequence identity to the amino acid sequence of SEQ ID NO:55; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:56; (g) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:57, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:58, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:59; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:60, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:61; (h) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:83, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:84, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:85; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:86, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:61; or (i) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:62; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:63, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:64. In some embodiments, (a) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:30, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:31, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:32; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35; (b) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:37, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:38; and

wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35; (c) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:39, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:40; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35; (d) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:41, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:42, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:43; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:44, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:46; (e) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:49; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:51, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:52; (f) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:54, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:55; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:56; (g) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:57, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:58, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:59; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:60, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61; (h) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:83, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:84, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:85; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:86, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61; or (i) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:62; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:63, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:64. In some embodiments, the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein: (a) the VH domain comprises a CDR-H1 comprising an amino acid

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SEQ ID NO:64. In some embodiments, (a) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:88, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:89; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35; (b) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:92, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:93; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:350; (c) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:92, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:94; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35; (d) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:95, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:96, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:97; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:98, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:99, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:100; (e) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:109, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:110, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:114; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:115, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:99, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:52; (f) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:116, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:117, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:118; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:115, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:99, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:56; (g) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:101, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:102, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:103; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:104, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61; (h) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:105, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:106, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:107; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:108, a CDR-L2 comprising the amino acid

sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61; or (i) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:109, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:110, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:111; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:112, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:113, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:64. In some embodiments, (a) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:65, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:66; (b) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:67, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:68; (c) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:69, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:70; (d) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:71, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:72; (e) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:73, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:74; (f) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:75, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:76; (g) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:77, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:78; (h) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:79, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:80; or (i) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:81, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:82. In some embodiments, (a) the VH domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:65, and the VL domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:66; (b) the VH domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:67, and the VL domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:68; (c) the VH domain comprises an amino acid sequence with at least 90% sequence identity to the amino acid sequence of SEQ ID NO:69, and the VL domain

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comprises the amino acid sequence of SEQ ID NO:76; (g) the VH domain comprises the amino acid sequence of SEQ ID NO:77, and the VL domain comprises the amino acid sequence of SEQ ID NO:78; (h) the VH domain comprises the amino acid sequence of SEQ ID NO:79, and the VL domain comprises the amino acid sequence of SEQ ID NO:80; or (i) the VH domain comprises the amino acid sequence of SEQ ID NO:81, and the VL domain comprises the amino acid sequence of SEQ ID NO:82.

[0014] In further aspects, provided herein are antibodies that bind the same epitope as an antibody according to any one of the above embodiments. In some embodiments, the antibodies of the present disclosure bind the same epitope as a reference antibody. In some embodiments, the reference antibody comprises a VH domain comprising a CDR-H1 comprising the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and a VL domain comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6. In some embodiments, the reference antibody comprises a VH domain comprising a CDR-H1 comprising the amino acid sequence of SEQ ID NO:7, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:8, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:9; and a VL domain comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO:10, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:11, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:12. In some embodiments, the reference antibody comprises a VH domain comprising a CDR-H1 comprising the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15; and a VL domain comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18. In some embodiments, the reference antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein: (a) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:30, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:31, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:32; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35; (b) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:37, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:38; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35; (c) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:39, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:40; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid

sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35; (d) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:41, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:42, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:43; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:44, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:46; (e) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:49; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:51, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:52; (f) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:54, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:55; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:56; (g) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:57, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:58, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:59; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:60, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61; (h) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:83, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:84, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:85; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:86, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61; or (i) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:62; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:63, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:64.

[0015] In further aspects, provided herein are antibodies that compete with an antibody according to any one of the above embodiments for binding to human CD94. In some embodiments, the antibodies of the present disclosure compete for binding to human CD94 with a reference antibody. In some embodiments, the reference antibody comprises a VH domain comprising a CDR-H1 comprising the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and a VL domain comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6. In some

embodiments, the reference antibody comprises a VH domain comprising a CDR-H1 comprising the amino acid sequence of SEQ ID NO:7, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:8, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:9; and a VL domain comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO:10, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:11, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:12. In some embodiments, the reference antibody comprises a VH domain comprising a CDR-H1 comprising the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15; and a VL domain comprising a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18. In some embodiments, the reference antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein: (a) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:30, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:31, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:32; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35; (b) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:37, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:38; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35; (c) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:39, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:40; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35; (d) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:41, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:42, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:43; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:44, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:46; (e) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:49; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:51, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:52; (f) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:54, and a CDR-H3 comprising the amino acid

sequence of SEQ ID NO:55; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:56; (g) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:57, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:58, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:59; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:60, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61; (h) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:83, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:84, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:85; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:86, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61; or (i) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:62; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:63, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:64.

[0016] In some embodiments according to any of the embodiments described herein, the antibody is an antigen-binding antibody fragment or single chain antibody. In some embodiments, the antibody further comprises an Fc region, *e.g.*, a human IgG1 Fc region. In some embodiments, the antibody comprises a human Fc region that is non-fucosylated. In some embodiments, the antibody is produced in a cell line (*e.g.*, a CHO cell line) deficient in an alpha-1,6-fucosyltransferase gene, such as FUT8. In some embodiments, the antibody binds to a human cellular Fc gamma receptor IIIA to a greater extent than an antibody comprising a wild type human IgG1 Fc region. In some embodiments, the antibody is capable of inducing antibody-dependent cellular cytotoxicity (ADCC) against a cell expressing human CD94 on its surface.

[0017] In further aspects, provided herein are polynucleotide(s) encoding the antibody according to any one of the above embodiments. Further provided herein are vectors (*e.g.*, expression vectors) comprising the polynucleotide(s) according to any one of the above embodiments. Further provided herein are host cells (*e.g.*, isolated host cells or cell lines) comprising the polynucleotide(s) or vectors according to any one of the above embodiments. Further provided herein are methods for producing an antibody, comprising culturing the host cell according to any one of the above embodiments under conditions suitable for production of the antibody. In some embodiments, the methods further comprise recovering the antibody from the host cell.

[0018] Further provided herein are compositions (*e.g.*, pharmaceutical compositions) comprising the antibody according to any one of the above embodiments and a pharmaceutically acceptable carrier.

[0019] In further aspects, provided herein are methods for treating a disease or disorder in a subject, comprising administering to the subject an effective amount of the antibody or composition according to any one of the above embodiments. In some embodiments, administration of the antibody results in a reduction in the number of peripheral blood LGL or NK cells in the subject. In some embodiments, the disease or disorder is Felty's syndrome, and wherein administration of the antibody to the subject results in a reduction of one or more Felty's syndrome symptoms in the subject. In some embodiments, the disease or disorder is inclusion body myositis, and wherein administration of the antibody to the subject results in a reduction of one or more inclusion body myositis symptoms in the subject. In some embodiments, the disease or disorder is aggressive NK leukemia, and wherein administration of the antibody to the subject results in a reduction of one or more aggressive NK leukemia symptoms in the subject. In some embodiments, the disease or disorder is rheumatoid arthritis, and wherein administration of the antibody to the subject results in a reduction of one or more rheumatoid arthritis symptoms in the subject. In some embodiments, the disease or disorder is LGL leukemia, and wherein administration of the antibody to the subject results in a reduction of one or more LGL leukemia symptoms in the subject. In some embodiments, the disease or disorder is CLPD-NK, and wherein administration of the antibody to the subject results in a reduction of one or more CLPD-NK symptoms in the subject. In some embodiments, the disease or disorder is natural killer (NK) cell or T-cell lymphoma, and wherein administration of the antibody to the subject results in a reduction of one or more lymphoma symptoms in the subject. In some embodiments, the NK cell or T-cell lymphoma is extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL, angioimmunoblastic TCL, adult TCL, monomorphic epitheliotropic intestinal TCL, epidermotropic CD8+ cutaneous TCL, primary cutaneous gamma/delta TCL, or subcutaneous panniculitis TCL. In some embodiments, the NK cell or T-cell lymphoma is extranodal NK/T cell lymphoma, hepatosplenic TCL, or enteropathy-associated TCL. In some embodiments, the disease or disorder is microscopic colitis, and wherein administration of the antibody to the subject results in a reduction of one or more microscopic colitis symptoms in the subject.

[0020] In further aspects, provided herein are methods for reducing the number of peripheral blood LGL and/or NK cells in a subject, comprising administering to the subject an effective amount of the antibody or composition according to any one of the above embodiments. In further aspects, provided herein are methods for inducing ADCC activity in a subject comprising administering to the subject an effective amount of the antibody or composition according to any one of the above embodiments. In further aspects, provided herein are methods for treating CLPD-NK in a human subject in need thereof comprising administering to the subject an effective amount of the antibody or composition according to any one of the above embodiments. In some embodiments, administration of the antibody results in an improvement of one or more CLPD-NK symptoms in the subject.

[0021] In further aspects, provided herein are methods of treating natural killer (NK) cell or T-cell lymphoma, comprising administering to a subject in need thereof an effective amount of the antibody or

composition according to any one of the above embodiments. In some embodiments, the antibody does not bind to the same epitope on human CD94 as anti-CD94 antibody clones HP-3D9, HP-3B1, DX22, 131412, or 12K45. In some embodiments, the antibody binds to human CD94 with a greater affinity than anti-CD94 antibody clones HP-3D9, HP-3B1, DX22, 131412, and 12K45. In some embodiments, the NK cell or T-cell lymphoma is extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL, angioimmunoblastic TCL, or adult TCL. In some embodiments, the NK cell or T-cell lymphoma is extranodal NK/T cell lymphoma, hepatosplenic TCL, or enteropathy-associated TCL.

[0022] In further aspects, provided herein are methods of enhancing chimeric antigen receptor T cell (CAR-T) therapy in a human subject in need thereof, comprising administering to the subject an effective amount of the antibody or composition according to any one of the above embodiments prior to administration of a CAR-T treatment to the subject. In some embodiments, administration of the antibody or composition results in depletion of NK cells in the subject prior to administration of the CAR-T treatment.

[0023] In further aspects, provided herein are methods of depleting CD8+ CD94+ T cells in a human subject in need thereof, comprising administering to the subject an effective amount of the antibody or composition according to any one of the above embodiments. In some embodiments, administration of the antibody or composition results in depletion of CD8+ CD94+ T cells in the subject.

[0024] In some embodiments according to any of the embodiments described herein, the methods further comprise administering an IL-2 polypeptide to the subject.

[0025] In some embodiments according to any of the embodiments described herein, the subject is a human.

[0026] In further aspects, provided herein are the antibodies or compositions according to any one of the above embodiments for use in: treating a disease or disorder in a subject, reducing the number of peripheral blood LGL and/or NK cells in a subject, treating CLPD-NK in a human subject in need thereof, treating natural killer (NK) cell or T-cell lymphoma, treating microscopic colitis in a subject, or enhancing CAR-T therapy in a subject in need thereof. In some embodiments, the NK cell or T-cell lymphoma is extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL, angioimmunoblastic TCL, adult TCL, monomorphic epitheliotropic intestinal TCL, epidermotropic CD8+ cutaneous TCL, primary cutaneous gamma/delta TCL, or subcutaneous panniculitis TCL. In some embodiments, the NK cell or T-cell lymphoma is extranodal NK/T cell lymphoma, hepatosplenic TCL, or enteropathy-associated TCL.

[0027] In further aspects, provided herein is the use of the antibodies or compositions according to any one of the above embodiments for manufacture of a medicament, *e.g.*, for use in: treating a disease or disorder in a subject, reducing the number of peripheral blood LGL and/or NK cells in a subject, treating

CLPD-NK in a human subject in need thereof, treating natural killer (NK) cell or T-cell lymphoma, treating microscopic colitis in a subject, or enhancing CAR-T therapy in a subject in need thereof. In some embodiments, the NK cell or T-cell lymphoma is extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL, angioimmunoblastic TCL, or adult TCL. In some embodiments, the NK cell or T-cell lymphoma is extranodal NK/T cell lymphoma, hepatosplenic TCL, or enteropathy-associated TCL.

[0028] In further aspects, provided herein are kits or articles of manufacture comprising the antibodies or compositions according to any one of the above embodiments. In some embodiments, the kits further comprise instructions for using the kits, *e.g.*, in treating a disease or disorder in a subject, reducing the number of peripheral blood LGL and/or NK cells in a subject, treating CLPD-NK in a human subject in need thereof, treating natural killer (NK) cell or T-cell lymphoma, treating microscopic colitis in a subject, or enhancing CAR-T therapy in a subject in need thereof. In some embodiments, the NK cell or T-cell lymphoma is extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL, angioimmunoblastic TCL, adult TCL, monomorphic epitheliotropic intestinal TCL, epidermotropic CD8+ cutaneous TCL, primary cutaneous gamma/delta TCL, or subcutaneous panniculitis TCL. In some embodiments, the NK cell or T-cell lymphoma is extranodal NK/T cell lymphoma, hepatosplenic TCL, or enteropathy-associated TCL.

[0029] In some embodiments, which may be combined with any of the preceding embodiments, an antibody of the disclosure comprises six CDRs from a single antibody listed in Table 1 (*e.g.*, antibody 18H3, 1M4, 1E4, ATX-122, ATX-123, ATX-124, ATX-125, ATX-126, ATX-127, ATX-128, ATX-129, or ATX-130). In some embodiments, which may be combined with any of the preceding embodiments, an antibody of the disclosure comprises a VH and VL domain from a single antibody listed in Table 2 (*e.g.*, antibody 18H3, 1M4, 1E4, ATX-122, ATX-123, ATX-124, ATX-125, ATX-126, ATX-127, ATX-128, ATX-129, or ATX-130).

[0030] All references cited herein, including patent applications and publications, are incorporated by reference in their entirety.

BRIEF DESCRIPTION OF THE DRAWINGS

[0031] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0032] **FIG. 1** shows the affinity of anti-CD94 antibody 18H3 for human primary natural killer (NK) cells as measured by flow cytometry. Peripheral blood mononuclear cells (PBMCs) of healthy donor HD-40 were used for antibody staining. 18H3 antibody was titrated from 100nM to 0.046nM in 1:3 dilutions and incubated with PBMCs. CD3 and CD56 antibodies were used to identify NK cells on the flow scatter.

18H3 antibody binding on CD3+ and CD56 bright NK cells was used to assess affinity of 18H3. Titration curves and EC50 were generated using Graphpad Prism. 18H3 bound to CD3+CD56 bright NK cells with an affinity of 2.6nM. Human IgG1 isotype control with secondary antibody (hIgG1) and goat (Fab)2 fragment anti-human Fcy-specific secondary antibody AF647 only (2ndary Ab) were used as controls.

[0033] FIG. 2 shows the binding of anti-CD94 antibodies to human primary NK cells as measured by flow cytometry. Anti-CD94 hybridoma supernatants were screened on human primary NK cells by flow cytometry. HP-3D9 is a commercial anti-CD94 antibody that was used as a positive control. Mouse IgG1, IgG2a, IgG2b and IgG3 were used as negative controls. Anti-CD94 antibodies 18H3, 1M4 and 1E4 bound to CD94 expressed on human primary NK cells.

[0034] FIGS. 3A-3B show the cross-reactivity of anti-CD94 antibodies to cynomolgus CD94. FIG. 3A shows the cross-reactivity of hybridoma antibodies to cynomolgus CD94. Anti-CD94 hybridoma supernatants were screened on cynomolgus CD94-expressing HEK293 cells by flow cytometry for cross-reactivity to cynomolgus CD94. HP-3D9 is a commercial anti-CD94 antibody that was used as a negative control. Mouse IgG1, IgG2a, IgG2b and IgG3 were used as negative controls. 18H3, 1M4 and 1E4 cross-reacted with cynomolgus CD94, while 20F2 is an example of another CD94 antibody clone that reacts with human CD94 but did not cross-react with cynomolgus CD94. FIG. 3B shows the cross-reactivity of commercial antibodies to cynomolgus CD94. Commercially available anti-CD94 antibodies were used to test cynomolgus cross-reactivity. 18H3 was used as a positive control. The MFI of each antibody was normalized to the MFI of its respective isotype. HP-3B1, 131412, 12K45, DX22 and HP-3D9 did not cross-react with cynomolgus CD94, unlike 18H3.

[0035] FIG. 4 shows the results of HLA-E tetramer blocking assays performed with anti-CD94 and commercially available anti-CD94 antibodies using flow cytometry. Healthy donor PBMCs were incubated with anti-CD94 antibodies. PE labeled HLA-E tetramer was then incubated with the cell and antibody mixture, and detected using flow cytometry. For HP-3B1, 131412, 12K45, DX22, 1M4 and 1E4, 2.5 µl of HLA-E tetramer reagent was used, while 5 µl was used for 18H3 and HP-3D9. Saturating concentrations of each antibody was used in this assay. The percent blocking was calculated as $100 - ((\text{percent HLA-E positive for anti-CD94 antibody})/(\text{percent HLA-E positive for isotype}) * 100)$. The 18H3 and 1E4 antibodies did not block HLA-E binding to CD94.

[0036] FIGS. 5A-5B show the results of competition assays performed for 18H3 anti-CD94 antibody evaluation. For all competition assays, 18H3 was incubated with PBMCs at a concentration of 1.3 µg/ml. FIG. 5A shows competition assays between 18H3 and commercially available anti-CD94 antibodies. Commercially available anti-CD94 antibodies were titrated and incubated with PBMCs concurrently with 18H3. FIG. 5B shows competition assays with 18H3 and other hybridoma anti-CD94 antibodies disclosed herein (1M4 and 1E4). To test competition between 18H3 and 1M4/1E4, 1M4 and 1E4 were incubated with cells at concentrations of 8.5 µg/ml and 11 µg/ml, respectively. 18H3 was fluorescently tagged with AF647 and incubated with cells concurrently with 18H3-AF647. 18H3 only partially competed with HP-

3D9, and did not compete with DX22, HP-3B1, 131412, 12K45, 1E4 and 1M4. These results suggest that 18H3 antibody binds to an epitope that is not shared with commercially available antibodies.

[0037] **FIGS. 6A-6B** show the results of competition assays performed for 1M4 anti-CD94 antibody evaluation. For all competition assays, 1M4 was incubated with PBMCs at a concentration of 8.5 µg/ml. **FIG. 6A** shows competition assays between 1M4 and commercially available anti-CD94 antibodies. Commercially available anti-CD94 antibodies were titrated and incubated with PBMCs concurrently with 1M4. **FIG. 6B** shows competition assays with 1M4 and 1E4 antibody. To test competition between 1M4 and 1E4, 1E4 was incubated with cells at a concentration of 11 µg/ml. 1M4 with anti-mouse secondary antibody were incubated with cells concurrently with 1E4. 1M4 antibody did not compete with commercially available antibodies, but did compete with 1E4.

[0038] **FIG. 7** shows the results of competition assays performed for 1E4 anti-CD94 antibody evaluation. For all competition assays, 1E4 was incubated with PBMCs at a concentration of 11 µg/ml. Commercially available anti-CD94 antibodies were titrated and incubated with PBMCs concurrently with 1E4. 1E4 antibody did not compete with four out of the five commercially available anti-CD94 antibodies tested, but partially competed with 12K45.

[0039] **FIGS. 8A-8B** show the results of an anti-CD94 antibody internalization assay. Healthy donor peripheral blood mononuclear cells (PBMCs) were incubated with unconjugated anti-CD94 antibodies at multiple time points ranging from 30 minutes to 24 hours. The cells were either kept at 4 °C to prevent internalization or 37 °C to induce internalization. **FIG. 8A** shows the results for commercially available antibodies HP-3D9 and DX22. Commercially available anti-CD94 antibodies were internalized in a time-dependent manner. **FIG. 8B** shows the results for 18H3, 1M4 and 1E4 antibodies. 18H3, 1M4 and 1E4 antibodies were not significantly internalized upon binding to CD94.

[0040] **FIGS. 9A-9B** show the results of an antibody-dependent cellular cytotoxicity (ADCC) assay for anti-CD94 antibody using healthy donor PBMCs. The 18H3 antibody was produced in Expi-CHO cells cultured in the presence of kifunensine, a potent inhibitor of the mannosidase I enzyme, which is used to produce 18H3-KIF mimicking non-fucosylated antibody. Fucosylated 1E4 antibody was used for the ADCC assay. PBMCs were plated in 96-well plates and incubated in the presence of anti-CD94 antibody ranging from 1x10⁻⁶ to 10 µg/ml in 10-fold dilutions overnight. The number of NK cells was quantified by flow cytometry. The number of NK cells in the human IgG1 and anti-CD94 antibody treated conditions were normalized to NK cell number from human IgG1 treated wells. **FIG. 9A** shows the results for the ADCC assay using human IgG1 18H3 antibody, while **FIG. 9B** shows the results for the ADCC assay using fucosylated 1E4 antibody. Both human IgG1 18H3 and fucosylated 1E4 depleted human primary NK cells in a concentration dependent manner.

[0041] **FIG. 10** shows the results of an anti-CD94 antibody ADCC assay using CLPD-NK patient PBMCs. 18H3 was produced in Expi-CHO cells cultured in the presence of kifunensine, a potent inhibitor of the mannosidase I enzyme, to produce 18H3-KIF mimicking non-fucosylated antibody. PBMCs were plated in 96-well plates and incubated in the presence of anti-CD94 antibody ranging from 1x10⁻⁶ to

10 μ g/ml in 10-fold dilutions overnight. The number of CD3-CD16⁺ leukemic cells was quantified by flow cytometry. The number of leukemic cells in the human IgG1 and anti-CD94 antibody treated conditions were normalized to leukemic cell number from human IgG1 treated wells. Partially non-fucosylated, human IgG1 18H3 depleted human CLPD-NK leukemic cells in a concentration dependent manner.

[0042] FIG. 11 depicts a summary of anti-CD94 antibody characteristics and functional assessment relative to commercially available anti-CD94 antibodies.

[0043] FIG. 12 shows the affinity of anti-CD94 antibody ATX-130 for human primary natural killer (NK) cells and anti-CD94 antibody ATX-130-KIF for cynomolgus primary natural killer (NK) cells, chronic lymphoproliferative disorder of NK cells (CLPD-NK), and T- large granular lymphocyte leukemia cells (T-LGLL) as measured by flow cytometry. The ATX-130 antibody was produced in Expi-CHO cells cultured in the presence of kifunensine, a potent inhibitor of the mannosidase I enzyme, which is used to produce ATX-130-KIF mimicking non-fucosylated antibody. PBMCs of healthy donors were used for antibody staining. ATX-130 antibody was titrated from 50 nM to 0.02 nM. Secondary anti-human antibody labeled with Alexa Fluor 647 was used to detect binding on CD3-CD56 bright NK cells. ATX-130-KIF antibody conjugated with Alexa Fluor 647 was titrated from 50 nM to 0.02 nM. T-LGLL cells were identified using CD3+CD16⁺ gating, while CLPD-NK cells were identified using CD3-CD16⁺ gating strategy. Titration curves and EC₅₀ were generated using Graphpad Prism. ATX-130 bound to CD3-CD56 bright NK cells with an affinity of 0.6 nM. ATX-130-KIF showed an affinity of 1 nM on primary cynomolgus NK cells, 1.4 nM on CLPD-NK cells, and 3 nM on T-LGLL cells. Fluorescently labeled human IgG1-KIF isotype-KIF antibody was used as control. Arrows indicate ATX-130 and Human IgG1-KIF data points.

[0044] FIG. 13 shows affinity of anti-CD94 antibody ATX-130 on CD94 homodimer or heterodimer. BaF3 cells overexpressing CD94 homodimer (top panel), CD94/NKG2A heterodimer (lower left panel), and CD94/NKG2C heterodimer (lower right panel) were incubated with unconjugated ATX-130 antibody in a dilution series from 50 nM to 0.02 nM. Secondary anti-human antibody labeled with Alexa Fluor 647 was used to detect ATX-130 binding on cells. ATX-130 binds to CD94 homodimer, CD94/NKG2A, and CD94/NKG2C heterodimer BaF3 cells with affinity of 0.3, 0.8, and 1.8nM, respectively.

[0045] FIG. 14 shows IFN-gamma secretion on human NK cells in the presence of ATX-130 antibodies as assessed by ELISA. NK cells were isolated from healthy donor PBMCs and cultured in the presence of ATX-130 with mouse IgG1 inactive Fc (mATX-130), human IgG1-KIF isotype control, ATX-130 (hATX-130), and media alone. After 24 hours of incubation, cell culture supernatants were collected and ELISA was performed to detect secreted IFN-gamma. Concentration of ATX-130 (10 μ g/mL, 5 μ g/mL, 1 μ g/mL, or media) is depicted at the top of each bar and corresponds to concentrations depicted in figure legend.

[0046] FIG. 15 shows the results of competition assays performed for ATX-130 anti-CD94 antibody evaluation. For all competition assays, ATX-130 was incubated with PBMCs at a concentration of 7.5

µg/ml. Commercially available anti-CD94 antibodies (clones HP-3D9, DX22, 131412, 12K45, and HP-3B1) were titrated and incubated with PBMCs concurrently with ATX-130. Competition was assessed by plotting the MFI of the titrated commercially available anti-CD94 antibodies. ATX-130 does not compete with HP-3D9, DX22, 131412, 12K45, or HP-3B1.

[0047] FIG. 16 shows the results of HLA-E tetramer blocking assays performed with ATX-130-KIF and isotype control antibody using flow cytometry. Healthy donor PBMCs were incubated with ATX-130-KIF. PE labeled HLA-E tetramer was then incubated with cells and antibody mixture and detected by flow cytometry. Saturating concentrations of ATX-130-KIF were used in this assay. The percent blocking was calculated as $100 - ((\text{percent HLA-E positive for anti-CD94 antibody})/(\text{percent HLA-E positive for isotype}) * 100)$. Arrows indicate ATX-130-KIF and isotype histograms. ATX-130-KIF did not block HLA-E binding to CD94.

[0048] FIG. 17 shows the results of an anti-CD94 antibody internalization assay. Healthy donor PBMCs were incubated with unconjugated ATX-130 at multiple time points ranging from 30 minutes to 24 hours. Cells were either kept at 4 °C to prevent internalization or at 37 °C to induce internalization. ATX-130 does not become significantly internalized within 24 hours.

[0049] FIG. 18 shows the binding of ATX-130-KIF to immune cell types as measured by flow cytometry. Immune cell types (monocytes, CD4 T cells, B cells, CD8 T cells, and NK cells) of PBMCs from normal human, cynomolgus, and LGL leukemia patient samples were stained with ATX-130-KIF Alexa Fluor 647 (50 nM) and assessed for binding. ATX-130-KIF selectively binds to NK cells (CD3-CD56+/CD16+), subset of normal CD8 T cells (CD3+CD8+), and all LGLL cells (CD3-CD16+). Arrows indicate ATX-130-KIF and isotype histograms.

[0050] FIG. 19 shows the results of an ADCC assay for ATX-130-KIF using healthy donor PBMCs. Healthy donor PBMCs were plated in 96-well plates and incubated with ATX-130 (titrated in 10-fold dilutions) for 24 hours. Depletion of different immune cell types was assessed by quantifying the remaining number of cells by flow cytometry. Arrows indicate ATX-130-KIF and isotype curves. ATX-130 depletes human NK cells with a potency of 0.8 ng/ml while sparing other immune cell types.

[0051] FIG. 20 shows the results of an anti-CD94 antibody ADCC assay using cynomolgus PBMCs. Cynomolgus PBMCs were plated in 96-well plates and incubated with ATX-130-KIF (titrated in 10-fold dilutions) for 24 hours. Depletion of different immune cell types (NK cells, CD8 T cells, CD4 T cells, and B cells) was assessed by quantifying the remaining number of cells by flow cytometry. Arrows indicate ATX-130-KIF and isotype curves. ATX-130-KIF depletes cynomolgus NK cells with a potency of 0.3 ng/ml while sparing other immune cell types.

[0052] FIG. 21 shows the results of an anti-CD94 antibody ADCC assay using T-LGLL and CLPD-NK PBMCs. T-LGLL and CLPD-NK PBMCs were plated in 96-well plates and incubated with ATX-130-KIF (titrated in 10-fold dilutions) for 24 hours. Depletion of different immune cell types was assessed by quantifying the remaining number of cells by flow cytometry. Arrows indicate ATX-130-KIF and isotype

curves. ATX-130-KIF depletes T-LGLL and CLPD-NK cells with a potency of 0.2 and 0.6 ng/ml, respectively while sparing other immune cell types.

[0053] **FIG. 22A** shows study design examining effects of ATK-130 or isotype control on humanized IL-15 transgenic mice engrafted with healthy human donor PBMCs.

[0054] **FIG. 22B** shows depletion of normal human NK and CD8 T cells in IL-15 transgenic mice. Mice were engrafted with healthy donor PBMCs for three days. One dose of human IgG1 isotype control or ATX-130 (5 mg/kg) were injected into mice (5 mice per arm), and depletion of NK cells (top panel) and CD8 T cells (lower panel) in the blood, spleen, and bone marrow were assessed by flow cytometry 48 hours post-dose. Depletion was quantified by the number of NK and CD8 T cells remaining in respective samples.

[0055] **FIG. 23** shows depletion of LGLL cells in blood, spleen, bone marrow, and liver in IL-15 transgenic mice. Mice are engrafted with LGLL PBMCs for 28 days. One dose of human IgG1 isotype control or ATX-130 (5 mg/kg) were injected into mice (5 mice per arm), and depletion of LGLL cells in the blood, spleen, bone marrow, and liver were assessed by flow cytometry 48 hours post-dose. Depletion was quantified by the number of CD94+ LGLL cells remaining in respective samples.

[0056] **FIG. 24A** shows the design of an exploratory pharmacodynamic (PD) study in non-human primates to evaluate efficacy of ATK-130 *in vivo*.

[0057] **FIG. 24B** shows depletion of cynomolgus NK cells *in vivo* with ATX-130-KIF dosing at 2mg/kg as assessed by flow cytometry. Two naïve cynomolgus macaques (Cyno #1 and Cyno #2) were administered ATX-130-KIF (2 mg/kg) via intravenous (IV) infusion for 60 minutes. An additional 2 mg/kg of ATX-130-KIF was administered to Cyno #1 at 8 weeks and Cyno #2 at 16 weeks. Body weight and clinical observations were recorded periodically. PBMCs were isolated from 5 mL blood draws per time point per animal. 0.3×10^6 cells were plated per well in technical triplicates and stained with antibody panel. CD3-CD8+ gating strategy was used to identify cynomolgus NK cells. NK cells were quantified by calculating the percentage of the cell population out of total PBMCs. Arrows indicate time points at which doses were administered.

[0058] **FIGS. 25A-25B** show the assessment of depletion of cynomolgus CD4 T, CD8 T, and B cells. PBMCs were isolated from 5 mL blood draws per time point for Cyno #1 and Cyno #2. 0.3×10^6 cells were plated per well in technical triplicates and stained with antibody panel. CD3+CD4+, CD3+CD8+, and CD3-CD20+ gating strategy were used to identify Cyno #1 (**FIG. 25A**) and Cyno #2 (**FIG. 25B**) CD4+ T cells, CD8+ T cells, and B cells, respectively. Cells were quantified by calculating the percentage of the cell population out of total PBMCs.

[0059] **FIG. 26** shows the results of assessment of monocyte depletion by flow cytometry. PBMCs were isolated from 5 mL blood draws per time point for Cyno #1 (left panel) and Cyno #2 (right panel). 0.3×10^6 cells were plated per well in technical triplicates and stained with antibody panel. CD3-CD14+ gating strategy was used to identify monocytes. Cells were quantified by calculating the percentage of the cell population out of total PBMCs.

[0060] FIG. 27 shows the results of assessment of CD16 expression on monocytes by flow cytometry. PBMCs were isolated from 5 mL blood draws per time point for Cyno #1 (left panel) and Cyno #2 (right panel). 0.3×10^6 cells were plated per well in technical triplicates and stained with antibody panel. CD3-CD14+ gating strategy was used to identify monocytes. CD16 MFI was assessed on monocytes.

[0061] FIG. 28A shows design of a non-GLP PD study in non-human primates to evaluate efficacy of ATK-130 *in vivo*.

[0062] FIG. 28B shows depletion of cynomolgus NK cells *in vivo* with ATX-130 dosing at 5, 50, and 100 mg/kg. PBMCs were isolated from 0.5 mL blood draws per time point per animal. 0.3×10^6 cells were plated per well in technical triplicates and stained with antibody panel. CD3-CD16+ gating strategy was used to identify cynomolgus NK cells. NK cells were quantified by calculating the percentage of the cell population out of total PBMCs.

[0063] FIG. 29 shows depletion of cynomolgus CD94+CD8+NKG2A+ cells *in vivo* with ATX-130 dosing at 5, 50, and 100mg/kg. PBMCs were isolated from 0.5 mL blood draws per time point per animal. 0.3×10^6 cells were plated per well in technical triplicates and stained with antibody panel. CD3+CD8+NKG2A+ gating strategy was used to identify cynomolgus CD8+ T cells. CD8 T cells were quantified by calculating the percentage of the cell population out of total PBMCs. Identifiers at the top of each bar indicate time point at which PMBCs were isolated and correspond to time points depicted in figure legend.

[0064] FIG. 30 shows depletion of cynomolgus NK and CD94+CD8+NKG2A+ T cells *in vivo* with ATX-130 dosing at 5, 50, and 100mg/kg or vehicle control at 0mg/kg (using Dulbecco's Phosphate Buffered Saline, PBS). Duodenum, liver, spleen, and bone marrow were harvested at study endpoint. Tissues were dissociated into single cell suspensions and 0.3×10^6 cells were plated per well in technical triplicates and stained with antibody panel. CD3+CD8+NKG2A+ gating strategy was used to identify cynomolgus CD8+ T cells. CD45+CD3-NKG2A+ markers were used to identify cynomolgus NK cells. Identifiers at the top of each boxplot indicate antibody used in the experiment.

[0065] FIGS. 31A & 31B show binding of depicted anti-CD94 antibodies to normal human NK cells (FIG. 31A) or HEK293 cells expressing cynomolgus CD94 (FIG. 31B). Antibodies are shown by ATX numbers. The results showed that ATX-# anti-CD94 antibodies bound to human NK cells or cells expressing cynomolgus CD94.

[0066] FIGS. 32A-32I show results of HLA-E tetramer blocking assays to determine whether the indicated anti-CD94 antibodies block HLA-E binding. Healthy donor PBMCs were incubated with anti-CD94 antibodies. PE labeled HLA-E tetramer was then incubated with cells and antibody mixture and detected by flow cytometry.

DETAILED DESCRIPTION OF THE INVENTION

[0067] Several aspects are described below with reference to example applications for illustration. It should be understood that numerous specific details, relationships, and methods are set forth to provide a full understanding of the features described herein. One having ordinary skill in the relevant art, however,

will readily recognize that the features described herein can be practiced without one or more of the specific details or with other methods. The features described herein are not limited by the illustrated ordering of acts or events, as some acts can occur in different orders and/or concurrently with other acts or events. Furthermore, not all illustrated acts or events are required to implement a methodology in accordance with the features described herein.

[0068] As used herein, the singular forms “a”, “an”, and “the” are intended to include the plural forms as well, unless the context clearly indicates otherwise. Furthermore, to the extent that the terms “including”, “includes”, “having”, “has”, “with”, or variants thereof are used in either the detailed description and/or the claims, such terms are intended to be inclusive in a manner similar to the term “comprising”. The term “comprising” as used herein is synonymous with “including” or “containing”, and is inclusive or open-ended.

[0069] Any reference to “or” herein is intended to encompass “and/or” unless otherwise stated. As used herein, the term “about” with reference to a number refers to that number plus or minus 10% of that number. The term “about” with reference to a range refers to that range minus 10% of its lowest value and plus 10% of its greatest value.

I. Antibodies

[0070] In some embodiments, provided herein are antibodies that bind to CD94, e.g., human CD94 expressed on the surface of NK cells or T cells. Also provided herein are antibodies that bind to CD94 and that have immunoglobulin Fc part with modifications including reduced fucosylation, non-fucosylation, or mutations that enhance ADCC activities and/or improve affinity of the Fc region to Fc receptors such as CD16 (e.g., CD16a). Also provided herein are antibodies that bind to CD94 and that have one or more of the following characteristics: bind to human CD94 and cynomolgus monkey CD94, do not block binding of HLA-E to the CD94/NKG2A heterodimer, have a low degree of target (e.g., CD94) internalization, are non-fucosylated or have reduced fucosylation, and/or induce or promote ADCC activity.

A. Antibody Targets and Affinities

[0071] In some embodiments, the antibodies provided herein bind to CD94. In some embodiments, the antibodies provided herein bind to human CD94 (e.g., an extracellular domain of human CD94). In some embodiments, the antibodies provided herein bind to cynomolgus monkey CD94 (e.g., an extracellular domain of cynomolgus CD94). In some embodiments, the antibodies provided herein bind to human CD94 and to cynomolgus monkey CD94. In some embodiments, an antibody of the disclosure binds to CD94 on the surface of NK cells and/or T cells.

[0072] In some embodiments, an antibody of the disclosure binds to a human CD94 protein or a part thereof, or a protein having at least 80% (e.g., any of at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100%) homology to a human CD94 protein or a part thereof. Amino acid sequences of exemplary human CD94 proteins are provided in the sequences of SEQ ID NOS: 25-27:

MAVFKTTLWRLISGTLGIICLSLMSTLGILLKNSFTKLSIEPAFTPGPNIELQKDSGCCS
CQEKWVGRCNCYFISSEQKTWNESRHLCASQKSSLLQLQNTDELDFMSSSQFYWIGLS
YSEEHTAWLWENGSAQSQYLFPSFETFNTKNCIAYNPNGNALDESCEDKNRYICKQQLI (SEQ ID NO:
25)

MAVFKTTLWRLISGTLGIICLSLMSTLGILLKNSFTKLSIEPAFTPGPNIELQKDSGCCS
CQEKWVGRCNCYFISSEQKTWNESRHLCASQKSSLLQLQNTDELDFMSSSQFYWIGLS
SYSEEHTAWLWENGSAQSQYLFPSFETFNTKNCIAYNPNGNALDESCEDKNRYICKQQLI (SEQ ID
NO: 26)

MAAFTKLSIEPAFTPGPNIELQKDSGCCSCQEKWVGRCNCYFISSEQKTWNESRHLCAS
QKSSLLQLQNTDELDFMSSSQFYWIGLSYSEEHTAWLWENGSAQSQYLFPSFETFNTKN
CIAYNPNGNALDESCEDKNRYICKQQLI
SYSEEHTAWLWENGSAQSQYLFPSFETFNTKNCIAYNPNGNALDESCEDKNRYICKQQLI (SEQ ID
NO: 27)

[0073] In some embodiments, the terms bind, specifically binds to, or is specific for refer to measurable and reproducible interactions such as binding between a target and an antibody, which is determinative of the presence of the target in the presence of a heterogeneous population of molecules including biological molecules. For example, an antibody that binds to or specifically binds to a target (which can be an epitope) is an antibody that binds this target with greater affinity, avidity, more readily, and/or with greater duration than it binds to other targets. In one embodiment, the extent of binding of an antibody to an unrelated target is less than about 10% of the binding of the antibody to the target as measured, e.g., by a radioimmunoassay (RIA). In certain embodiments, an antibody that specifically binds to a target has a dissociation constant (K_D) of $< 1\mu\text{M}$, $< 100\text{ nM}$, $< 10\text{ nM}$, $< 1\text{ nM}$, or $< 0.1\text{ nM}$. In certain embodiments, an antibody specifically binds to an epitope on a protein that is conserved among the protein from different species. In another embodiment, specific binding can include, but does not require exclusive binding.

[0074] In some embodiments, the antibodies provided herein bind to human CD94 (Natural killer cells antigen CD94; CD94 Entrez Gene ID: 3824; KLRD1 (HGNC Symbol); UniProtKB identifier: Q13241; HGNC:6378; Ensembl: ENSG00000134539 OMIM: 602894; KP43).

[0075] In some embodiments, an antibody of the disclosure binds to a cynomolgus monkey CD94 protein or a part thereof, or a protein having at least 80% (e.g., any of at least 80%, at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100%) homology to a cynomolgus monkey CD94 protein or a part thereof. The amino acid sequences of cynomolgus monkey CD94 proteins are known in the art, for example, UniProtKB identifier: Q68VD4.

[0076] In certain embodiments, the affinity of an antibody for its target (e.g., CD94) may be represented by the dissociation constant (K_D). Affinity can be measured by common methods known in the art, such as flow cytometry or Western blotting, and using assays described herein (e.g., in the Examples). In some embodiments, the K_D is measured using a radiolabeled antigen binding assay (RIA) performed with the Fab version of an antibody of the disclosure and its target (e.g., CD94). In some embodiments, the K_D is

measured using surface plasmon resonance assays. Exemplary assays are described, *e.g.*, in Drake, A.W. and Klakamp, S.L. (2007) *J. Immunol. Methods* 318:147-152.

[0077] In some embodiments, the binding of an antibody of the disclosure to CD94, *e.g.*, human CD94 and/or cynomolgus monkey CD94, may be assessed using any method known in the art. For example, binding of an antibody of the disclosure to human CD94 may be assessed in an *ex vivo* flow cytometry-based assay using peripheral blood mononuclear cells (PMBCs) and/or NK cells, *e.g.*, as described in the Examples. Titration curves and EC50 may be generated and evaluated using methods known in the art, such as using Graphpad prism. In another example, binding of an antibody of the disclosure to cynomolgus monkey CD94 may be assessed in an *ex vivo* or *in vitro* flow cytometry-based assay using cynomolgus monkey CD94-expressing cells such as cynomolgus monkey CD94-expressing HEK293 cells, *e.g.*, as described in the Examples.

[0078] In certain embodiments, an antibody of the disclosure has a K_D of less than about 10 μM for binding to its target (*e.g.*, human and/or cynomolgus CD94). In certain embodiments, an antibody of the disclosure has a K_D of less than about 1 μM for binding to its target (*e.g.*, human and/or cynomolgus CD94). In certain embodiments, an antibody of the disclosure has a K_D of any of less than about 1000 nM, less than about 900 nM, less than about 800 nM, less than about 700 nM, less than about 600 nM, less than about 500 nM, less than about 400 nM, less than about 300 nM, less than about 200 nM, less than about 100 nM, less than about 90 nM, less than about 80 nM, less than about 70 nM, less than about 60 nM, less than about 50 nM, less than about 40 nM, less than about 30 nM, less than about 20 nM, less than about 10 nM, less than about 9 nM, less than about 8 nM, less than about 7 nM, less than about 6 nM, less than about 5 nM, less than about 4 nM, less than about 3 nM, less than about 2 nM, less than about 1 nM, less than about 0.5 nM, or less than about 0.1 nM for binding to its target (*e.g.*, human and/or cynomolgus CD94). In some embodiments, an antibody of the disclosure has a K_D of any of less than about 100 pM, less than about 75 pM, less than about 50 pM, less than about 25 pM, less than about 10 pM, less than about 5 pM, less than about 1 pM, less than about 0.5 pM, or less than about 0.1 pM for binding to its target (*e.g.*, human and/or cynomolgus CD94).

[0079] In certain embodiments, an antibody of the disclosure has a K_D of less than about 100 nM, less than about 90 nM, less than about 80 nM, less than about 70 nM, less than about 60 nM, less than about 50 nM, less than about 40 nM, less than about 30 nM, less than about 20 nM, less than about 10 nM, less than about 9 nM, less than about 8 nM, less than about 7 nM, less than about 6 nM, less than about 5 nM, less than about 4 nM, less than about 3 nM, less than about 2 nM, less than about 1 nM, less than about 0.5 nM, or less than about 0.1 nM for binding to human CD94 on human NK cells or T cells. In certain embodiments, an antibody of the disclosure has a K_D of less than about 75 nM, less than about 60 nM, less than about 50 nM, less than about 40 nM, less than about 30 nM, less than about 20 nM, less than about 10 nM, less than about 9 nM, less than about 8 nM, less than about 7 nM, less than about 6 nM, less than about 5 nM, less than about 4 nM, less than about 3 nM, less than about 2 nM, less than about 1 nM, less than about 0.5 nM, or less than about 0.1 nM for binding

to human CD94 on human NK cells or T cells. In certain embodiments, an antibody of the disclosure has a K_D of between about 2 nM and about 80 nM for binding to human CD94 on human NK cells or T cells.

[0080] In certain embodiments, an antibody of the disclosure has a K_D of less than about 100 nM, less than about 90 nM, less than about 80 nM, less than about 70 nM, less than about 60 nM, less than about 50 nM, less than about 40 nM, less than about 30 nM, less than about 20 nM, less than about 10 nM, less than about 9 nM, less than about 8 nM, less than about 7 nM, less than about 6 nM, less than about 5 nM, less than about 4 nM, less than about 3 nM, less than about 2 nM, less than about 1 nM, less than about 0.5 nM, or less than about 0.1 nM for binding to cynomolgus CD94 on cells expressing cynomolgus monkey CD94. In certain embodiments, an antibody of the disclosure has a K_D of less than about 75 nM, less than about 80 nM, less than about 70 nM, less than about 60 nM, less than about 50 nM, less than about 40 nM, less than about 30 nM, less than about 20 nM, less than about 10 nM, less than about 9 nM, less than about 8 nM, less than about 7 nM, less than about 6 nM, less than about 5 nM, less than about 4 nM, less than about 3 nM, less than about 2 nM, less than about 1 nM, less than about 0.5 nM, or less than about 0.1 nM for binding to cynomolgus CD94 on cells expressing cynomolgus monkey CD94. In certain embodiments, an antibody of the disclosure has a K_D of between about 2 nM and about 80 nM for binding to cynomolgus CD94 on cells expressing cynomolgus monkey CD94.

[0081] In some embodiments, an antibody of the disclosure binds to its target (e.g., CD94) in the same or a different epitope as an antibody known in the art for that target. In some embodiments, an antibody of the disclosure binds to a different epitope as an antibody known in the art. In some embodiments, an antibody of the disclosure specifically binds to human CD94, wherein the antibody does not bind to the same epitope on human CD94 as anti-CD94 antibody clones HP-3D9, DX22, HP-3B1, 131412, or 12K45. In some embodiments, an antibody of the disclosure specifically binds to human CD94, wherein the antibody does not bind to the same epitope on human CD94 as anti-CD94 antibody clones DX22, HP-3B1, or 131412. In some embodiments, an antibody of the disclosure specifically binds to human CD94, wherein the antibody binds to the same epitope on human CD94 as anti-CD94 antibody clones HP-3D9, DX22, HP-3B1, 131412, or 12K45. In some embodiments, an antibody of the disclosure specifically binds to human CD94, wherein the antibody binds to the same epitope on human CD94 as anti-CD94 antibody clone HP-3D9. In some embodiments, an antibody of the disclosure specifically binds to human CD94, wherein the antibody binds to the same epitope on human CD94 as anti-CD94 antibody clone 12K45.

[0082] In some embodiments, if an antibody of the disclosure does not bind to its target (e.g., CD94,) in the same epitope as another antibody for that target, e.g., a commercially available antibody or an antibody known in the art for that target, then the antibody of the disclosure does not block binding of the other antibody to the target in a competition assay (e.g., as described in the Examples), e.g., by 50% or more.

[0083] In some embodiments, an antibody of the disclosure binds to its target (e.g., CD94) with a higher affinity than an antibody known in the art for that target. In some embodiments, an antibody of the

disclosure binds to its target (e.g., CD94) with a higher affinity than anti-CD94 antibody clones HP-3D9, DX22, HP-3B1, 131412, or 12K45. In some embodiments, an antibody of the disclosure binds to its target (e.g., CD94) with a higher affinity than anti-CD94 antibody clones HP-3B1, 131412, or 12K45.

[0084] In some embodiments, an antibody of the disclosure specifically binds to human CD94, wherein the antibody binds to human CD94 with a greater affinity than anti-CD94 antibody clones HP-3D9, DX22, HP-3B1, 131412, or 12K45. In some embodiments, an antibody of the disclosure specifically binds to human CD94, wherein the antibody binds to human CD94 with a greater affinity than anti-CD94 antibody clones HP-3B1, 131412, or 12K45.

[0085] In some embodiments, an antibody of the disclosure binds to its target (e.g., CD94) with any of at least 1.5-fold, at least 2-fold, at least 2.5-fold, at least 3-fold, at least 3.5-fold, at least 4-fold, at least 4.5-fold, at least 5-fold, at least 5.5-fold, at least 6-fold, at least 6.5-fold, at least 7-fold, at least 7.5-fold, at least 8-fold, at least 8.5-fold, at least 9-fold, at least 9.5-fold, at least 10-fold, or more, greater affinity than another antibody known in the art for that target.

B. Exemplary Anti-CD94 Antibodies

[0086] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising an amino acid sequence with at least 80%, at least

81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:6.

[0087] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:6.

[0088] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6.

[0089] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:19, and the VL domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:20.

[0090] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:19, and the VL domain comprises the amino acid sequence of SEQ ID NO:20.

[0091] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:7, a CDR-H2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:8, and a CDR-H3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:9; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:10, a CDR-L2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:11, and a CDR-L3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:12.

[0092] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:7, a CDR-H2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:8, and a CDR-H3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:9; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:10, a CDR-L2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:11, and a CDR-L3 comprising an amino

acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:12.

[0093] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:7, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:8, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:9; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:10, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:11, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:12.

[0094] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:21, and the VL domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:22.

[0095] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:21, and the VL domain comprises the amino acid sequence of SEQ ID NO:22.

[0096] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least

86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:18.

[0097] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:18.

[0098] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18.

[0099] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:23, and the VL domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least

87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:24.

[0100] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:23, and the VL domain comprises the amino acid sequence of SEQ ID NO:24.

[0101] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:30, a CDR-H2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:31, and a CDR-H3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:32; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:35.

[0102] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:30, a CDR-H2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:31, and a CDR-H3

comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:32; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:35.

[0103] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:30, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:31, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:32; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35.

[0104] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:65, and the VL domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:66.

[0105] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:65, and the VL domain comprises the amino acid sequence of SEQ ID NO:66.

[0106] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:37, and a CDR-H3 comprising an amino acid sequence with at

least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:38; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:35.

[0107] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:37, and a CDR-H3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:38; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:35.

[0108] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:37, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:38; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35.

[0109] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises an amino acid

sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:67, and the VL domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:68.

[0110] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:67, and the VL domain comprises the amino acid sequence of SEQ ID NO:68.

[0111] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:39, and a CDR-H3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:40; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:35.

[0112] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:39, and a CDR-H3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:40; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:35.

[0113] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:39, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:40; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35.

[0114] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:69, and the VL domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:70.

[0115] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:69, and the VL domain comprises the amino acid sequence of SEQ ID NO:70.

[0116] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100%

sequence identity to the amino acid sequence of SEQ ID NO:41, a CDR-H2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:42, and a CDR-H3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:43; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:44, a CDR-L2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:46.

[0117] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:41, a CDR-H2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:42, and a CDR-H3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:43; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:44, a CDR-L2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:46.

[0118] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:41, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:42, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:43; and wherein the VL

domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:44, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:46.

[0119] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:71, and the VL domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:72.

[0120] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:71, and the VL domain comprises the amino acid sequence of SEQ ID NO:72.

[0121] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:49; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid

sequence of SEQ ID NO:51, and a CDR-L3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:52.

[0122] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:49; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:51, and a CDR-L3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:52.

[0123] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:49; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:51, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:52.

[0124] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:73, and the VL domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:74.

[0125] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:73, and the VL domain comprises the amino acid sequence of SEQ ID NO:74.

[0126] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:54, and a CDR-H3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:55; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:56.

[0127] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:54, and a CDR-H3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:55; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:45, and a CDR-L3

comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:56.

[0128] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:54, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:55; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:56.

[0129] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:75, and the VL domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:76.

[0130] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:75, and the VL domain comprises the amino acid sequence of SEQ ID NO:76.

[0131] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:57, a CDR-H2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:58, and a CDR-H3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:59; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least

86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:60, a CDR-L2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:61.

[0132] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:57, a CDR-H2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:58, and a CDR-H3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:59; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:60, a CDR-L2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:61.

[0133] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:57, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:58, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:59; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:60, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61.

[0134] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:77, and the VL domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least

87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:78.

[0135] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:77, and the VL domain comprises the amino acid sequence of SEQ ID NO:78.

[0136] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:83, a CDR-H2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:84, and a CDR-H3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:85; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:86, a CDR-L2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:61.

[0137] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:83, a CDR-H2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:84, and a CDR-H3

comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:85; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:86, a CDR-L2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:61.

[0138] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:83, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:84, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:85; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:86, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61.

[0139] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:79, and the VL domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:80.

[0140] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:79, and the VL domain comprises the amino acid sequence of SEQ ID NO:80.

[0141] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising an amino acid sequence with at

least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:62; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:63, a CDR-L2 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:64.

[0142] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:62; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:63, a CDR-L2 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence comprising one, two, or three amino acid substitutions relative to the amino acid sequence of SEQ ID NO:64.

[0143] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:62; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:63, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:64.

[0144] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises an amino acid

sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:81, and the VL domain comprises an amino acid sequence with at least 80%, at least 81%, at least 82%, at least 83%, at least 84%, at least 85%, at least 86%, at least 87%, at least 88%, at least 89%, at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or 100% sequence identity to the amino acid sequence of SEQ ID NO:82.

[0145] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:81, and the VL domain comprises the amino acid sequence of SEQ ID NO:82.

[0146] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:88, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:89; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35.

[0147] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:92, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:93; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35.

[0148] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:92, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:94; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35.

[0149] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:95, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:96, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:97; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:98, a CDR-L2

comprising the amino acid sequence of SEQ ID NO:99, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:100.

[0150] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:109, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:110, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:114; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:115, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:99, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:52.

[0151] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:116, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:117, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:118; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:115, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:99, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:56.

[0152] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:101, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:102, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:103; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:104, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61.

[0153] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:105, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:106, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:107; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:108, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61.

[0154] In some embodiments, an antibody of the disclosure comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:109, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:110, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:111; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:112, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:113, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:64.

[0155] In some embodiments, an antibody of the disclosure comprises a VH domain comprising 1, 2, or 3 CDRs from a single antibody listed in Table 1 and/or a VL domain comprising 1, 2, or 3 CDRs from a single antibody listed in Table 1. In some embodiments, an antibody of the disclosure comprises a VH and/or VL domain from a single antibody listed in Table 2.

Table 1. Anti-CD94 antibody CDR sequences

<i>Name</i>	<i>CDR-H1</i>	<i>CDR-H2</i>	<i>CDR-H3</i>	<i>CDR-L1</i>	<i>CDR-L2</i>	<i>CDR-L3</i>
18H3	SYWIG (SEQ ID NO:1)	IIYPGDS D TRYSPSF QG (SEQ ID NO:2)	PFDYGGSP GYFDY (SEQ ID NO:3)	RASQSIR SWLA (SEQ ID NO:4)	KASSLES (SEQ ID NO:5)	QQYNTFWT (SEQ ID NO:6)
1M4	NYAMN (SEQ ID NO:7)	VISGSGD TTYCADS VKG (SEQ ID NO:8)	NCYGSGSY YNHFDY (SEQ ID NO:9)	KSSQSVL YSSNRM NYLA (SEQ ID NO:10)	WASTRES (SEQ ID NO:11)	QQYYSIPT (SEQ ID NO:12)
1E4	TSDLCVS (SEQ ID NO:13)	LIDWND DKYYSTS LQT (SEQ ID NO:14)	TIAAAGPY DAFDI (SEQ ID NO:15)	KSSQSVL YGSNNK NYLA (SEQ ID NO:16)	WASTRKS (SEQ ID NO:17)	QEYYSRFT (SEQ ID NO:18)
ATX-122 (Kabat)	SYGVS (SEQ ID NO: 30)	WISPYNG NTNYAH NLQG (SEQ ID NO: 31)	DRGRFGEL FFDY (SEQ ID NO: 32)	RASQGIS NYLA (SEQ ID NO: 33)	AASSLQS (SEQ ID NO: 34)	LQHNSYPFT (SEQ ID NO: 35)
ATX-122 (IMGT)	GYTFTSY G (SEQ ID NO: 87)	ISPYNGN T (SEQ ID NO: 88)	ARDRGRFG ELFFDY (SEQ ID NO: 89)	QGISNY (SEQ ID NO: 90)	AAS (SEQ ID NO: 91)	LQHNSYPFT (SEQ ID NO: 35)
ATX-123 (Kabat)	SYGIS (SEQ ID NO: 36)	WISAYNG NTNYAQ KFQG (SEQ ID NO: 37)	DRGRFGEL LSDY (SEQ ID NO: 38)	RASQGIS NYLA (SEQ ID NO: 33)	AASSLQS (SEQ ID NO: 34)	LQHNSYPFT (SEQ ID NO: 35)

ATX-123 (IMGT)	GYTFTSY G (SEQ ID NO: 87)	ISAYNGN T (SEQ ID NO: 92)	ARDRGRFG ELLSDY (SEQ ID NO: 93)	QGISNY (SEQ ID NO: 90)	AAS (SEQ ID NO: 91)	LQHNSYPFT (SEQ ID NO: 35)
ATX-124 (Kabat)	SYGIS (SEQ ID NO: 36)	WISAYNG NTNYAQ KLQG (SEQ ID NO: 39)	DRGRFGEL FFDH (SEQ ID NO: 40)	RASQGIS NYLA (SEQ ID NO: 33)	AASSLQS (SEQ ID NO: 34)	LQHNSYPFT (SEQ ID NO: 35)
ATX-124 (IMGT)	GYTFTSY G (SEQ ID NO: 87)	ISAYNGN T (SEQ ID NO: 92)	ARDRGRFG ELFFDH (SEQ ID NO: 94)	QGISNY (SEQ ID NO: 90)	AAS (SEQ ID NO: 91)	LQHNSYPFT (SEQ ID NO: 35)
ATX-125 (Kabat)	SIYYWG (SEQ ID NO: 41)	SIYYSGS TYYNPSL KS (SEQ ID NO: 42)	LPLTGEFAP DI (SEQ ID NO: 43)	RASQSVS TYLA (SEQ ID NO: 44)	GASSRAT (SEQ ID NO: 45)	QQYGSSPIT (SEQ ID NO: 46)
ATX-125 (IMGT)	GGSISSII YY (SEQ ID NO: 95)	IYYSGST (SEQ ID NO: 96)	ARLPLTGE FAFDI (SEQ ID NO: 97)	QSVSTY (SEQ ID NO: 98)	GAS (SEQ ID NO: 99)	QQYGSSPIT (SEQ ID NO: 100)
ATX-126 (Kabat)	SYSMN (SEQ ID NO: 47)	SISTSSNF IYYADSV KG (SEQ ID NO: 48)	DMGPFYSF YYMDV (SEQ ID NO: 49)	RASQSVS SSYLA (SEQ ID NO: 50)	GASNRAT (SEQ ID NO: 51)	LQHNSYPPT (SEQ ID NO: 52)
ATX-126 (IMGT)	GFTFSSY S (SEQ ID NO: 109)	ISTSSNFI (SEQ ID NO: 110)	VRDMGPFY SFYYMDV (SEQ ID NO: 114)	QSVSSSY (SEQ ID NO: 115)	GAS (SEQ ID NO: 99)	LQHNSYPPT (SEQ ID NO: 52)
ATX-127 (Kabat)	SRYWWT (SEQ ID NO: 53)	EIYHSGT TNYNPSL ES (SEQ ID NO: 54)	SPNWGY YYYMDV (SEQ ID NO: 55)	RASQSVS SSYLA (SEQ ID NO: 50)	GASSRAT (SEQ ID NO: 45)	QQYGRSLT (SEQ ID NO: 56)
ATX-127 (IMGT)	GGSISSR YW (SEQ ID NO: 116)	IYHSGTT (SEQ ID NO: 117)	ARSPNWG YYYYYMD V (SEQ ID NO: 118)	QSVSSSY (SEQ ID NO: 115)	GAS (SEQ ID NO: 99)	QQYGRSLT (SEQ ID NO: 56)

ATX-128 (Kabat)	GSTIQ (SEQ ID NO: 57)	RIRSKAN SYATASA ASVKG (SEQ ID NO: 58)	EGLGYYNV GYYYFYM DV (SEQ ID NO: 59)	RASQSISS YLN (SEQ ID NO: 60)	AASSLQS (SEQ ID NO: 34)	QQSYSTPIT (SEQ ID NO: 61)
ATX-128 (IMGT)	GFTFSGS T (SEQ ID NO: 101)	IRSKANS YAT (SEQ ID NO: 102)	TREGLGYY NVGYYYF YMDV (SEQ ID NO: 103)	QSISSY (SEQ ID NO: 104)	AAS (SEQ ID NO: 91)	QQSYSTPIT (SEQ ID NO: 61)
ATX-129 (Kabat)	SYWMS (SEQ ID NO: 83)	NIKQDGS AKYYVD SVKG (SEQ ID NO: 84)	GYFFDY (SEQ ID NO: 85)	RVSQGIS SYLN (SEQ ID NO: 86)	AASSLQS (SEQ ID NO: 34)	QQSYSTPIT (SEQ ID NO: 61)
ATX-129 (IMGT)	GFTFSSY W (SEQ ID NO: 105)	IKQDGSA K (SEQ ID NO: 106)	ARGYYFDY (SEQ ID NO: 107)	QGISSY (SEQ ID NO: 108)	AAS (SEQ ID NO: 91)	QQSYSTPIT (SEQ ID NO: 61)
ATX-130 (Kabat)	SYSMN (SEQ ID NO: 47)	SISTSSNF IYYADSV KG (SEQ ID NO: 48)	DLGRYYY YMDV (SEQ ID NO: 62)	RASQSISS WLA (SEQ ID NO: 63)	AASSLQS (SEQ ID NO: 34)	QKYNAPFT (SEQ ID NO: 64)
ATX-130 (IMGT)	GFTFSSY S (SEQ ID NO: 109)	ISTSSNFI (SEQ ID NO: 110)	ARDLGRYY YYMDV (SEQ ID NO: 111)	QSISSW (SEQ ID NO: 112)	ASS (SEQ ID NO: 113)	QKYNAPFT (SEQ ID NO: 64)

Table 2. Anti-CD94 antibody variable domain sequences

<i>Name</i>	<i>VH</i>	<i>VL</i>
18H3	EVQLVQSGAEVKKPGESLKISCKGS GYRFTSYWIGWVRQMPGKGLEWM GIIYPGDSDFTRYSPSFQGGQVHISADKS ITTAFLQWSSLKASDTAMYYCARPF DYGGSPGYFDYWGGQGLVTVSS (SEQ ID NO:19)	DIQMTQSPSTLSASVGDRVTITCRASQSIRSW LAWYQQKPGKAPKLLIYKASSLESGVPSRFS GSGSGTEFTLTISSLQPDDFATYYCQQYNLF WTFGQGTKVEIK (SEQ ID NO:20)
1M4	QLVESGGGLVQPGLSLRLACAASGF TFSNYAMNWVRQAPGKGLEWVSVI	EIVMTQSPDSLAVSLGERATINCKSSQSVLYS SNRMNYLAWYQQKPGQPPNLLIYWASTRES

	SGSGDTTYCADSVKGRFTISRDNK NTLHLQLNSLRAEDTAVYYCAKNC YSGGSYYNHFDYWGGTLVTVSS (SEQ ID NO:21)	GVPDRFSGSGSGTDFTLTISLQAEDVAVYY CQQYYSIPLTFGGGKVEIK (SEQ ID NO:22)
1E4	QVTLRSEGPALVKPTQTLTLCTFSG FSLSTSDLCVSWIRQPPGKALEWLA LIDWNDDKYYSTSLQTRLTISKDTS KNQVVLMTNMDPVDATYYCAR TIAAAGPYDAFDIWGGGTMVTVSS (SEQ ID NO:23)	DIVMTQSPDSLVSLSGERATINCKSSQSVLY GSNNKNYLAWYQQKPGQPPKLLIYWASTR KSGVPDRFSGSGSGTDFTLTISLQAEDVAV YYCQEYYSLRFTFGPGTKVDIK (SEQ ID NO:24)
ATX- 122	QVQLVQSGAEVKKPGASLVKSCKA SGYTFTSYGVSWVRQAPGQGLEWV GWISPYNGNTNYAHNLQGRVAMTT DTSTSTAYMELRSLRSDDMAVYYC ARDRGRFGELFFDYWGQGTLLTVSS (SEQ ID NO: 65)	DIVMTQSPSSVSASVGDRVITTCRASQGISNY LAWYQQKPGKAPKLLIYAASSLQSGVPSRFS GSGSGTDFTLTISLQPEDFATYYCLQHNSYP FTFGPGTKVDIK (SEQ ID NO: 66)
ATX- 123	QVQLVQSGAEVKKPGASLVKSCKA SGYTFTSYGISWVRQAPGQGLEWM GWISAYNGNTNYAQKFQGRVTMTT DTSTNTAYMELRSLRSDDTAVYYC ARDRGRFGELLSDYWGGQGTLLTVSS (SEQ ID NO: 67)	DIVMTQSPSSVSASVGDRVITTCRASQGISNY LAWYQQKPGKAPKLLIYAASSLQSGVPSRFS GSGSGTDFTLTISLQPEDFATYYCLQHNSYP FTFGPGTKVDIK (SEQ ID NO: 68)
ATX- 124	QVQLVQSGAEVKKPGASLVKSCKA SGYTFTSYGISWVRQAPGQGLEWM GWISAYNGNTNYAQKLQGRVTMTT DTSTSTAYMEVRSLSDDTAVYYC ARDRGRFGELFFDHWGGQGTLLTVSS (SEQ ID NO: 69)	DIVMTQSPSSVSASVGDRVITTCRASQGISNY LAWYQQKPGKAPKLLIYAASSLQSGVPSRFS GSGSGTDFTLTISLQPEDFATYYCLQHNSYP FTFGPGTKVDIK (SEQ ID NO: 70)
ATX- 125	QVQLQQSGPGLVKPSETLSLTCTVS GGSISSIIYYWGWIRQPPGKGLEWIG SIYYSGSTYYNPSLKSRTISVDTSK NQFSLNLSSVTAADTAVYYCARLPL TGEFAFDIWGGGTMVTVSS (SEQ ID NO: 71)	EIVLTQSPATLSLSPGERATLSCRASQSVSTY LAWFQQKPGQAPRLLIYGASSRATGIPDRFS GSGSGTDFTLTISRLEPEDFAVYYCQQYGSS PITFGQGTRLEIK (SEQ ID NO: 72)
ATX- 126	QVQLQESGGGLVQPGGSLKLSAAS GFTFSSYSMNWVRQAPGKGLEWVS SISTSSNFIYYADSVKGRFTISRDNK	DIQVTQSPATLSLSPGERATLSCRASQSVSSS YLAWYQQKPGQAPRLLIYGASNATGIPAR

	NTLYLQMNSLRAEDTAVYYCVRD MGPFYSFYMDVWNGTTVTVSS (SEQ ID NO: 73)	FSGSGSGTDFTLTISLQPEDFATYYCLQHNS YPPTFGGGTKVDIK (SEQ ID NO: 74)
ATX- 127	QVQLQQSGPGLVKPSGTLSTCAVS GGSISSRYWWTWVRQPPGKGLEWI GEIYHSGTTNYPNPSLESRTISVDKS KNQFSLKVSSVTAADTAVYYCARSP NWGYYYYYMDVWGKGTTVTVSS (SEQ ID NO: 75)	EIVMTQSPATLSVSPGERATLSCRASQSVSSS YLAWYQQKPGQAPRLLIYGASSRATGIPDRF SGSGSGTDFTLTISRLESEDFAVYYCQYGR SLTFGGGTKEIK (SEQ ID NO: 76)
ATX- 128	QVQLQESGGGLVQPGGSLKLSAAS GFTFSGSTIQWVRQASGKGLEWVG RIRSKANSYATASAASVKGRFTISRD DSKNMAYLQMNSLKTEDTAVYYCT REGLGYYNVGYFFYMDVWGKGT TVTVSS (SEQ ID NO: 77)	DIVMTQSPSSLSASVGDRVTITCRASQSISSY LNWYQQKPGKAPKLLIYAASSLQSGVPSKFS GSGSGTDFTLTISLQPEDFATYYCQSYSTP ITFGQGRLEIK (SEQ ID NO: 78)
ATX- 129	EVQLVQSGGGLVQPGGSLRLSAAAS GFTFSSYWMSWVRQAPGKGLEWV ANIKQDGSAYYYVDSVKGRFTISRD NAKNSLYLQMNSLRAEDTAVYYCA RGYYFDYWGQGLTVTVSS (SEQ ID NO: 79)	EIVLTQSPSTLSASVGDRVTITCRVSQGISSYL NWYRQKPGKVPKLLIYAASSLQSGVPSRFSG SGSGTDFTLTISLQPEDFATYYCQSYSTPI TFGQGRLEIK (SEQ ID NO: 80)
ATX- 130	EVQLLES GGGLVKPGGSLRLSAAAS GFTFSSYSMNWVRQAPGKGLEWVS SISTSSNFIYYADSVKGRFTISRDN KNSLYLQMNSLRAEDTAVYYCARD LGRYYYYMDVWGKGTTVTVSS (SEQ ID NO: 81)	DIVMTQSPSSLSASVGDRVTITCRASQSISSW LAWYQQKPGKAPKSLIYAASSLQSGVPSKFS GSGSGTDFTLTISLQPEDVATYYCQKYN SA PFTFGPGTKVDIK (SEQ ID NO: 82)

[0156] Many definitions for CDR sequences of an antibody variable domain are known in the art and may be used to describe an antibody of the present disclosure, *e.g.*, by CDR sequences. In some embodiments, antibody CDR sequences are defined as in Kabat (*see, e.g.*, Kabat et al., Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md., 1991). In some embodiments, antibody CDR sequences are defined as in Chothia (*see, e.g.*, Chothia and Lesk *J. Mol. Biol.* 196:901-917 (1987)). In some embodiments, antibody CDR sequences are defined as in IMGT (*see, e.g.*, Lefranc, M.P. (1999) *The Immunologist* 7:132-136). In some embodiments, CDR sequences of a single antibody are defined as by mixing two or more definitions, *e.g.*, Kabat, Chothia, and/or IMGT. In some embodiments, an antibody of the present disclosure comprises a VH domain

[illegible]

or HVR sequences present in the VH domain sequence of ATX-127 as described herein (*see, e.g.*, Table 2) and/or a VL domain comprising 1, 2, or all 3 CDR or HVR sequences present in the VL domain sequence of ATX-127 as described herein (*see, e.g.*, Table 2). In some embodiments, an antibody of the present disclosure comprises a VH domain comprising 1, 2, or all 3 CDR or HVR sequences present in the amino acid sequence of SEQ ID NO:77 and/or a VL domain comprising 1, 2, or all 3 CDR or HVR sequences present in the amino acid sequence of SEQ ID NO:78. In some embodiments, an antibody of the present disclosure comprises a VH domain comprising 1, 2, or all 3 CDR or HVR sequences present in the VH domain sequence of ATX-128 as described herein (*see, e.g.*, Table 2) and/or a VL domain comprising 1, 2, or all 3 CDR or HVR sequences present in the VL domain sequence of ATX-128 as described herein (*see, e.g.*, Table 2). In some embodiments, an antibody of the present disclosure comprises a VH domain comprising 1, 2, or all 3 CDR or HVR sequences present in the amino acid sequence of SEQ ID NO:79 and/or a VL domain comprising 1, 2, or all 3 CDR or HVR sequences present in the amino acid sequence of SEQ ID NO:80. In some embodiments, an antibody of the present disclosure comprises a VH domain comprising 1, 2, or all 3 CDR or HVR sequences present in the VH domain sequence of ATX-129 as described herein (*see, e.g.*, Table 2) and/or a VL domain comprising 1, 2, or all 3 CDR or HVR sequences present in the VL domain sequence of ATX-129 as described herein (*see, e.g.*, Table 2). In some embodiments, an antibody of the present disclosure comprises a VH domain comprising 1, 2, or all 3 CDR or HVR sequences present in the amino acid sequence of SEQ ID NO:81 and/or a VL domain comprising 1, 2, or all 3 CDR or HVR sequences present in the amino acid sequence of SEQ ID NO:82. In some embodiments, an antibody of the present disclosure comprises a VH domain comprising 1, 2, or all 3 CDR or HVR sequences present in the VH domain sequence of ATX-130 as described herein (*see, e.g.*, Table 2) and/or a VL domain comprising 1, 2, or all 3 CDR or HVR sequences present in the VL domain sequence of ATX-130 as described herein (*see, e.g.*, Table 2).

[0157] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6.

[0158] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:19, and the VL domain comprises the amino acid sequence of SEQ ID NO:20.

[0159] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:7, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:8, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:9; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:10, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:11, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:12.

[0160] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:21, and the VL domain comprises the amino acid sequence of SEQ ID NO:22.

[0161] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18.

[0162] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:23, and the VL domain comprises the amino acid sequence of SEQ ID NO:24.

[0163] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:30, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:31, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:32; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35.

[0164] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH

domain comprises the amino acid sequence of SEQ ID NO:65, and the VL domain comprises the amino acid sequence of SEQ ID NO:66.

[0165] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:37, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:38; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35.

[0166] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:67, and the VL domain comprises the amino acid sequence of SEQ ID NO:68.

[0167] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:39, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:40; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35.

[0168] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:69, and the VL domain comprises the amino acid sequence of SEQ ID NO:70.

[0169] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:41, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:42, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:43; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:44, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:46.

[0170] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:71, and the VL domain comprises the amino acid sequence of SEQ ID NO:72.

[0171] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:49; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:51, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:52.

[0172] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:73, and the VL domain comprises the amino acid sequence of SEQ ID NO:74.

[0173] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:54, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:55; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:56.

[0174] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:75, and the VL domain comprises the amino acid sequence of SEQ ID NO:76.

[0175] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:57, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:58, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:59; and wherein the VL domain comprises a CDR-L1 comprising the amino acid

sequence of SEQ ID NO:60, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61.

[0176] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:77, and the VL domain comprises the amino acid sequence of SEQ ID NO:78.

[0177] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:83, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:84, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:85; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:86, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61.

[0178] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:79, and the VL domain comprises the amino acid sequence of SEQ ID NO:80.

[0179] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:62; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:63, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:64.

[0180] In some embodiments, an antibody of the disclosure binds to an epitope on human or cynomolgus monkey CD94 that is the same as the CD94 epitope bound by an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:81, and the VL domain comprises the amino acid sequence of SEQ ID NO:82.

[0181] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:2,

and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6.

[0182] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:19, and the VL domain comprises the amino acid sequence of SEQ ID NO:20.

[0183] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:7, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:8, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:9; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:10, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:11, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:12.

[0184] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:21, and the VL domain comprises the amino acid sequence of SEQ ID NO:22.

[0185] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18.

[0186] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:23, and the VL domain comprises the amino acid sequence of SEQ ID NO:24.

[0187] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:30, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:31, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:32; and wherein the VL

domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35.

[0188] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:65, and the VL domain comprises the amino acid sequence of SEQ ID NO:66.

[0189] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:37, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:38; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35.

[0190] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:67, and the VL domain comprises the amino acid sequence of SEQ ID NO:68.

[0191] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:39, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:40; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35.

[0192] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:69, and the VL domain comprises the amino acid sequence of SEQ ID NO:70.

[0193] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:41, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:42, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:43; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:44, a CDR-L2

comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:46.

[0194] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:71, and the VL domain comprises the amino acid sequence of SEQ ID NO:72.

[0195] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:49; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:51, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:52.

[0196] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:73, and the VL domain comprises the amino acid sequence of SEQ ID NO:74.

[0197] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:54, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:55; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:56.

[0198] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:75, and the VL domain comprises the amino acid sequence of SEQ ID NO:76.

[0199] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:57, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:58, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:59; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:60, a CDR-L2

comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61.

[0200] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:77, and the VL domain comprises the amino acid sequence of SEQ ID NO:78.

[0201] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:83, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:84, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:85; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:86, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61.

[0202] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:79, and the VL domain comprises the amino acid sequence of SEQ ID NO:80.

[0203] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:62; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:63, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:64.

[0204] In some embodiments, an antibody of the disclosure competes for binding to human or cynomolgus monkey CD94 with an anti-CD94 antibody comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:81, and the VL domain comprises the amino acid sequence of SEQ ID NO:82.

[0205] In some embodiments, an antibody of the disclosure comprises an Fc region. In some embodiments, the Fc region is a human IgG1 Fc region. In some embodiments, the antibody comprises a human Fc region that is non-fucosylated. In some embodiments, the antibody binds to a human cellular Fc gamma receptor IIIA to a greater extent than an antibody comprising a wild type human IgG1 Fc region. In some embodiments, the antibody is capable of inducing antibody-dependent cellular cytotoxicity (ADCC) against a cell expressing human CD94 on its surface.

[0206] In some embodiments, the term antibody is used in the broadest sense and encompasses various antibody structures, including but not limited to monoclonal antibodies, polyclonal antibodies, multispecific antibodies (e.g., bispecific antibodies), and antibody fragments so long as they exhibit the desired antigen-binding activity. In some embodiments, an antibody of the disclosure is an isolated antibody. An "isolated" antibody is one which has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials which would interfere with research, diagnostic, and/or therapeutic uses for the antibody, and may include enzymes, hormones, and other proteinaceous or nonproteinaceous solutes. In some embodiments, an antibody is purified (1) to greater than 95% by weight of antibody as determined by, for example, the Lowry method, and in some embodiments, to greater than 99% by weight; (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of, for example, a spinning cup sequenator, or (3) to homogeneity by SDS-PAGE under reducing or nonreducing conditions using, for example, Coomassie blue or silver stain. An isolated antibody includes the antibody in situ within recombinant cells since at least one component of the antibody's natural environment will not be present. Ordinarily, however, an isolated antibody will be prepared by at least one purification step.

[0207] In some embodiments, a monoclonal antibody is an antibody obtained from a population of substantially homogeneous antibodies, *i.e.*, the individual antibodies comprising the population are identical and/or bind the same epitope, except for possible variant antibodies, e.g., containing naturally occurring mutations or arising during production of a monoclonal antibody preparation, such variants generally being present in minor amounts. In contrast to polyclonal antibody preparations, which typically include different antibodies directed against different determinants (epitopes), each monoclonal antibody of a monoclonal antibody preparation is directed against a single determinant on an antigen. Thus, in some embodiments, a monoclonal antibody is obtained from a substantially homogeneous population of antibodies. Monoclonal antibodies may be produced using any method known in the art. For example, monoclonal antibodies to be used in accordance with the present disclosure may be made by a variety of techniques, including but not limited to the hybridoma method, recombinant DNA methods, phage-display methods, and methods utilizing transgenic animals containing all or part of the human immunoglobulin loci.

C. Blocking of HLA-E binding

[0208] Major histocompatibility complex class I, E (HLA-E) is the ligand of the CD94/NKG2A heterodimer and plays a crucial role in the inhibition of NK cell and CD8⁺ T cell activity when bound to the CD94/NKG2A heterodimer. Thus, without wishing to be bound to theory, blocking HLA-E and CD94/NKG2A interaction may result in activation and proliferation of target cells, e.g., cells expressing CD94. Thus, it may be beneficial that an anti-CD94 antibody does not block HLA-E interaction with the CD94/NKG2A heterodimer, e.g., in a subject with an NK/T cell lymphoma administered the anti-CD94 antibody. In some embodiments, HLA-E is human HLA-E, also known as QA1 and HLA-6.2. For an

exemplary HLA-E gene, *see, e.g.*, NCBI Gene ID No. 3133; for an exemplary HLA-E polypeptide, *see, e.g.*, NP_005507.3.

[0209] In some embodiments, blocking of binding of HLA-E to the CD94/NKG2A heterodimer refers to blocking of binding of HLA-E to the CD94/NKG2A heterodimer, blocking of binding of HLA-E to CD94, and/or blocking of binding of HLA-E to NKG2A.

[0210] Blocking of binding of HLA-E to the CD94/NKG2A heterodimer by an antibody of the disclosure may be assessed using any method known in the art. For example, blocking of binding of HLA-E to the CD94/NKG2A heterodimer by an antibody of the disclosure may be assessed using an *ex vivo* assay using PBMCs and/or NK cells, *e.g.*, as described in the Examples. In an exemplary assay, PBMCs, *e.g.*, obtained from healthy donors, are incubated with human Fc block (Biolegend, San Diego, CA) and cell viability dye (Thermo Fisher, Carlsbad, CA) for 30 minutes on ice and protected from light. Cells are then washed once with FACS buffer (PBS with 2% IgG low FBS). Anti-CD94 antibodies or isotype control antibodies at saturating concentrations are incubated with the cells for 30 minutes on ice and protected from light. Cells are then washed and incubated with HLA-E tetramer PE (Creative Biolabs, Shirley, NY), CD3 pacific blue, and CD56 FITC antibodies (Biolegend, San Diego, CA) for 30 minutes on ice and protected from light. Cells then receive a final wash in FACS buffer before quantification on a flow cytometer. Data acquisition and fluorescence compensation may be performed using methods known in the art, such as using a CytoFlex flow cytometer (Beckman Coulter, Chaska, MN). Data analysis may be performed using any method known in the art, such as using the FlowJo software. NK cells are identified through gating on lymphocytes on the forward and side scatter, followed by doublet and dead cell exclusion, and gated on the CD3-CD56+ population. HLA-E is then quantified on the CD3-CD56+ NK cell population. Percent blocking of binding of HLA-E to the CD94/NKG2A heterodimer by an anti-CD94 antibody compared to a control antibody, *e.g.*, an isotype control antibody, is calculated as: $100 - ((\text{percent HLA-E positive for anti-CD94 antibody})/(\text{percent HLA-E positive for isotype}) * 100)$.

[0211] In some embodiments, an antibody blocks binding of HLA-E to the CD94/NKG2A heterodimer if it blocks more than about 20% of HLA-E binding to the CD94/NKG2A heterodimer, *e.g.*, compared to an isotype control antibody. In some embodiments, an antibody blocks binding of HLA-E to the CD94/NKG2A heterodimer if it blocks about 21%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 99%, or 100% of HLA-E binding to the CD94/NKG2A heterodimer, *e.g.*, compared to an control antibody, *e.g.*, an isotype control antibody.

[0212] In some embodiments, an antibody does not block binding of HLA-E to the CD94/NKG2A heterodimer if it blocks about 20% or less of HLA-E binding to the CD94/NKG2A heterodimer, *e.g.*, compared to an isotype control antibody. In some embodiments, an antibody does not block binding of HLA-E to the CD94/NKG2A heterodimer if it blocks about 20%, about 18%, about 16%, about 14%, about 12%, about 10%, about 8%, about 6%, about 4%, about 2%, about 1%, about 0.5%, or 0% of HLA-

E binding to the CD94/NKG2A heterodimer, e.g., compared to an control antibody, e.g., an isotype control antibody.

[0213] In some embodiments, an antibody provided herein does not block binding of HLA-E to the CD94/NKG2A heterodimer. In some embodiments, an antibody provided herein blocks about 20% or less, about 19% or less, about 18% or less, about 17% or less, about 16% or less, about 15% or less, about 14% or less, about 13% or less, about 12% or less, about 11% or less, about 10% or less, about 9% or less, about 8% or less, about 6% or less, about 5% or less, about 4% or less, about 3% or less, about 2% or less, about 1% or less, about 0.5% or less, or 0% of binding of HLA-E to the CD94/NKG2A heterodimer, compared to a control antibody, e.g., an isotype control antibody. In some embodiments, an antibody provided herein blocks 0% of binding of HLA-E to the CD94/NKG2A heterodimer, compared to a control antibody, e.g., an isotype control antibody.

D. Enhanced ADCC Activity

[0214] In some embodiments, antibody-dependent cell-mediated cytotoxicity, antibody-dependent cellular cytotoxicity, antibody directed cell cytotoxicity, or ADCC refer to a cell-mediated reaction in which non-specific cytotoxic cells producing Fc receptors, e.g. natural killer cells (NK cells), neutrophils, and macrophages, recognize an antibody bound to a target cell and then cause lysis of the target cell. The primary mediator cells are natural killer (NK) cells. NK cells express FcγRIII (Ravetch et al. (1991) *Annu. Rev. Immunol.*, 9:457-92). In some embodiments, ADCC activity refers to the ability of an antibody or Fc fusion protein to elicit an ADCC reaction.

[0215] In some embodiments, the antibodies provided herein have enhanced antibody-dependent cellular cytotoxicity (ADCC) activity. In some embodiments, enhanced ADCC activity refers to an antibody or an Fc region of an antibody mediating or inducing ADCC more efficiently and/or more effectively than a native or wild type antibody and/or a native or wild type Fc region of an antibody in the presence of effector cells *in vitro* or *in vivo*, which may be determined using an ADCC assay, e.g., as described herein or as is commonly known in the art. In some embodiments, effector cells are leukocytes that produce one or more Fc receptors and perform effector functions. In some embodiments, such cells produce at least FcγRIII and perform the ADCC effector function. Examples of ADCC-mediated human leukocytes include peripheral blood mononuclear cells (PBMCs), natural killer cells (NK), monocytes, cytotoxic T cells, and neutrophils.

[0216] In some embodiments, ADCC activity can be assessed directly using an *in vitro* assay, using a ⁵¹Cr release assay using peripheral blood mononuclear cells (PBMC) and/or NK effector cells, *see e.g.*, Shields et al. (2001) *J. Biol. Chem.*, 276:6591-6604, or another suitable method. ADCC activity may be expressed as the number of remaining cells following an ADCC assay, or a concentration of antibody or Fc fusion protein at which the lysis of target cells is half-maximal (e.g., EC50 or IC50). In some embodiments, ADCC activity is determined using an *ex vivo* assay using PBMCs, LGL cells, and/or NK cells, e.g., as described in the Examples, and the ADCC activity of an antibody of the disclosure is described as the percent of target cells remaining after the ADCC assay and/or the IC50 or EC50 of the

antibody (*i.e.*, the concentration of an antibody of the disclosure at which half the maximum target cell depletion or cell lysis is achieved). The IC₅₀ or EC₅₀ of an antibody may be determined using any method known in the art, *e.g.*, using a dosage response curve and GraphPad Prism.

[0217] In some embodiments, the antibodies provided herein induce ADCC activity with an IC₅₀ or EC₅₀ measured using an *ex vivo* assay of between about 1 ng/ml to about 100 ng/ml (*e.g.*, any of about 1 ng/ml, about 2 ng/ml, about 3 ng/ml, about 4 ng/ml, about 5 ng/ml, about 10 ng/ml, about 15 ng/ml, about 20 ng/ml, about 25 ng/ml, about 30 ng/ml, about 35 ng/ml, about 40 ng/ml, about 45 ng/ml, about 50 ng/ml, about 55 ng/ml, about 60 ng/ml, about 65 ng/ml, about 70 ng/ml, about 75 ng/ml, about 80 ng/ml, about 85 ng/ml, about 90 ng/ml, about 95 ng/ml, or about 100 ng/ml). In some embodiments, the antibodies provided herein induce ADCC activity with an IC₅₀ or EC₅₀ measured using an *ex vivo* assay of about 20 ng/ml or less. In some embodiments, the antibodies provided herein induce ADCC activity with an IC₅₀ or EC₅₀ measured using an *ex vivo* assay of about 60 ng/ml or less. In some embodiments, an antibody of the disclosure exhibits an IC₅₀ or EC₅₀ that is at least 1%, at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% lower than the IC₅₀ or EC₅₀ of a control antibody (*e.g.*, a wild type control antibody, or an antibody known in the art or commercially available against the same target).

[0218] In some embodiments, IC₅₀ or EC₅₀ refers to the concentration of a compound (*e.g.*, an antibody) which induces a response halfway between the baseline and maximum after a specified exposure time. For example, IC₅₀ or EC₅₀ may be used to measure the potency of an antibody for mediating and/or inducing an effector function, *e.g.*, ADCC activity. In some embodiments, the IC₅₀ or EC₅₀ of a dose response curve represents the concentration of a compound (*e.g.*, an antibody) where 50% of its maximal effect is observed.

[0219] In some embodiments, an antibody of the disclosure has a higher maximal target cell lysis compared to a control antibody (*e.g.*, a wild type control antibody, or an antibody known in the art or commercially available against the same target). For example, antibodies of the disclosure may exhibit a maximal target cell lysis that is at least 5%, at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 100% higher than that of a control antibody (*e.g.*, a wild type control antibody, or an antibody known in the art or commercially available against the same target).

(i) Enhanced Binding to Fc Receptors

[0220] In some embodiments, the antibodies provided herein include a human immunoglobulin Fc region that has enhanced ADCC activity compared to a wild type Fc region. In some embodiments, the antibodies provided herein bind to a human cellular Fc receptor to a greater extent than an antibody comprising a wild type Fc region. In some embodiments, an Fc receptor (FcR) is a receptor that is capable of binding to an Fc region of an antibody. Certain Fc receptors can bind to IgG (*i.e.*, γ -receptor); such

receptors include subclasses of FcγRI, FcγRII and FcγRIII, as well as their allelic variants and alternative splicing events. For an overview of the Fc receptors see Ravetch and China: *Annu. Port. Immunol.* 9, 457 (1991); Capel et al. *Immunomethods*, 4, 25 (1994); and de Haas et al., *J. Leg. Clin. Med.* 126, 330 (1995).

[0221] In some embodiments, the antibodies provided herein bind to a human cellular Fc gamma receptor IIIA to a greater extent than an antibody comprising a wild type Fc region. In some embodiments, the human cellular Fc gamma receptor IIIA comprises a valine residue or a phenylalanine residue at amino acid residue position 158. *See, e.g.*, UniProt Accession P08637 or VAR_003960. In some embodiments, the human cellular Fc gamma receptor IIIA comprises the sequence of SEQ ID NO: 28 or 29.

Human cellular Fc gamma receptor IIIA 158F

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MWQLLLPTALLLLVSAGMRTEDLPKAVVFLEPQWYRVLEKDSVTLKCQGA
YSPEDNSTQWFHNESLISSQASSYFIDAATVDDSGEYRCQTNLSTLSDPV
QLEVHIGWLLLQAPRWVFKEEDPIHLRCHSWKNTALHKVTYLQNGKGRKY
FHHNSDFYIPKATLKDSGSYFCRGLFGSKNVSSETVNITITQGLAVSTIS
SFFPPGYQVSFCLVMVLLFAVDTGLYFSVKTNIRSSTRDWKDHKFKWRKD
PQDK (SEQ ID NO: 28)
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Human cellular Fc gamma receptor IIIA 158V

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MWQLLLPTALLLLVSAGMRTEDLPKAVVFLEPQWYRVLEKDSVTLKCQGA
YSPEDNSTQWFHNESLISSQASSYFIDAATVDDSGEYRCQTNLSTLSDPV
QLEVHIGWLLLQAPRWVFKEEDPIHLRCHSWKNTALHKVTYLQNGKGRKY
FHHNSDFYIPKATLKDSGSYFCRGLVGSKNVSSETVNITITQGLAVSTIS
SFFPPGYQVSFCLVMVLLFAVDTGLYFSVKTNIRSSTRDWKDHKFKWRKD
PQDK (SEQ ID NO: 29)
```

[0222] In some embodiments, an antibody provided herein is of the IgG (e.g., IgG1, IgG2, IgG3, or IgG4), IgA (IgA1 or IgA2), IgD, IgM, or IgE isotype. In some embodiments, an antibody provided herein is of the IgG, isotype. In some embodiments, an antibody provided herein is of the IgG1, isotype. In some embodiments, antibodies provided herein bind to a human cellular Fc gamma receptor IIIA (FcγRIIIA) to a greater extent than an antibody comprising a wild type human IgG1 Fc region. In some embodiments, the human cellular Fc gamma receptor IIIA comprises a valine residue or a phenylalanine residue at amino acid residue position 158. Exemplary assays for determining binding to a human cellular Fc gamma receptor IIIA are known in the art; *see, e.g.*, Lazar, G.A. *et al.* (2006) *Proc. Natl. Acad. Sci.* 103:4005-1010; and Ferrara, C. *et al.* (2011) *Proc. Natl. Acad. Sci.* 108:12669-12674.

[0223] In some embodiments, an Fc region is a C-terminal region of an immunoglobulin heavy chain that contains at least a portion of the constant region. In some embodiments, an Fc region includes a native Fc region or a variant Fc region. In one embodiment, a human IgG heavy chain Fc region extends from Cys226, or from Pro230, to the carboxyl-terminus of the heavy chain. However, the C-terminal

lysine (Lys447) of the Fc region may or may not be present. In some embodiments, numbering of amino acid residues in an Fc region or constant region is according to the EU numbering system, also called the EU index, as described in Kabat et al., *Sequences of Proteins of Immunological Interest*, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md., 1991. In some embodiments, a wild type Fc region or a native Fc region are an Fc region that comprises an amino acid sequence that is identical to the amino acid sequence of the Fc region found in nature. In some embodiments, a variant Fc region is an Fc region that comprises an amino acid sequence that differs from the native or wild type sequence of the Fc region in at least one amino acid. In some embodiments, a variant Fc region has at least one amino acid substitution, e.g., approximately 1-10 or 1-5 amino acid substitutions. In some embodiments, the Fc region variant is at least approximately 80% (e.g., at least about 90%, or at least about 95%) homologous to a native or wild type sequence Fc region and/or an Fc region of an original polypeptide. In some embodiments, the at least one amino acid substitution in the variant Fc region enhances the effector function of the variant Fc region compared to a native or wild type Fc region. In some embodiments, an effector function is a biological activity attributable to the Fc region of an antibody, which vary with the antibody isotype. Examples of antibody effector functions include: Clq binding and complement dependent cytotoxicity (CDC); Fc receptor binding; antibody-dependent cell-mediated cytotoxicity (ADCC); antibody-dependent cell-mediated phagocytosis (ADCP); down regulation of cell surface receptors (e.g., B-cell receptor); and B-cell activation.

[0224] The binding affinity of an antibody for an Fc receptor may be assessed using any method known in the art, such as using surface plasmon resonance, and/or ELISA, e.g., as described in Shields et al. (2001) *J. Biol. Chem.*, 276:6591-6604. In some embodiments, the affinity of an antibody of the disclosure for FcγRIIIA may be above that of the wild-type control by any of at least about 1.5-fold, at least about 2-fold, at least about 3-fold, at least about 4-fold, at least about 5-fold, at least about 6-fold, at least about 7-fold, at least about 8-fold, at least about 9-fold, at least about 10-fold, at least about 20 fold, at least about 30-fold, at least about 40-fold, at least about 50-fold, or higher.

[0225] In some embodiments, affinity refers to the strength of the sum total of noncovalent interactions between a single binding site of a molecule (e.g., an antibody) and its binding partner (e.g., an antigen or a target). For example, 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.

[0226] In some embodiments, statements that a molecule (e.g., an antibody and/or an Fc region) binds to a greater extent than another molecule (e.g., an antibody and/or an Fc region), or that a molecule (e.g., an antibody and/or an Fc region) binds with a greater affinity than another molecule (e.g., an antibody and/or an Fc region), or other grammatical equivalents, refer to a molecule (e.g., an antibody and/or an Fc region) binding more tightly (e.g., having a lower dissociation constant) to a target (e.g., an Fc receptor, a cell surface protein) than another molecule (e.g., an antibody and/or an Fc region) in binding assays (e.g., as described herein and/or as commonly known in the art) under substantially the same conditions. For

example, the statement that an antibody “X” binds to an Fc receptor to a greater extent than an antibody “Y” indicates that antibody “X” binds more tightly (e.g., has a lower dissociation constant) to an Fc receptor than antibody “Y” in binding assays (e.g., as described herein and/or as commonly known in the art) under substantially the same conditions. In another example, the statement that an antibody “X” binds to a target (e.g., a cell surface protein, such as CD94) with a greater affinity than an antibody “Y” indicates that antibody “X” binds more tightly (e.g., has a lower dissociation constant) to a target (e.g., a cell surface protein, such as CD94) than antibody “Y” in binding assays (e.g., as described herein and/or as commonly known in the art) under substantially the same conditions.

(ii) Reduced Fucosylation

[0227] In some embodiments, an antibody of the present disclosure is non-fucosylated or fucose-deficient, e.g., a glycosylation antibody variant comprising an Fc region wherein a carbohydrate structure attached to the Fc region has reduced fucose or lacks fucose. In some embodiments, an antibody with reduced fucose or lacking fucose has improved ADCC function. Non-fucosylated or fucose-deficient antibodies have reduced fucose relative to the amount of fucose on the same antibody produced in a cell line. In some embodiments, a non-fucosylated or fucose-deficient antibody composition of the present disclosure is a composition in which less than about 50% of the N-linked glycans attached to the Fc region of the antibodies in the composition comprise fucose.

[0228] In some embodiments, fucosylation or fucosylated refers to fucose residues within the oligosaccharides attached to the peptide backbone of an antibody of the present disclosure. Specifically, a fucosylated antibody comprises α (1,6)-linked fucose at the innermost N-acetylglucosamine (GlcNAc) residue in one or both of the N-linked oligosaccharides attached to the antibody Fc region, e.g., at position Asn 297 of the human IgG1 Fc domain (EU numbering of Fc region residues). Asn297 may also be located about + 3 amino acids upstream or downstream of position 297, i.e., between positions 294 and 300, due to minor sequence variations in immunoglobulins.

[0229] In some embodiments, a degree of fucosylation is a percentage of fucosylated oligosaccharides relative to all oligosaccharides, e.g., as identified by methods known in the art, such as in an N-glycosidase F treated antibody composition assessed by matrix-assisted laser desorption-ionization time-of-flight mass spectrometry (MALDI-TOF MS). In a composition of a fully fucosylated antibody, at least 90% or essentially all oligosaccharides comprise fucose residues, *i.e.* are fucosylated. Accordingly, an individual antibody in such a composition typically comprises fucose residues in each of the two N-linked oligosaccharides in the Fc region. In some embodiments, in a composition of a fully non-fucosylated antibody, less than about 10% or essentially none of the oligosaccharides are fucosylated, and an individual antibody in such a composition does not contain fucose residues in either of the two N-linked oligosaccharides in the Fc region. In a composition of a partially fucosylated antibody, only part of the oligosaccharides comprise fucose. An individual antibody in such a composition can comprise fucose residues in none, one or both of the N-linked oligosaccharides in the Fc region, provided that the composition does not comprise essentially all individual antibodies that lack fucose residues in the N-

linked oligosaccharides in the Fc region, nor essentially all individual antibodies that contain fucose residues in both of the N-linked oligosaccharides in the Fc region. In one embodiment, a composition of a partially fucosylated antibody has a degree of fucosylation of about 10% to about 80% (e.g., about 50% to about 80%, about 60% to about 80%, or about 70% to about 80%).

[0230] In some embodiments, a glycosylation antibody variant comprises an Fc region, wherein a carbohydrate structure attached to the Fc region lacks fucose. Such variants have improved ADCC function. Examples of defucosylated or fucose-deficient antibodies are described in: US 2003/0157108; WO 2000/61739; WO 2001/29246; US 2003/0115614; US 2002/0164328; US 2004/0093621; US 2004/0132140; US 2004/0110704; US 2004/0110282; US 2004/0109865; WO 2003/085119; WO 2003/084570; WO 2005/035586; WO 2005/035778; WO2005/053742; Okazaki et al. J. Mol. Biol. 336:1239-1249 (2004); Yamane-Ohnuki et al. Biotech. Bioeng. 87: 614 (2004).

[0231] Antibodies with reduced fucosylation, or antibodies that are non-fucosylated may be produced using any method known in the art. In some embodiments of the antibodies of the disclosure, at least one or two of the heavy chains of the antibody can be non-fucosylated. For example, antibodies of the disclosure with reduced fucosylation, or antibodies of the disclosure that are non-fucosylated may be produced in a cell line having a α 1,6-fucosyltransferase (Fut8) knockout, and/or overexpressing β 1,4-N-acetylglycosaminyltransferase III (GnT-III), and/or overexpressing Golgi μ -mannosidase II (ManII). Antibodies with reduced fucosylation, or antibodies that are non-fucosylated may also be generated using a cell line that is deficient for 'FUT8', α -1,6 fucosyltransferase, which catalyzes the transfer of fucose; using Chinese hamster ovary (CHO) cells, e.g., that are deficient in FUT8 (Yamane-Ohnuki et al., 2004); or using small interfering RNAs (siRNAs) to block the expression of the FUT8 gene (Mori et al., 2004). Other cell lines that may be used to produce non-fucosylated or defucosylated antibodies or antibodies with reduced fucosylation are known in the art, e.g., include Lec13 CHO cells deficient in protein fucosylation (Ripka et al. Arch. Biochem. Biophys. 249:533-545 (1986); US Pat Appl No US 2003/0157108 A1, Presta, L; and WO 2004/056312 A1, Adams et al., especially at Example 11), and knockout cell lines, such as α -1,6-fucosyltransferase gene, FUT8, knockout CHO cells (Yamane-Ohnuki et al. Biotech. Bioeng. 87: 614 (2004)), and cells overexpressing β 1,4-N-acetylglycosaminyltransferase III (GnT-III) and Golgi μ -mannosidase II (ManII).

[0232] In some embodiments, antibodies of the present disclosure have reduced fucose relative to the amount of fucose on the same antibody produced in a wild-type CHO cell. For example, an antibody can have a lower amount of fucose than it would otherwise have if produced by native CHO cells (e.g., a CHO cell that produce a native glycosylation pattern, such as, a CHO cell containing a native FUT8 gene). In some embodiments, an antibody provided herein is one wherein less than about 50%, 40%, 30%, 20%, 10%, 5% or 1% of the N-linked glycans thereon comprise fucose. In certain embodiments, an antibody provided herein is one wherein none of the N-linked glycans thereon comprise fucose, i.e., wherein the antibody is completely without fucose, or has no fucose, or is non-fucosylated, or is afucosylated. The amount of fucose can be determined by one of skill in the art, e.g., by calculating the average amount of

fucose within the sugar chain at Asn297, relative to the sum of all glycostructures attached to Asn297 (e.g., complex, hybrid and high mannose structures) as measured by MALDI-TOF mass spectrometry, as described in WO 2008/077546, for example. Asn297 refers to the asparagine residue located at about position 297 in the Fc region (Eu numbering of Fc region residues); however, Asn297 may also be located about ± 3 amino acids upstream or downstream of position 297, i.e., between positions 294 and 300, due to minor sequence variations in antibodies. In some embodiments, at least one or two of the heavy chains of the antibody is non-fucosylated.

[0233] Antibodies lacking 1,6-fucose on their heavy chain glycosylation may have enhanced binding affinity to the Fc γ RIII receptor and increased ADCC activity (*see, e.g.*, Shields et al., 2002; Shinkawa et al., 2002; Okazaki, 2004; Dall'Ozzo, 2004). In some embodiments, the antibodies provided herein include an Fc region with modifications including reduced fucosylation, non-fucosylation, and/or mutations that enhance ADCC activities and/or improve affinity of the Fc region for Fc receptors such as Fc γ RIII and CD16 (e.g., CD16a). In some embodiments, the molecules (e.g., the antibodies provided herein) induce antibody directed cell cytotoxicity (ADCC) and deplete or reduce the number of NK cells and/or T cells that express CD94 to a higher extent over a fucosylated or wild type antibody.

[0234] In some embodiments, an antibody of the disclosure is engineered to improve ADCC activity by reducing fucosylation. In some embodiments, the molecules provided herein (e.g., the antibodies provided herein) can induce antibody directed cell cytotoxicity (ADCC) and deplete or reduce number of NK cells and/or T cells that express CD94 to a higher extent than a fucosylated or wild type antibody. In some embodiments, at least one or two of the heavy chains of an antibody of the disclosure are non-fucosylated. In some embodiments, an antibody of the disclosure is modified such that the carbohydrates of the antibody are non-fucosylated. In some embodiments, an antibody of the disclosure is modified such that less than about 90%, e.g., less than any of about 90%, about 80%, about 70%, about 60%, about 50%, about 40%, about 30%, about 20%, about 10%, about 5%, or about 1%, of the carbohydrates of the antibody contain fucose. In some embodiments, an antibody of the disclosure is modified such that less than about 40% of the carbohydrates of the antibody contain fucose. In some embodiments, the antibodies provided herein are non-fucosylated.

[0235] In some embodiments, the molecules (e.g., antibodies) provided herein induce antibody directed cell cytotoxicity (ADCC) and deplete or reduce the number of NK cells and/or T cells that express CD94 to a higher extent over a fucosylated or wild type antibody.

(iii) Mutations that Enhance ADCC Activity

[0236] An antibody of the disclosure may comprise a variant Fc region. In some embodiments, the variant Fc region includes at least one amino acid substitution in the Fc region that improves ADCC activity. For example, an antibody of the disclosure may have a variant IgG1 Fc region which comprises one or more of the Fc mutations selected from S239D, A330L, I332E, F243L and G236A. In another example, an antibody of the disclosure may have a human IgG1 Fc variant region which comprises one or more of the Fc mutations selected from S239D, A330L, I332E, F243L and G236A. Other amino acid

substitutions that are known to enhance ADCC activity may be used, for example, as described in Lazar et al., PNAS 103, 4005–4010 (2006); Shields et al., J. Biol. Chem. 276, 6591–6604 (2001); Stewart et al., Protein Engineering, Design and Selection 24, 671–678 (2011), and Richards et al., Mol Cancer Ther 7, 2517–2527 (2008).

(iv) *Reduced Internalization*

[0237] In some embodiments, an antibody of the disclosure has a low degree of internalization, e.g., receptor-induced internalization or target internalization (i.e., internalization of surface expressed CD94), e.g., as compared to a wild type control antibody, or an antibody known in the art or commercially available for the same target. Antibodies with lower internalization have a higher receptor (e.g., CD94) occupancy on the cell surface and higher level of the receptor-antibody complexes on the cell surface, which may enhance ADCC activity. An antibody of the disclosure may be tested *in vitro* for its internalization capabilities. An antibody of the disclosure may be tested in an *ex vivo* assay, e.g., using PBMCs and/or NK cells, for its internalization capabilities, e.g., as described in the Examples. The internalization of the target (e.g., CD94) may be expressed as the percent decrease in mean fluorescence intensity (MFI) over a period of time using a flow cytometry-based assay, e.g., as described in the Examples. For example, the internalization of the target (i.e., the internalization capabilities of an antibody of the disclosure) may be expressed as the percent decrease in MFI, calculated by computing the difference in MFI over a 24 hour period (e.g., between 0.5 and 24 hours) in cells incubated with the antibody at 37 degrees Celsius, and multiplying by 100, e.g., as described in the Examples.

[0238] In some embodiments, an antibody has a high degree of internalization if it results in an MFI decrease of greater than 50%, calculated by computing the difference in MFI over a 24 hour period (e.g., between 0.5 and 24 hours) in cells incubated with antibody at 37°C, and multiplying by 100, as measured by an *ex vivo* assay, e.g., using PBMCs and/or NK cells, as described in the Examples. In some embodiments, an antibody has a high degree of internalization if incubating the antibody with a cell expressing human CD94 on its surface for 24 hours at 37°C results in a decrease in surface antibody staining of greater than 50% due to internalization, assessed using methods known in the art and/or as described above.

[0239] In some embodiments, an antibody has a low degree of internalization if it results in an MFI decrease of less than 50% (e.g., any of about 50% or less, 45% or less, 40% or less, 35% or less, 30% or less, 25% or less, 20% or less, 15% or less, 10% or less, 5% or less, 1% or less, or 0%), calculated by computing the difference in MFI over a 24 hour period (e.g., between 0.5 and 24 hours) in cells incubated with antibody at 37°C, and multiplying by 100, as measured by an *ex vivo* assay, e.g., using PBMCs and/or NK cells, as described in the Examples. In some embodiments, an antibody of the disclosure has a low degree of internalization and results in an MFI decrease of about 50% or less, about 40% or less, about 35% or less, about 30% or less, about 25% or less, about 20% or less, about 15% or less, about 10% or less, about 5% or less, about 2.5% or less, about 1% or less, or about 0%, calculated as described above. In some embodiments, an antibody has a low degree of internalization if incubating the antibody

with a cell expressing human CD94 on its surface for 24 hours at 37°C results in a decrease in surface antibody staining of less than 50% due to internalization, assessed using methods known in the art and/or as described above.

[0240] In some embodiments, an antibody of the disclosure has or results in internalization activity that is at least about 5%, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 99%, or about 100% lower the internalization of a control antibody, e.g., a commercial or wild type control antibody, or an isotype control antibody, wherein internalization is assessed as described above and/or using any suitable method known in the art.

[0241] Antibody candidates with no or low internalization activity may be further tested for binding to a target from cynomolgus monkeys and/or from humans (e.g., cynomolgus and/or human CD94).

Antibodies that bind to a cynomolgus monkey and/or human target may be used for cell killing assays (e.g., ADCC assays) in vitro and in vivo. The cell killing activity (e.g., ADCC activity) of the selected antibodies may be compared to the commercially available antibodies or antibodies known in the art.

E. Generation of Antibodies

[0242] An antibody of the disclosure may be generated using any technologies and/or methods known in the art. Techniques for preparing antibodies, e.g., monoclonal antibodies (mAbs), against virtually any target antigen are well known in the art. See, for example, Köhler and Milstein, *Nature* 256: 495 (1975), and Coligan et al. (eds.), *CURRENT PROTOCOLS IN IMMUNOLOGY*, VOL. 1, pages 2.5.1-2.6.7 (John Wiley & Sons 1991). Briefly, monoclonal antibodies can be obtained by injecting mice with a composition comprising an antigen (e.g., CD94, or a part thereof), removing the spleen to obtain B-lymphocytes, fusing the B-lymphocytes with myeloma cells to produce hybridomas, cloning the hybridomas, selecting positive clones which produce antibodies to the antigen, culturing the clones that produce antibodies to the antigen, and isolating the antibodies from the hybridoma cultures. The person of ordinary skill will realize that where antibodies are to be administered to human subjects, the antibodies will bind to human antigens (e.g., human CD94, or a part thereof).

[0243] MAbs can be isolated and purified from hybridoma cultures by a variety of well-established techniques. Such isolation techniques include affinity chromatography with Protein-A or Protein-G Sepharose, size-exclusion chromatography, and ion-exchange chromatography. See, for example, Coligan at pages 2.7.1-2.7.12 and pages 2.9.1-2.9.3. Also, see Baines et al., "Purification of Immunoglobulin G (IgG)," in *METHODS IN MOLECULAR BIOLOGY*, VOL. 10, pages 79-104 (The Humana Press, Inc. 1992).

[0244] After the initial raising of antibodies to the immunogen (e.g., CD94, or a part thereof), the antibodies can be sequenced and subsequently prepared by recombinant techniques. Humanization and chimerization of murine antibodies and antibody fragments are well known to those skilled in the art, as discussed below.

[0245] In an exemplary method of generating an antibody of the disclosure, recombinant targets (e.g., CD94) may be utilized for immunization of mice. Antibodies generated following immunization of mice, e.g., as described above, may be analyzed for specific or selective binding to its target (e.g., CD94) by ELISA and flow cytometry. Antibodies may be selected based on their ability to bind to a target (e.g., CD94).

[0246] In some embodiments, non-human primate antibodies may be generated. General techniques for raising therapeutically useful antibodies in baboons may be found, for example, in Goldenberg et al., WO 91/11465 (1991), and in Losman et al., Int. J. Cancer 46: 310 (1990).

[0247] In some embodiments, an antibody may be a human antibody. In some embodiments, an antibody may be a monoclonal human antibody. In some embodiments, a human antibody possesses an amino acid sequence which corresponds to that of an antibody produced by a human or a human cell or derived from a non-human source that utilizes human antibody repertoires or other human antibody-encoding sequences. Such antibodies may be obtained from transgenic mice that have been engineered to produce specific human antibodies in response to antigenic challenge e.g., CD94, or a part thereof. Methods for producing fully human antibodies using either combinatorial approaches or transgenic animals transformed with human immunoglobulin loci are known in the art (e.g., Mancini et al., 2004, New Microbiol. 27:315-28; Conrad and Scheller, 2005, Comb. Chem. High Throughput Screen. 8:117-26; Brekke and Loset, 2003, Curr. Opin. Pharmacol. 3:544-50). In certain embodiments, the claimed methods and procedures may utilize human antibodies produced by such techniques. Other methods of producing fully human antibodies include phage display, e.g., as described in Dantas-Barbosa et al., 2005, Genet. Mol. Res. 4:126-40, generation of antibodies in normal humans or from humans that exhibit a particular disease state, e.g., as described in Dantas-Barbosa et al., 2005, or using transgenic animals (e.g., mice) that have been genetically engineered to produce human antibodies using standard immunization protocols as discussed above, e.g., as described in Green et al., 1999, J. Immunol. Methods 231:11-23, Green et al., Nature Genet. 7:13 (1994), Lonberg et al., Nature 368:856 (1994), and Taylor et al., Int. Immun. 6:579 (1994).

(i) In Vitro Cell Killing Assays

[0248] Generation of an antibody of the disclosure may involve testing the *in vitro* ADCC activity of the antibody. The improved cell killing or ADCC activity of an antibody of the disclosure may be tested as described above, as described in the Examples, and/or using methods known in the art. The improved cell killing or ADCC activity of an antibody of the disclosure may be tested for depletion of NK cells and/or T cells that express CD94. Depletion of NK cells and/or T cells that express CD94 may be tested using an exemplary *in vitro* model that recapitulates activity in humans (Tomasevic, et al, Growth Factors, 2014; 32(6): 223–235; Huang, et al, JCI insight, 2016;1(7):e86689). Peripheral blood lymphocytes (PBL) isolated from the blood of normal (i.e., healthy) donors are incubated with antibodies that have a human Fc region with and without fucose and/or with and without Fc region mutations. The level of killing of NK cells and/or T cells that express CD94 in the PBLs (e.g., in a PBL sample) is measured using any

method known in the art, such as flow cytometry (e.g., as described in the Examples). The cell killing activity (e.g., ADCC activity) of antibodies may be tested as described above, e.g., using the assay described above, using a variety of biospecimens such as blood, synovial fluid, bone marrow and spleen intact cell homogenates from patients with diseases such as NK/T cell lymphomas, e.g., extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL (not otherwise specified), angioimmunoblastic TCL, adult TCL, chronic lymphoproliferative disorder of NK cells (CLPD-NK), LGL leukemia, Felty's syndrome, CLPD-NK, IBM and RA with LGL and/or aggressive NK leukemia.

[0249] In addition to the cell killing assay described above, *in vitro* ADCC and antibody-dependent cellular phagocytosis (ADCP) assays using antibodies of the disclosure, purified target cells (e.g., NK cells and/or T cells that express CD94), and/or effector cells such as NK cells or monocytes/macrophages may be performed to assay the cell killing, ADCC and/or ADCP activity of antibodies of the disclosure. Cell killing, ADCC and/or ADCP assays, and other assay methods known in the art may be used, for example, as described in Kolbeck et al., J Allergy Clin Immunol. 2010;125(6):1344-1353.e2; Gomez-Roman et al., J. Immunol. Methods, 2006, 308, pp. 53-67; and Ackerman et al., J. Immunol. Methods, 2011, 366, pp. 8-19. The *in vitro* activity of an antibody of the disclosure may be compared to a commercially available antibody or an antibody known in the art against the same target.

(ii) In Vivo Cell Killing Assays

[0250] Generation of an antibody of the disclosure may involve testing the *in vivo* ADCC activity of the antibody, e.g., to show activity of the selected antibody candidates *in vivo* for depletion or reduction in the levels of NK cells and/or T cells that express CD94. The *in vivo* cell killing activity (e.g., ADCC and/or ADCP activity) of an antibody of the disclosure may be determined using any method known in the art. For example, the ability of an antibody of the disclosure to deplete or reduce NK cells and/or T cells that express CD94 *in vivo* may be tested in cynomolgus monkeys using methods known in the art. For example, in an exemplary method to test the *in vivo* cell killing activity (e.g., ADCC and/or ADCP activity) of an antibody of the disclosure, a cohort of cynomolgus monkeys are bled one day prior to administration of a single dose of an antibody of the disclosure, e.g., antibody treatment, to identify the pre-dose levels of NK cells and/or T cells that express CD94 by flow cytometry. After administration of an antibody of the disclosure, e.g., upon treatment with antibodies of the disclosure, the monkeys are bled at the following time points: 1 hour, 1 day, 7 days, 14 days and 30 days. The levels of NK cells and/or T cells that express CD94 in blood and other biospecimens such as synovial fluids, bone marrow and spleen are determined by flow cytometry at each of the time points. The *in vivo* activity of an antibody of the disclosure may be compared to a commercially available antibody or an antibody known in the art against the same target. An anti-CD94 antibody of the disclosure may be compared to anti-CD94 antibody clones DX22, HP-3D9, HP-3B1, 131412, or 12K45.

[0251] A skilled artisan will readily appreciate that other methods known in the art for testing ADCC activity *in vivo* may be used to assay the *in vivo* ADCC activity of antibodies of the disclosure (e.g., transgenic animals such as transgenic mice).

[0252] Other known antibodies against the target (e.g., CD94) may also be used in the methods provided herein. For example, an anti-CD94 antibody of the disclosure may be tested (e.g., for *in vitro* or *in vivo* ADCC activity, or for any other characteristic described herein) together with the following anti-CD94 antibodies: HP-3D9 (LSBio Catalog # LS-C134679-100; Abnova Catalog #: MAB6947); 2I2; 131412 (R&D Systems Catalog #: MAB1058); 13B146 (US Biological Catalog #: 030068); 13B147 (US Biological Catalog #: 030069); 1H1 (Abnova Catalog #: MAB10543); 3G2 (Biorbyt Catalog #: orb69389); DX22 (Biolegend Catalog # 305502); REA113 (Miltenyi Biotec Catalog #: 130-098-967); KP43; EPR21003; AT13E3 (ATGen Catalog: ATGA0487); HP-3B1; 12K45; and B-D49.

(iii) *Humanization*

[0253] An antibody of the disclosure may be humanized according to any method known in the art. In some embodiments, a humanized antibody is a chimeric antibody comprising amino acid residues from non-human hypervariable regions (HVRs) and amino acid residues from human framework regions (FRs). In certain embodiments, a humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the HVRs (e.g., CDRs) correspond to those of a non-human antibody, and all or substantially all of the FRs correspond to those of a human antibody. A humanized antibody optionally may comprise at least a portion of an antibody constant region derived from a human antibody. In some embodiments, a humanized form of an antibody, e.g., a non-human antibody, refers to an antibody that has undergone humanization.

[0254] For example, a monoclonal antibody may be humanized by transferring mouse CDRs from the heavy and light variable chains of a mouse immunoglobulin into the corresponding variable domains of a human antibody. The mouse framework regions (FR) in the chimeric monoclonal antibody may also be replaced with human FR sequences. To preserve the stability and antigen specificity of the humanized monoclonal antibody, one or more human FR residues may be replaced by the mouse counterpart residues. Humanized monoclonal antibodies may be used for therapeutic treatment of subjects.

Techniques for the production of humanized monoclonal antibodies are well known in the art, e.g., as described in Jones et al., 1986, *Nature*, 321:522; Riechmann et al., *Nature*, 1988, 332:323; Verhoeyen et al., 1988, *Science*, 239:1534; Carter et al., 1992, *Proc. Nat'l Acad. Sci. USA*, 89:4285; Sandhu, *Crit. Rev. Biotech.*, 1992, 12:437; Tempest et al., 1991, *Biotechnology* 9:266; Singer et al., *J. Immun.*, 1993, 150:2844.

[0255] An antibody of the disclosure may have one or more of the characteristics described above, e.g., enhanced *in vitro* and/or *in vivo* cell killing activity (e.g., ADCC and/or ADCP activity), enhanced binding to one or more Fc receptors, reduced fucosylation or non-fucosylation, cross-reactivity (e.g., binding to human CD94 and to cynomolgus monkey CD94), lack of blocking of HLA-E binding to the CD94/NKG2A heterodimer, competition with commercially available antibodies (e.g., commercially

available anti-CD94 antibodies), low internalization, and/or desirable affinity for its target protein (e.g., CD94, human CD94, and/or cynomolgus CD94).

[0256] In some embodiments, an antibody of the disclosure is soluble at concentrations higher than about 10 mg/mL. In some embodiments, an antibody of the disclosure forms a low level of soluble aggregates (e.g., less than 5%, less than 4%, less than 3%, less than 2%, or less than 1% soluble aggregates). In some embodiments, an antibody of the disclosure has an ability to maintain binding to its target (e.g., CD94) during storage, e.g., for at least 1 week, at least 2 weeks, at least 3 weeks, at least 1 month, at least 2 months, at least 3 months, at least 4 months, or more, at any of about 2°C, about 3°C, about 4°C, about 5°C, about 6°C, about 7°C, about 8°C. In some embodiments, an antibody of the disclosure has stability (e.g., lack of degradation products, e.g., as measured by SDS-PAGE) during storage, e.g., for at least 1 week, at least 2 weeks, at least 3 weeks, at least 1 month, at least 2 months, at least 3 months, at least 4 months, or more, at any of about 2°C, about 3°C, about 4°C, about 5°C, about 6°C, about 7°C, or about 8°C.

[0257] In some embodiments, an antibody of the disclosure is tested for toxicology. Toxicology analysis of an antibody of the disclosure may be carried out using any method known in the art. In an exemplary toxicology analysis, an antibody of the disclosure is tested for toxicity in cynomolgus monkeys at doses that are more than 5 times higher (e.g., any of about 5 times higher, about 10 times higher, about 15 times higher, about 20 times higher, about 25 times higher, about 30 times higher, about 35 times higher, about 40 times higher, about 45 times higher, about 50 times higher, about 55 times higher, about 60 times higher, about 65 times higher, about 70 times higher, about 75 times higher, about 80 times higher, about 85 times higher, about 90 times higher, about 95 times higher, about 100 times higher, or more) than the doses anticipated to be used in human subjects.

[0258] In some embodiments, an antibody of the disclosure is capable of depleting or reducing the level of NK cells and/or T cells that express CD94 *in vitro* and/or *in vivo*. Depletion or reduction in the level of NK cells and/or T cells that express CD94 may be measured using any method known in the art. For example, depletion of NK cells and/or T cells that express CD94 may be measured using a cell killing, ADCC, and/or ADCP assay, e.g., as described above and/or as described in the Examples.

[0259] In some embodiments, an antibody of the disclosure is soluble at concentrations higher than 10mg/mL, has low level of soluble aggregates (<5%), maintains its binding to the target as measured by ELISA (>90% potency), with no degradation products as measured by SDS PAGE when incubated for 3 months at 2-8°C. In some embodiments, toxicology analysis of an antibody of the disclosure can be performed in cynomolgus monkeys at doses that are more than 5 times higher than the doses anticipated to be used in human subjects.

[0260] In some embodiments, the antibodies that bind to CD94 may deplete or reduce the level of NK cells and/or T cells that express CD94 and may have clear benefits for patients (e.g., human patients) with diseases or disorders such as LGL leukemia, Rheumatoid arthritis, Felty's syndrome, CLPD-NK, aggressive NK leukemia, IBM, IBD, or an NK/T cell lymphoma, such as extranodal NK/T cell

lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL (not otherwise specified), angioimmunoblastic TCL, adult TCL, monomorphic epitheliotropic intestinal TCL, epidermotropic CD8+ cutaneous TCL, primary cutaneous gamma/delta TCL, or subcutaneous panniculitis TCL. In addition, the antibody treatment may have better tolerability and fewer side-effects over the first and second line of therapies including chemotherapy, such as cyclophosphamide, doxorubicin, vincristine, prednisone; stem cell transplant; splenectomy; Alemtuzumab; Bevacizumab; Pralatrexate; Avelumab; proteasome inhibitors such as Carfilzomib and Bortezomib; HDAC inhibitors such as Romidepsin, Belinostat, and Vorinostat; and antibody-drug conjugates such as Brentuximab vedotin. The antibody treatment may demonstrate more selective depletion of the disease-inducing cells compared to the current therapies that are non-selective. Non-limiting examples of diseases and disorders in which NK cells and/or T cells that express CD94 may play a role are: LGL leukemia, Rheumatoid arthritis, Felty's syndrome, CLPD-NK, aggressive NK leukemia, IBM, IBD, or an NK/T cell lymphoma, such as extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL (not otherwise specified), angioimmunoblastic TCL, adult TCL, monomorphic epitheliotropic intestinal TCL, epidermotropic CD8+ cutaneous TCL, primary cutaneous gamma/delta TCL, or subcutaneous panniculitis TCL. Accordingly, the invention provides a method of reducing the number of or depleting NK cells and/or T cells that express CD94 in a human subject upon administration of molecule that binds to CD94 and that comprises (a) a region that specifically binds to the target (e.g., CD94) and (b) an immunoglobulin Fc region.

II. Uses and Methods of Treatment

[0261] As discussed above, NK cells, CD4+ T cells, CD8+ T cells, and/or CD8+ and CD4+ T cells have been implicated in the pathogenesis of numerous diseases and disorders, such as NK/T cell lymphomas. Many of these disorders or diseases are characterized by a clonal expansion of NK cells and/or CD8+ and CD4+ T cells.

[0262] In some embodiments, provided herein are molecules (e.g., antibodies) that bind to CD94, e.g., expressed on the surface of NK cells and/or T cells. Also provided herein are molecules (e.g., antibodies) that bind to CD94 and that have reduced fucosylation, non-fucosylation (e.g., that have an immunoglobulin Fc part with modifications or mutations that reduce or eliminate fucosylation). Also provided herein are molecules (e.g., antibodies) that bind to CD94 and that have modifications or mutations that enhance ADCC activities and/or improve affinity of the Fc region to Fc receptors such as CD16 (e.g., CD16a). Also provided herein are molecules (e.g., antibodies) that bind to CD94 and that have one or more of the following characteristics: bind to human CD94 and cynomolgus CD94, do not block binding of HLA-E to the CD94/NKG2A heterodimer, have a low degree of internalization, are non-fucosylated or have reduced fucosylation, and/or induce, promote, or enhance ADCC activity.

[0263] In some embodiments, provided herein is a method for treating a disease or disorder in a subject, comprising administering to the subject an effective amount of an antibody described herein, that specifically binds to human CD94. In some embodiments, provided herein is a method for treating a disease or disorder in a subject, comprising administering to the subject an effective amount of an antibody that specifically binds to human CD94, wherein the antibody has one or more of the following characteristics: does not block binding of HLA-E to the CD94/NKG2A heterodimer, has a low degree of internalization, is non-fucosylated or has reduced fucosylation, and/or induces, promotes or enhances ADCC activity. In some embodiments, the disease or disorder is selected from chronic lymphoproliferative disorder of NK cells (CLPD-NK), LGL leukemia, Felty's syndrome, rheumatoid arthritis, aggressive NK leukemia, inclusion body myositis, inflammatory bowel disease, or an NK/T cell lymphoma, such as extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL (not otherwise specified), angioimmunoblastic TCL, adult TCL, monomorphic epitheliotropic intestinal TCL, epidermotropic CD8+ cutaneous TCL, primary cutaneous gamma/delta TCL, subcutaneous panniculitis TCL, or microscopic colitis. In some embodiments, administration of the antibody results in a reduction in the number of NK cells and/or T cells that express CD94. In some embodiments, administration of the antibody results in a reduction in the number of peripheral blood NK cells, CD8+, CD4+, or CD8+/CD4+ T cells, and/or LGL cells in the subject, e.g., that express CD94. In some embodiments, administration of the antibody results in a reduction in the number of peripheral blood LGL cells, e.g., that express CD94, in the subject. In some embodiments, administration of the antibody results in a reduction in the number of peripheral blood NK cells, e.g., that express CD94, in the subject. In some embodiments, administration of the antibody results in a reduction in the number of peripheral blood CD8+/CD4+ T cells, e.g., that express CD94, in the subject. In some embodiments, administration of the antibody results in a reduction in the number of peripheral blood CD8+ T cells, e.g., that express CD94, in the subject. In some embodiments, administration of the antibody results in a reduction in the number of peripheral blood CD4+ T cells, e.g., that express CD94, in the subject.

[0264] Also provided herein is a method for reducing the number of peripheral blood NK cells and/or T cells that express CD94, comprising administering to the subject an effective amount of an antibody of the disclosure that specifically binds to human CD94. In some embodiments, the antibody has one or more of the following characteristics: does not block binding of HLA-E to the CD94/NKG2A heterodimer, has a low degree of internalization, is non-fucosylated or has reduced fucosylation, and/or induces, promotes or enhances ADCC activity. In some embodiments, the subject has a disease or disorder selected from chronic lymphoproliferative disorder of NK cells (CLPD-NK), LGL leukemia, Felty's syndrome, rheumatoid arthritis, aggressive NK leukemia, inclusion body myositis, inflammatory bowel disease, or an NK/T cell lymphoma, such as extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL (not otherwise specified), angioimmunoblastic

TCL, adult TCL, monomorphic epitheliotropic intestinal TCL, epidermotropic CD8+ cutaneous TCL, primary cutaneous gamma/delta TCL, subcutaneous panniculitis TCL, or microscopic colitis. In some embodiments, administration of the antibody to the subject results in a reduction in the number of peripheral blood NK cells and/or T cells that express CD94 compared to prior to administration of the antibody.

[0265] Also provided herein is a method for inducing ADCC activity in a subject, comprising administering to the subject an effective amount of an antibody of the disclosure that specifically binds to human CD94. In some embodiments, the antibody has one or more of the following characteristics: does not block binding of HLA-E to the CD94/NKG2A heterodimer, has a low degree of internalization, is non-fucosylated or has reduced fucosylation, and/or induces, enhances or promotes ADCC activity. In some embodiments, the subject has a disease or disorder selected from chronic lymphoproliferative disorder of NK cells (CLPD-NK), LGL leukemia, Felty's syndrome, rheumatoid arthritis, aggressive NK leukemia, inclusion body myositis, inflammatory bowel disease, or an NK/T cell lymphoma, such as extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL (not otherwise specified), angioimmunoblastic TCL, adult TCL, monomorphic epitheliotropic intestinal TCL, epidermotropic CD8+ cutaneous TCL, primary cutaneous gamma/delta TCL, subcutaneous panniculitis TCL, or microscopic colitis. In some embodiments, administration of the antibody to the subject results in a reduction in the number of peripheral blood NK cells and/or T cells that express CD94 compared to prior to administration of the antibody.

[0266] In some embodiments, the disease or disorder is CLPD-NK. In some embodiments, the disease or disorder is LGL leukemia. In some embodiments, the disease or disorder is Felty's syndrome. In some embodiments, the disease or disorder is rheumatoid arthritis. In some embodiments, the disease or disorder is aggressive NK leukemia. In some embodiments, the disease or disorder is inclusion body myositis. In some embodiments, the disease or disorder is inflammatory bowel disease. In some embodiments, the disease or disorder is T- large granular lymphocyte leukemia (T-LGLL). In some embodiments, the disease or disorder is Natural Killer-large granular lymphocyte leukemia (NK-LGLL). In some embodiments, the disease or disorder is an NK/T cell lymphoma. In some embodiments, the disease or disorder is extranodal NK/T cell lymphoma. In some embodiments, the disease or disorder is hepatosplenic T cell lymphoma (TCL). In some embodiments, the disease or disorder is enteropathy-associated TCL. In some embodiments, the disease or disorder is cutaneous TCL. In some embodiments, the disease or disorder is anaplastic large cell lymphoma (ALK+). In some embodiments, the disease or disorder is anaplastic large cell lymphoma (ALK-). In some embodiments, the disease or disorder is peripheral TCL (not otherwise specified). In some embodiments, the disease or disorder is angioimmunoblastic TCL. In some embodiments, the disease or disorder is adult TCL. In some embodiments, the disease or disorder is monomorphic epitheliotropic intestinal TCL. In some embodiments, the disease or disorder is epidermotropic CD8+ cutaneous TCL. In some embodiments, the

disease or disorder is primary cutaneous gamma/delta TCL. In some embodiments, the disease or disorder is subcutaneous panniculitis TCL. In some embodiments, the disease or disorder is microscopic colitis.

[0267] Also provided herein is a method for treating CLPD-NK in a human subject in need thereof, comprising administering to the human subject an effective amount of an antibody of the disclosure, wherein the antibody specifically binds to human CD94. In some embodiments, administration of the antibody to the human subject results in an improvement of CLPD-NK symptoms in the human.

[0268] Also provided herein is a method for treating NK/T cell lymphoma in a human subject in need thereof, comprising administering to the human subject an effective amount of an antibody of the disclosure, wherein the antibody specifically binds to human CD94. In some embodiments, administration of the antibody to the human subject results in an improvement of NK/T cell lymphoma symptoms in the human. In some embodiments, the NK/T cell lymphoma is selected from extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL (not otherwise specified), angioimmunoblastic TCL, adult TCL, monomorphic epitheliotropic intestinal TCL, epidermotropic CD8+ cutaneous TCL, primary cutaneous gamma/delta TCL, or subcutaneous panniculitis TCL.

[0269] Also provided herein is a method for treating CLPD-NK in a human subject in need thereof, comprising administering to the human subject an effective amount of an antibody of the disclosure, wherein the antibody specifically binds to human CD94, wherein the antibody has one or more of the following characteristics: does not block binding of HLA-E to the CD94/NKG2A heterodimer, has a low degree of internalization, is non-fucosylated or has reduced fucosylation, and/or induces, enhances or promotes ADCC activity. In some embodiments, administration of the antibody to the human subject results in an improvement of CLPD-NK symptoms in the human.

[0270] Also provided herein is a method for treating NK/T cell lymphoma in a human subject in need thereof, comprising administering to the human subject an effective amount of an antibody of the disclosure, wherein the antibody specifically binds to human CD94, wherein the antibody has one or more of the following characteristics: does not block binding of HLA-E to the CD94/NKG2A heterodimer, has a low degree of internalization, is non-fucosylated or has reduced fucosylation, and/or induces, enhances, or promotes ADCC activity. In some embodiments, administration of the antibody to the human subject results in an improvement of NK/T cell lymphoma symptoms in the human. In some embodiments, the NK/T cell lymphoma is selected from extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL (not otherwise specified), angioimmunoblastic TCL, adult TCL, monomorphic epitheliotropic intestinal TCL, epidermotropic CD8+ cutaneous TCL, primary cutaneous gamma/delta TCL, or subcutaneous panniculitis TCL. In some embodiments, the NK cell or T-cell lymphoma is extranodal NK/T cell lymphoma, hepatosplenic TCL, or enteropathy-associated TCL.

In some embodiments, the NK cell or T-cell lymphoma is characterized by NK cells and/or T cells expressing CD94 (*e.g.*, human CD94).

[0271] Also provided herein is a method for treating microscopic colitis in a human subject in need thereof, comprising administering to the human subject an effective amount of an antibody of the disclosure, wherein the antibody specifically binds to human CD94, wherein the antibody has one or more of the following characteristics: does not block binding of HLA-E to the CD94/NKG2A heterodimer, has a low degree of internalization, is non-fucosylated or has reduced fucosylation, and/or induces, enhances, or promotes ADCC activity. In some embodiments, administration of the antibody to the human subject results in an improvement of microscopic colitis symptoms in the human. Microscopic colitis is a gastrointestinal disease characterized by inflammation of the colon leading to persistent non-bloody, watery diarrhea. It is termed microscopic because tissue destruction can only be seen under a microscope, not through gross examination. The colon in these patients appear macroscopically normal or have near normal colonic mucosa. Two subtypes of microscopic colitis currently exists: Collagenous colitis, which is characterized by the buildup of a layer of collagen in the intestinal lining and Lymphocytic colitis, which is characterized by an increase in lymphocytes in colon tissue. It currently affects 100/100,000 individuals worldwide, of which 39.3% of the cases are of the lymphocytic subtype (Hisamatsu et al. (2016) *Inflamm. Intest. Dis.* 2:52-62). The current causes of microscopic colitis are unknown, but common factors include medication, bacterial and viral infections, autoimmune disease such as rheumatoid arthritis, celiac disease or psoriasis and buildup of bile acid. Current methods for diagnosis is histological examination of intestinal tissue, as the disease cannot be diagnosed without histopathological examination of biopsy material. Common symptoms of microscopic colitis include persistent, watery diarrhea, resulting in weight loss, bloating, anemia, malnourishment, etc. There is no cure or proper treatment for microscopic colitis except anti-diarrhetic medication, low-fat, low-fiber and low-dairy diet, steroids, bile acid blockers, anti-inflammatory meds, TNF inhibitors or in the rarest circumstances surgery to remove part or all of the colon. Although it is not clear what are the major disease-causing cells in microscopic colitis, studies have shown that there are elevations in the CD8+ intraepithelial lymphocytes (IELs) in the colon of microscopic colitis patients (Goranzon et al. (2013) *J. Crohns Colitis* 7:e434-442). There is evidence in the literature to suggest that CD94 is highly expressed on IELs in microscopic colitis (Barmeyer et al. (2016) *Inflamm. Bowel Dis.* 22:539-547). Without wishing to be bound to theory, it is thought that anti-CD94 (*e.g.*, a non-fucosylated IgG1 antibody) could execute ADCC on the IEL cells via fratricide. The literature has also suggested that CD16 is highly elevated in microscopic colitis biopsies vs. normal controls, suggesting that IELs may engage anti-CD94 to induce ADCC on other IEL cells (Barmeyer et al. (2016) *Inflamm. Bowel Dis.* 22:539-547). Without wishing to be bound to theory, it is thought that the IEL cells are cytotoxic and could serve as an effector as well as target cells.

[0272] Also provided herein is a method for enhancing chimeric antigen receptor T cell (CAR-T) therapy in a human subject in need thereof, comprising administering to the human subject an effective amount of an antibody of the disclosure prior to administration of a CAR-T treatment to the subject,

wherein the antibody specifically binds to human CD94, wherein the antibody has one or more of the following characteristics: does not block binding of HLA-E to the CD94/NKG2A heterodimer, has a low degree of internalization, is non-fucosylated or has reduced fucosylation, and/or induces, enhances, or promotes ADCC activity. In some embodiments, administration of the antibody to the human subject results in depletion of NK cells in the subject prior to administration of the CAR-T treatment. In some embodiments, the CAR-T therapy is for treatment of cancer, *i.e.*, the subject has/is being treated for cancer. The short half-life of CAR-T cells for the treatment of various hematological and solid cancers significantly hampers the development of cell therapy. Lymphodepleting chemotherapy is commonly used prior to CAR-T treatments such as cyclophosphamide with or without fludarabine (Flu). However, these standard chemotherapies do not adequately deplete NK cells, resulting in elimination of off the shelf CAR-T cells shortly after infusion. Without wishing to be bound to theory, it is thought that anti-CD94 antibody treatment could potentially transiently deplete NK cells to enable engraftment of HLA class I-deficient cells ("universal CAR T cells") or organs to prevent NK cell-mediated rejection. Transient depletion of NK cells should provide a window for engraftment of HLA class I-negative cells and pose no safety risk. After CD94 depleting antibodies are gone, NK cell numbers could return to normal. Newly arising NK cells should become tolerant to the transferred HLA class I-negative cells (based on mixed bone marrow chimera experiments). Thus, anti-CD94 antibody treatment could provide an opportunity for enhancing CAR-T therapy, *e.g.*, in cancer patients.

[0273] In some embodiments, the terms treat, treating, treatment, ameliorate, ameliorating, reducing one or more symptoms, reducing symptoms, reduce one or more symptoms, reduce symptoms, and other grammatical equivalents, refer to alleviating, abating or ameliorating one or more symptoms of a disease or disorder, preventing additional symptoms, ameliorating or preventing the underlying causes of symptoms, inhibiting the disease or disorder, *e.g.*, arresting the development of the disease or disorder, relieving the disease or disorder, causing regression of the disease or disorder, relieving a condition caused by the disease or disorder, or stopping the symptoms of the disease or disorder, and are intended to include prophylaxis. In some embodiments, the terms further include achieving a therapeutic benefit and/or a prophylactic benefit. In some embodiments, a therapeutic benefit refers to eradication or amelioration of the underlying disease or disorder being treated. Also, a therapeutic benefit is achieved with the eradication or amelioration of one or more of the physiological symptoms associated with the underlying disease or disorder such that an improvement is observed in the patient, notwithstanding that, in some embodiments, the patient is still afflicted with the underlying disease or disorder. For prophylactic benefit, the pharmaceutical compositions are administered to a patient at risk of developing a particular disease or disorder, or to a patient reporting one or more of the physiological symptoms of a disease or disorder, even if a diagnosis of the disease or disorder has not been made.

[0274] In some embodiments, an effective amount, a therapeutically effective amount or pharmaceutically effective amount may be a sufficient amount of at least one pharmaceutical composition

or compound (e.g., an antibody of the disclosure) being administered which will relieve to some extent one or more of the symptoms of the disease or condition being treated.

[0275] In some embodiments, the reduction in the number of peripheral blood NK cells and/or T cells that express CD94 in the subject occurs within the first 24 hours, e.g., any of within about 1 hour, within about 2 hours, within about 3 hours, within about 4 hours, within about 5 hours, within about 6 hours, within about 7 hours, within about 8 hours, within about 9 hours, within about 10 hours, within about 11 hours, within about 12 hours, within about 13 hours, within about 14 hours, within about 15 hours, within about 16 hours, within about 17 hours, within about 18 hours, within about 19 hours, within about 20 hours, within about 21 hours, within about 22 hours, within about 23 hours, or within about 24 hours after administration of the antibody to the subject.

[0276] In some embodiments, the number of peripheral blood NK cells and/or T cells that express CD94 in the subject (e.g., in a peripheral blood sample obtained from the subject) is reduced to below the limit for clinical diagnosis of the disease or disorder. In some embodiments, the number of peripheral blood NK cells and/or T cells that express CD94 in the subject is reduced to less than or equal to 2×10^9 cells/L (e.g., in a peripheral blood sample obtained from the subject). See, e.g., Lamy, T. *et al.* (2017) *Blood* 129:1082-1094. In some embodiments, the reduction in the number of peripheral blood NK cells and/or T cells that express CD94 in the subject to below the limit for clinical diagnosis of the disease or disorder is present in the subject for at least about 1 week, e.g., any of at least about 1 week, at least about 2 weeks, at least about 3 weeks, at least about 4 weeks, at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, or more, after administration of the antibody to the subject. In some embodiments, the reduction in the number of peripheral blood NK cells and/or T cells that express CD94 in the subject to less than or equal to 2×10^9 cells/L in the subject (e.g., in a peripheral blood sample obtained from the subject) is present in the subject for at least about 1 week, e.g., any of at least about 1 week, at least about 2 weeks, at least about 3 weeks, at least about 4 weeks, at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, or more, after administration of the antibody to the subject.

[0277] In some embodiments, the number of peripheral blood NK cells and/or T cells that express CD94 in the subject is reduced to below the limit of detection for the peripheral blood NK cells and/or T cells that express CD94 in the subject. In some embodiments, the reduction in the number of peripheral blood NK cells and/or T cells that express CD94 in the subject to below the limit of detection for the peripheral blood NK cells and/or T cells that express CD94 is present in the subject for at least about 1 week, e.g., any of at least about 1 week, at least about 2 weeks, at least about 3 weeks, at least about 4 weeks, at least about 1 month, at least about 2 months, at least about 3 months, at least about 4 months, at least about 5 months, at least about 6 months, or more, after administration of the antibody to the subject. In some embodiments, peripheral blood NK cells and/or T cells that express CD94 are detected by flow cytometry (e.g., as performed on a peripheral blood sample from the subject).

[0278] In some embodiments, the peripheral blood NK cells that express CD94 are CD3+ CD56 bright. In some embodiments, the peripheral blood T cells that express CD94 are CD4+, CD8+, or CD8+ and CD4+.

[0279] In some embodiments, the reduction in the number of peripheral blood NK cells and/or T cells that express CD94 in the subject is reversible. In some embodiments, the reduction in the number of peripheral blood NK cells and/or T cells that express CD94 in the subject is reversible within any of about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, or more, after administration of the antibody to the subject.

[0280] In some embodiments, a statement that a cell or a population of cells is positive (+) for, or expresses a particular marker (e.g., CD3, CD4, CD8, CD16, CD94, NKG2A, etc.), refers to the detectable presence on or in the cell of the particular marker. In some embodiments, a statement that a cell or a population of cells is positive for, +, or expresses a surface marker (e.g., a cell surface protein) refers to the presence of cell surface expression of the particular marker, for example, as detected by flow cytometry, for example, by staining with an antibody that specifically binds to the marker and detecting said antibody, wherein the staining is detectable by flow cytometry at a level substantially above the staining detected carrying out the same procedure with an isotype-matched control and/or fluorescence minus one (FMO) gating control under otherwise identical conditions, and/or at a level substantially similar to that for cell known to be positive for the marker, and/or at a level substantially higher than that for a cell known to be negative for the marker.

[0281] In some embodiments, a statement that a cell or a population of cells is negative (-) for, or does not express a particular marker (e.g., CD3, CD4, CD8, CD16, CD94, NKG2A, etc.) refers to the absence of a detectable presence on or in the cell of the particular marker. In some embodiments, a statement that a cell or a population of cells is negative for, -, or does not express a surface marker (e.g., a cell surface protein) refers to the absence of cell surface expression of the particular marker, for example, as detected by flow cytometry, for example, by staining with an antibody that specifically binds to the marker and detecting said antibody, wherein the staining is detectable by flow cytometry at a level substantially similar or below the staining detected carrying out the same procedure with an isotype-matched control and/or fluorescence minus one (FMO) gating control under otherwise identical conditions, and/or at a level below that for cell known to be positive for the marker, and/or at a level substantially similar or below that for a cell known to be negative for the marker.

[0282] In some embodiments, the antibody has an EC50 or IC50 for reducing peripheral blood NK cells and/or T cells that express CD94 in the subject of between about 1 ng/ml and about 100 ng/ml, e.g., any of about 1 ng/ml, about 5 ng/ml, about 10 ng/ml, about 15 ng/ml, about 20 ng/ml, about 25 ng/ml, about 30 ng/ml, about 35 ng/ml, about 40 ng/ml, about 45 ng/ml, about 50 ng/ml, about 55 ng/ml, about 60 ng/ml, about 65 ng/ml, about 70 ng/ml, about 75 ng/ml, about 80 ng/ml, about 85 ng/ml, about 90 ng/ml, about 95 ng/ml, or about 100 ng/ml. In some embodiments, the antibody has an IC50 or EC50 for reducing

peripheral blood NK cells and/or T cells that express CD94 in the subject of between about 10 ng/ml and about 80 ng/ml. In some embodiments, the antibody has an IC50 or EC50 for reducing peripheral blood NK cells and/or T cells that express CD94 in the subject of about 20 ng/ml. In some embodiments, the antibody has an IC50 or EC50 for reducing peripheral blood NK cells and/or T cells that express CD94 in the subject of about 60 ng/ml. EC50 or IC50 may be measured using any method known in the art, e.g., as described in the Examples.

[0283] In some embodiments, the subject is a human, a primate, a non-human primate (e.g., African green monkeys, cynomolgus monkey, rhesus monkeys, etc.), a farm mammal, a game mammal, or a domestic mammal. In some embodiments, the subject is a human. In some embodiments, the human subject is an infant, a toddler, a child, a young adult, an adult or a geriatric. In some embodiments, the subject has a disease involving T cells and/or NK cells that express CD94, e.g., CLPD-NK, LGL leukemia, Felty's syndrome, rheumatoid arthritis, aggressive NK leukemia, inclusion body myositis, inflammatory bowel disease, or an NK/T cell lymphoma, such as extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL (not otherwise specified), angioimmunoblastic TCL, adult TCL, monomorphic epitheliotropic intestinal TCL, epidermotropic CD8+ cutaneous TCL, primary cutaneous gamma/delta TCL, or subcutaneous panniculitis TCL.

[0284] In some embodiments, administration of the antibody to the subject does not result in tumor lysis syndrome in the subject. Tumor lysis syndrome may be measured or diagnosed according to any method known in the art, such as the Cairo-Bishop classification system for tumor lysis syndrome (*see, e.g.,* Cairo and Bishop (2004) *Br J Haematol*, 127(1):3-11.)

[0285] In some embodiments, an antibody of the disclosure binds to CD94. In some embodiments, an antibody of the disclosure depletes and/or reduces the level of NK cells and/or T cells that express CD94. In some embodiments, an antibody of the disclosure has clear benefits for a patient (e.g., a human patient) having a disease or disorder, such as CLPD-NK, LGL leukemia, rheumatoid arthritis, Felty's syndrome, aggressive NK leukemia, IBM, IBD, or an NK/T cell lymphoma, such as extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL (not otherwise specified), angioimmunoblastic TCL, adult TCL, monomorphic epitheliotropic intestinal TCL, epidermotropic CD8+ cutaneous TCL, primary cutaneous gamma/delta TCL, subcutaneous panniculitis TCL or other diseases associated with LGL, T cells, and/or NK cells. In some embodiments, an antibody of the disclosure has better tolerability and fewer side effects over the first and second line of therapies for the disease or disorder (e.g., CLPD-NK, LGL leukemia, Felty's syndrome, rheumatoid arthritis, aggressive NK leukemia, inclusion body myositis, inflammatory bowel disease, or an NK/T cell lymphoma, such as extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL (not otherwise specified), angioimmunoblastic TCL, or adult TCL), such as

chemotherapy, e.g., cyclophosphamide, doxorubicin, vincristine, prednisone; stem cell transplant; splenectomy; Alemtuzumab; Bevacizumab; Pralatrexate; Avelumab; proteasome inhibitors such as Carfilzomib and Bortezomib; HDAC inhibitors such as Romidepsin, Belinostat, and Vorinostat; and antibody-drug conjugates such as Brentuximab vedotin. In some embodiments, an antibody of the disclosure demonstrates more selective depletion of the disease-inducing cells, e.g., NK cells and/or T cells that express CD94, compared to current therapies that are non-selective, such as chemotherapy, e.g., cyclophosphamide, doxorubicin, vincristine, prednisone; stem cell transplant; splenectomy; Alemtuzumab; Bevacizumab; Pralatrexate; Avelumab; proteasome inhibitors such as Carfilzomib and Bortezomib; HDAC inhibitors such as Romidepsin, Belinostat, and Vorinostat; and antibody-drug conjugates such as Brentuximab vedotin. Accordingly, in some embodiments, the disclosure provides a method of reducing the number or depleting NK cells and/or T cells that express CD94 in a human subject upon administration of molecule (e.g., an antibody of the disclosure) that binds to a cell surface protein on NK cells and/or T cells, such as CD94, and that comprises (a) a region that specifically binds to the target and (b) an immunoglobulin Fc region.

[0286] In some embodiments, the methods provided herein further comprise administering to the subject an IL-2 polypeptide, e.g., a therapeutic IL-2 polypeptide. IL-2 polypeptides, e.g., therapeutic IL-2 polypeptides, suitable for administration to a subject (e.g., a subject having a disease or disorder described herein) according to the methods provided herein are known in the art. Exemplary IL-2 polypeptides include, without limitation, Aldesleukin, Interking, and Neoleukin 2/15.

A. Administration and Dosing Regimens

(i) Routes of Administration

[0287] In some embodiments, administer, administering, administration, and the like, refer to methods that are used to enable delivery of therapeutic or pharmaceutical compositions to the desired site of biological action. In some embodiments, an antibody of the disclosure (and any additional therapeutic agent) for use in any of the methods provided herein may be administered to the subject (e.g., a human) by any suitable means, including parenteral, intrapulmonary, intranasal, and intralesional administration. Parenteral infusions include intramuscular, intravenous, intraarterial, intraperitoneal, or subcutaneous administration. In some embodiments, an antibody of the disclosure is administered by intravenous infusion. Dosing of an antibody of the disclosure can be by any suitable route, e.g., by injections, such as intravenous or subcutaneous injections, depending in part on whether the administration is brief or chronic.

(ii) Dosing Regimens

[0288] An antibody of the disclosure for use in any of the methods provided herein may be administered to the subject using various dosing schedules or regimens, including but not limited to single or multiple administrations over various time-points, bolus administration, and pulse infusion. The specific dosage of the antibodies of the disclosure to be administered will vary according to the particular target specificity, the type of disease or disorder, the subject, and the nature and severity of the disease, the physical

condition of the subject, the therapeutic regimen (e.g., whether a combination therapeutic agent is used), and the selected route of administration. In some embodiments, a dose of an antibody of the disclosure may range from about 0.0001 mg/kg to 100 mg/kg of the subject's body weight. An exemplary dosage regimen of an antibody of the disclosure entails administration of the antibody in multiple dosages over a prolonged period, for example, of at least six months.

[0289] Other known antibodies against CD94 may also be used in the methods provided herein. For example, the following anti-CD94 antibodies may be used: HP-3D9 (LSBio Catalog # LS-C134679-100; Abnova Catalog #: MAB6947); 2I2; 131412 (R&D Systems Catalog #: MAB1058); 13B146 (US Biological Catalog #: 030068); 13B147 (US Biological Catalog #: 030069); 1H1 (Abnova Catalog #: MAB10543); 3G2 (Biorbyt Catalog #: orb69389); DX22 (Biolegend Catalog # 305502); REA113 (Miltenyi Biotec Catalog #: 130-098-967); KP43; EPR21003; AT13E3 (ATGen Catalog: ATGA0487); HP-3B1; 12K45; and B-D49.

B. Diseases

[0290] There are 9 distinct diseases involving NK/T cell lymphoma: extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL (not otherwise specified), angioimmunoblastic TCL and adult TCL. See, e.g., Bajaj, 2019. NK/T cell lymphoma affects various organs such as skin, GI, liver, spleen, bone marrow. Symptoms of NK/T cell lymphoma include enlarged lymph nodes of the neck. Advantageously, the methods described herein may be used, e.g., to reduce the number of abnormal or pathologic NK cells and/or T cells (e.g., CD4+ T cells, CD8+ T cells, CD4+ and CD8+ T cells) that express CD94 via mechanisms such as ADCC that employ NK cells, essentially using the pathologic cells to eliminate each other.

[0291] The methods described herein may also be used, e.g., to reduce the number of abnormal or pathologic NK and/or T cells that express CD94 and are associated with a NK/T cell lymphoma, such as extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL (not otherwise specified), angioimmunoblastic TCL, adult TCL, monomorphic epitheliotropic intestinal TCL, epidermotropic CD8+ cutaneous TCL, primary cutaneous gamma/delta TCL, or subcutaneous panniculitis TCL, via mechanisms such as ADCC that employ NK cells, essentially using the pathologic cells to eliminate each other.

[0292] There are 3 distinct diseases involving LGLs: T-cell LGL (T-LGL) leukemia; chronic lymphoproliferative disorders of NK cells (CLPD-NK, formerly NK-LGL); and aggressive NK-cell leukemias, such as aggressive natural killer leukemia (ANKL) and extranodal NK cell nasal type (ENKL).

[0293] In addition to the NK or T LGL leukemias, NK or LGL cells play key roles in rheumatoid arthritis (RA), Felty's syndrome, aggressive NK leukemia, Inclusion body myositis (IBM), inflammatory bowel disease (IBD), and other diseases. Non-limiting examples of diseases and disorders in which LGL and NK cells play a role include LGL leukemia, Rheumatoid arthritis, Felty's syndrome, aggressive NK

leukemia, IBM, and IBD. Advantageously, the methods described herein may be used, *e.g.*, to reduce the number of abnormal or pathologic NK cells (*e.g.*, CLPD-NK, ANKL, or ENKL cells) via mechanisms such as ADCC that employ NK cells, essentially using the pathologic cells to eliminate each other. For exemplary descriptions of symptoms of these diseases, *see, e.g.*, Lamy, et al, *Blood*, 2017 x Vol. 129, No. 9; Loughran *Blood*, VOI 82, NO 1 (July 1), 1993: pp 1-14; Semenzato G, et al, *Blood*. 1997;89(1):256-260; and Bourgault-Rouxel, et al, *Leuk Res.*2008;32(1):45-48.

(i) *CLPD-NK*

[0294] Chronic lymphoproliferative disorders of NK cells (CLPD-NK), also referred to as NK-LGL leukemia, chronic NK cell lymphocytosis, chronic NK-LGL lymphoproliferative disorder (LPD), NK cell lineage granular lymphocyte proliferative disorder, NK cell LGL lymphocytosis, or indolent granular NK cell LPD is generally characterized by a persistent (*e.g.*, 6 months or greater) increase in peripheral blood NK cells (*e.g.*, $\geq 2 \times 10^9/L$).

[0295] Symptoms of CLPD-NK include variable cytopenias such as neutropenia and anemia, fatigue, fever, night sweats, recurrent infections, rheumatoid arthritis, lymphadenopathy, hepatosplenomegaly, skin lesions, hematologic neoplasms, vasculitis, neuropathy, and autoimmune disorders.

[0296] In some embodiments of the methods provided herein, the disease or disorder is CLPD-NK, and administration of the antibody results in a reduction in one or more CLPD-NK symptoms in the subject. In some embodiments, the reduction in the number of peripheral blood LGL and/or NK cells in the subject after administration of the antibody results in a reduction in one or more CLPD-NK symptoms in the subject.

[0297] Symptoms of CLPD-NK may be measured by any method known in the art, such as using laboratory tests to measure anemia, neutropenia, complete blood counts, and/or magnetic resonance imaging (MRI), CT scan, palpation, or ultrasound (*e.g.*, to determine hepatosplenomegaly), bone marrow exams, and flow cytometry. Methods for measuring symptoms of CLPD-NK are described, *e.g.*, in Swerdlow, S.H. *et al.* (2016) *Blood* 127:2375-2390.

(ii) *LGL Leukemia*

[0298] Large granular lymphocytic (LGL) leukemia is a chronic lymphoproliferative disorder that exhibits a chronic elevation in large granular lymphocytes (LGLs) in the peripheral blood and is called T-cell LGL leukemia.

[0299] Symptoms of LGL leukemia include splenomegaly, B symptoms (*e.g.*, systemic symptoms such as fever, night sweats, and weight loss), anemia, neutropenia, and recurrent infections. Rheumatoid arthritis is often also found in people with T-cell LGL leukemia.

[0300] In some embodiments of the methods provided herein, the disease or disorder is LGL leukemia, and administration of the antibody results in a reduction in one or more LGL leukemia symptoms in the subject. In some embodiments, the reduction in the number of peripheral blood LGL and/or NK cells in the subject after administration of the antibody results in a reduction in one or more LGL leukemia symptoms in the subject.

[0301] Symptoms of LGL leukemia may be measured by any method known in the art, such as using laboratory tests to measure anemia, neutropenia, and other cytopenias, complete blood counts, magnetic resonance imaging (MRI), CT scan, palpation, or ultrasound (e.g., to determine splenomegaly), bone marrow exams, and flow cytometry. Methods for measuring symptoms of LGL leukemia are described, e.g., in Swerdlow, S.H. *et al.* (2016) *Blood* 127:2375-2390.

(iii) *Felty's Syndrome*

[0302] Felty's syndrome is an autoimmune disease characterized by rheumatoid arthritis, splenomegaly (e.g., inflammatory splenomegaly), and a reduced number of neutrophils in the blood. Symptoms of Felty's syndrome include painful, stiff, and/or swollen joints, physical findings associated with rheumatoid arthritis, splenomegaly, neutropenia, infections, keratoconjunctivitis sicca, fever, weight loss, fatigue, discoloration of the skin, sores (e.g., ulcers), hepatomegaly, anemia, thrombocytopenia, abnormal liver function, enlarged lymph nodes, and vasculitis.

[0303] In some embodiments of the methods provided herein, the disease or disorder is Felty's syndrome, and administration of the antibody results in a reduction in one or more Felty's syndrome symptoms in the subject. In some embodiments, the reduction in the number of peripheral blood LGL and/or NK cells in the subject after administration of the antibody results in a reduction in one or more Felty's syndrome symptoms in the subject. Symptoms of Felty's syndrome include, without limitation, joint inflammation, joint pain, and splenomegaly.

[0304] Symptoms of Felty's syndrome may be measured by any method known in the art, such as using laboratory tests to measure anemia, neutropenia, thrombocytopenia, and other cytopenias, complete blood counts, magnetic resonance imaging (MRI), CT scan, or ultrasound (e.g., to determine splenomegaly and/or hepatomegaly), laboratory tests for abnormal liver function, palpation to determine splenomegaly and/or hepatomegaly, flow cytometry, disease activity score-28 (DAS-28, e.g., as used for monitoring rheumatoid arthritis symptoms), and DAS-28 with erythrocyte sedimentation rate (ESR).

(iv) *Rheumatoid Arthritis*

[0305] Rheumatoid arthritis is an autoimmune disorder that primarily affects the joints, but can also affect other organs and can be associated with cardiovascular disease, osteoporosis, interstitial lung disease, infection, cancer, fatigue, and depression. Symptoms of rheumatoid arthritis include swollen, tender, and warm joints, joint inflammation, joint pain, joint stiffness, splenomegaly, rheumatoid nodules (e.g., in the skin), necrotizing granuloma, vasculitis, pyoderma gangrenosum, Sweet's syndrome, drug reactions, erythema nodosum, lobe panniculitis, atrophy of finger skin, palmar erythema, skin fragility, diffuse alopecia areata, lung fibrosis, Caplan's syndrome, exudative pleural effusions, atherosclerosis, myocardial infarction, stroke, pericarditis, endocarditis, left ventricular failure, valvulitis, fibrosis of the heart and/or blood vessels, anemia, increased platelet count, low white blood cell count, renal amyloidosis, episcleritis, scleritis, keratoconjunctivitis sicca, keratitis, loss of vision, liver problems, peripheral neuropathy, mononeuritis multiplex, carpal tunnel syndrome, myelopathy, atlanto-axial

subluxation, vertebrae slipping, fatigue, low grade fever, malaise, morning stiffness, loss of appetite, loss of weight, osteoporosis, cancer (e.g., lymphoma, skin cancer), and periodontitis.

[0306] In some embodiments of the methods provided herein, the disease or disorder is rheumatoid arthritis, and administration of the antibody results in a reduction in one or more rheumatoid arthritis symptoms in the subject. In some embodiments, the reduction in the number of peripheral blood LGL and/or NK cells in the subject after administration of the antibody results in a reduction in one or more rheumatoid arthritis symptoms in the subject.

[0307] In some embodiments, symptoms and disease status/progression of rheumatoid arthritis are measured according to the 2010 ACR/EULAR Rheumatoid Arthritis Classification Criteria (see, e.g., Aletaha et al., (2010) *Annals of Rheumatic Diseases*, 69(9):1580-8). Symptoms of rheumatoid arthritis may also be measured by any method known in the art, such as using laboratory tests to measure erythrocyte sedimentation rates, C-reactive protein, rheumatoid factor, anti-citrullinated protein antibodies, anemia and other cytopenias, increased platelet count, low white blood cell count, complete blood counts, renal amyloidosis, medical imaging such as X-rays, MRI, CT-scans, ultrasound (e.g., ultrasonography using a high-frequency transducer; Doppler ultrasound), flow cytometry, disease activity score-28 (DAS-28), and DAS-28 with erythrocyte sedimentation rate (ESR).

(v) Aggressive NK Leukemia

[0308] Aggressive NK-cell leukemia is an aggressive disease with systemic proliferation of NK cells and a rapidly declining clinical course. Aggressive NK leukemia may also be referred to as aggressive NK-cell lymphoma. Symptoms of aggressive NK-cell leukemia include constitutional symptoms (e.g., malaise, weight loss, fatigue), hepatosplenomegaly, lymphadenopathy, coagulopathies, hemophagocytic syndrome, multi-organ failure, infections such as Epstein-Barr virus, allergic reactions (e.g., allergic reactions to insect bites, such as mosquito bites) that may result in necrosis and systemic symptoms such as fever, swollen lymph nodes, abdominal pain, diarrhea, and anaphylaxis.

[0309] In some embodiments of the methods provided herein, the disease or disorder is aggressive NK-cell leukemia, and administration of the antibody results in a reduction in one or more aggressive NK-cell leukemia symptoms in the subject. In some embodiments, the reduction in the number of peripheral blood LGL and/or NK cells in the subject after administration of the antibody results in a reduction in one or more aggressive NK-cell leukemia symptoms in the subject.

[0310] Symptoms of aggressive NK leukemia may be measured by any method known in the art, such as using laboratory tests, e.g., to measure anemia, neutropenia, and other cytopenias, complete blood counts, and/or magnetic resonance imaging (MRI), CT scan, palpation, or ultrasound (e.g., to determine splenomegaly), bone marrow exams, and flow cytometry. Methods for measuring symptoms of aggressive NK leukemia are described, e.g., in Swerdlow, S.H. *et al.* (2016) *Blood* 127:2375-2390.

(vi) Inclusion Body Myositis

[0311] Inclusion Body Myositis (IBM), also referred to as sporadic inclusion body myositis, is an inflammatory muscle disease characterized by autoimmune and degenerative processes that result in

progressive weakness and wasting of distal and/or proximal muscles. Generally, IBM is characterized by invasion of immune cells into muscle tissues. In some cases, patients with IBM have elevated creatine kinase levels in the blood. Symptoms of IBM include progressive muscle weakness, muscle wasting/atrophy, frequent tripping and falling, difficulty manipulating fingers, foot drop, restricted mobility, impaired balance, muscle pain, dysphagia, and fatigue.

[0312] In some embodiments of the methods provided herein, the disease or disorder is IBM, and administration of the antibody results in a reduction in one or more IBM symptoms in the subject. In some embodiments, the reduction in the number of peripheral blood LGL and/or NK cells in the subject after administration of the antibody results in a reduction in one or more IBM symptoms in the subject.

[0313] Symptoms of IBM may be measured by any method known in the art, such as muscle biopsies, blood tests (e.g., to measure creatine kinase), electromyography (EMG) studies, blood tests to measure antibodies to NT5C1A, flow cytometry, and myositis disease activity assessment tools including without limitation Myositis Intention to Treat Activity Index (MITAX) and Myositis Disease Activity Assessment Visual Analogue Scales (MYOACT).

(vii) Inflammatory Bowel Disease

[0314] Inflammatory bowel disease (IBD) refers to a class of inflammatory conditions of the colon and small intestine. Types of IBD include ulcerative colitis and Crohn's disease. Symptoms of IBD include diarrhea, fever, fatigue, abdominal pain, abdominal cramping, blood in the stool, reduced appetite, and weight loss.

[0315] In some embodiments of the methods provided herein, the disease or disorder is IBD, and administration of the antibody results in a reduction in one or more IBD symptoms in the subject. In some embodiments, the reduction in the number of peripheral blood LGL and/or NK cells in the subject after administration of the antibody results in a reduction in one or more IBD symptoms in the subject.

[0316] Symptoms of IBD may be measured by any method known in the art, such as laboratory blood tests for anemia, other cytopenias, or infections, fecal occult blood tests, colonoscopies, flexible sigmoidoscopy, upper endoscopy, capsule endoscopy, balloon-assisted enteroscopy, X-rays, CT-scans, MRI scans, ultrasound, and flow cytometry.

III. Pharmaceutical Formulations

[0317] In some embodiments, a pharmaceutical composition, a composition, or a pharmaceutical formulation refer to a biologically active compound (e.g., an antibody of the disclosure), optionally mixed with at least one pharmaceutically acceptable chemical component, such as, though not limited to carriers, stabilizers, diluents, dispersing agents, suspending agents, thickening agents, excipients and the like.

[0318] Pharmaceutical compositions, pharmaceutical formulations, and/or compositions of any of the antibodies of the disclosure for use in any of the methods as described herein may be prepared by mixing such antibody having the desired degree of purity with one or more optional pharmaceutically acceptable

carriers (Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980)), in the form of lyophilized formulations or aqueous solutions.

[0319] Pharmaceutically acceptable carriers are generally nontoxic to recipients at the dosages and concentrations employed, and include, but are not limited to: buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid and methionine; preservatives (such as octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride; benzethonium chloride; phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol; and m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming counter-ions such as sodium; metal complexes (e.g., Zn-protein complexes); and/or non-ionic surfactants such as polyethylene glycol (PEG). Exemplary pharmaceutically acceptable carriers herein further include interstitial drug dispersion agents such as soluble neutral-active hyaluronidase glycoproteins (sHASEGP), for example, human soluble PH-20 hyaluronidase glycoproteins, such as rHuPH20 (HYLENEX®, Baxter International, Inc.). Certain exemplary sHASEGPs and methods of use, including rHuPH20, are described in US Patent Publication Nos. 2005/0260186 and 2006/0104968. In one aspect, a sHASEGP is combined with one or more additional glycosaminoglycanases such as chondroitinases.

[0320] The formulation herein may also contain more than one active ingredient as necessary for the particular indication (e.g., a disease or disorder) being treated, preferably those with complementary activities that do not adversely affect each other.

[0321] Active ingredients may be entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization, for example, hydroxymethylcellulose or gelatin-microcapsules and poly-(methylmethacrylate) microcapsules, respectively, in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles and nanocapsules) or in macroemulsions. Such techniques are disclosed in Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980).

[0322] Sustained-release preparations may be prepared. Suitable examples of sustained-release preparations include semipermeable matrices of solid hydrophobic polymers containing the antibody or immunoconjugate, which matrices are in the form of shaped articles, e.g., films, or microcapsules.

[0323] The formulations to be used for in vivo administration are generally sterile. Sterility may be readily accomplished, e.g., by filtration through sterile filtration membranes.

IV. Kits and Articles of Manufacture

[0324] In another aspect of the disclosure, a kit or an article of manufacture containing materials useful for the methods provided herein, e.g., treatment of the diseases or disorders described above, reducing the number of peripheral blood NK cells and/or T cells that express CD94 in a subject, or inducing ADCC activity in a subject, are provided. The kit or article of manufacture may comprise a container and a label or package insert on or associated with the container. Suitable containers include, for example, bottles, vials, syringes, IV solution bags, etc. The containers may be formed from a variety of materials such as glass or plastic. The container holds a composition which is by itself or combined with another composition effective for the methods provided herein, e.g., treatment of the diseases or disorders described above, reducing the number of peripheral blood NK cells and/or T cells that express CD94 in a subject, or inducing ADCC activity in a subject, and may have a sterile access port (for example the container may be an intravenous solution bag or a vial having a stopper pierceable by a hypodermic injection needle). At least one active agent in the composition is an antibody of the disclosure. The label or package insert indicates that the composition is used for the methods provided herein, e.g., treatment of the diseases or disorders described above, reducing the number of peripheral blood NK cells and/or T cells that express CD94 in a subject, or inducing ADCC activity in a subject. Moreover, the kit or article of manufacture may comprise (a) a first container with a composition contained therein, wherein the composition comprises an antibody of the disclosure; and (b) a second container with a composition contained therein, wherein the composition comprises a further therapeutic agent. The kit or article of manufacture in this embodiment of the invention may further comprise a package insert indicating that the compositions can be used to treat a particular disease or disorder, e.g., as described herein, to reduce the number of peripheral blood NK cells and/or T cells that express CD94 in a subject, or to induce ADCC activity in a subject. Alternatively, or additionally, the kit or article of manufacture may further comprise a second (or third) container comprising a pharmaceutically-acceptable buffer, such as bacteriostatic water for injection (BWFI), phosphate-buffered saline, Ringer's solution or dextrose solution. It may further include other materials desirable from a commercial and user standpoint, including other buffers, diluents, filters, needles, and syringes.

[0325] The following description is presented to enable a person of ordinary skill in the art to make and use the various embodiments. Descriptions of specific devices, techniques, and applications are provided only as examples. Various modifications to the examples described herein will be readily apparent to those of ordinary skill in the art, and the general principles defined herein may be applied to other examples and applications without departing from the spirit and scope of the various embodiments. Thus, the various embodiments are not intended to be limited to the examples described herein and shown, but are to be accorded the scope consistent with the claims.

EXAMPLES

Example 1: Anti-CD94 antibody production and evaluation

[0326] This example describes the production and characterization of antibodies specific to human CD94.

Materials and methods

Anti-CD94 antibody production and screening

[0327] Four-week old, ATX-Gx Alloy transgenic mice (mice that produce human antibodies) were immunized subcutaneously with C-terminal His-tagged CD94 for five weeks, with one boost of antigen per week. Antibody titers in mouse serum were assessed during pre- and post-boosts via ELISA and flow cytometry. The mice with the highest serum antibody titer were selected to supply B cells for the generation of hybridomas.

[0328] Prior to cell fusion, mice were administered with one additional boost of CD94-His antigen. The mice were then sacrificed and their spleens harvested. Spleen cells and SP2/0-Ag14 myeloma cells were mixed, and fusion was then induced by incubation at 37 °C in the presence of polyethylene glycol (PEG) or electroporation. The cells were then harvested and plated into 96-well plates with limited dilution to achieve one cell per well. The cells were subsequently treated with hypoxanthine, aminopterin and thymidine (HAT) medium and selected for over 2 weeks in culture.

[0329] Hybridoma supernatant were screened using ELISA and flow cytometry to identify candidates specific towards CD94. For ELISA, CD94-His antigen was immobilized on plates and 100 µl of each supernatant was incubated with antigen. A fluorescently labeled secondary antibody was used to detect antibodies captured on the ELISA plate, and positive hits were validated by analysis of antibody binding on human primary NK cells using flow cytometry. Cynomolgus CD94 cross-reactivity was assessed by antibody binding to cyno-CD94-expressing BaF3 cells using flow cytometry.

[0330] Verification of VH and VL sequences were performed using standard RNA extraction of hybridomas, followed by reverse transcription of RNA to cDNA and PCR using Alloy ATC-Gx specific primers.

Healthy donor and patient samples

[0331] Fresh healthy donor buffy coats were obtained from Stanford Blood Center. Peripheral blood mononuclear cells (PBMCs) were isolated via ficoll-paque (GE Healthcare, Chicago, IL) separation and cryopreserved in Bmbanker cell freezing media (Bulldog-Bio, Portsmouth, NH). Briefly, buffy coats were diluted in phosphate buffered saline (PBS) in a 1:1 ratio, followed by layering of the diluted buffy coat and centrifugation at 760g in ficoll. The PBMC layer was isolated and washed in PBS prior to downstream analysis. Peripheral blood leukocytes (PBLs) were isolated through red blood cell lysis.

Antibody affinity assays

[0332] Healthy donor PBMCs were seeded in 96 well plates at a density of 100,000 cells per well, incubated with human Fc block (Biolegend) and cell viability dye (Thermo Fisher) for 30 minutes on ice and protected from light. The cells were washed once with FACS buffer (PBS with 2% IgG low FBS). anti-CD94 antibodies at concentrations of 100 nM to 0.046 nM, 1:3-fold dilutions, were incubated with cells for 30 minutes on ice and protected from light. The cells were then washed and incubated with goat IgG anti-mouse Fc γ specific AF647 secondary antibody or goat (Fab)2 fragment anti-human Fc γ specific AF647 secondary antibody (Jackson immuno research), anti-CD3 pacific blue-labelled and anti-CD56 FITC-labelled antibodies (Biolegend) for 30 minutes on ice and protected from light. After incubation, the cells received a final wash in FACS buffer before quantification on the Cytoflex (Beckman Coulter). All data acquisition and fluorescence compensation were performed using CytoFlex (Beckman Coulter, Atlanta, GA). Data analysis was performed using FlowJo software. NK cells were identified through gating on lymphocytes on the forward and side scatter, followed by doublet and dead cell exclusion, and gated on the CD3-CD56 $^{+}$ population. CD94 expression was then quantified on the CD3-CD56 $^{+}$ NK cell population. Antibody titration curves and EC50s were generated using Graphpad Prism.

Antibody cynomolgus CD94 cross-reactivity assay

[0333] Cynomolgus CD94-expressing HEK293 cells were seeded in 96-well plates at a density of 100,000 cells per well, incubated with cell viability dye (Thermo Fisher) for 30 minutes on ice and protected from light. The cells were washed once with FACS buffer (PBS with 2% IgG low FBS). Hybridoma supernatants, anti-CD94 antibodies and isotype controls were incubated with cells for 30 minutes on ice and protected from light. The cells were then washed and incubated with goat IgG anti-mouse Fc γ specific AF647 secondary antibody or goat (Fab)2 fragment anti-human Fc γ specific AF647 secondary antibody (Jackson ImmunoResearch) for 30 minutes on ice and protected from light. After incubation, the cells received a final wash in FACS buffer before quantification on the Cytoflex (Beckman Coulter). All data acquisition and fluorescence compensation were performed using CytoFlex (Beckman Coulter, Atlanta, GA). Data analysis was performed using FlowJo software. HEK293 cells were identified through gating on the major cell population using forward and side scatter, followed by doublet and dead cell exclusion. CD94 expression was then quantified on this population. MFI bar graphs were generated using Graphpad Prism.

HLA-E blocking assay

[0334] Healthy donor PBMCs were seeded in 96-well plates at a density of 100,000 cells per well, incubated with human Fc block (Biolegend) and cell viability dye (Thermo Fisher) for 30 minutes on ice and protected from light. The cells were washed once with FACS buffer (PBS with 2% IgG low FBS). anti-CD94 antibodies at EC80 concentrations were incubated with cells for 30 minutes on ice and protected from light. After incubation with the anti-CD94 antibodies, the cells were washed and incubated

with HLA-E tetramer PE (Creative Biolabs), anti-CD3 pacific blue-labelled, and anti-CD56 FITC-labelled antibodies (Biolegend) for 30 minutes on ice and protected from light. The cells then received a final wash in FACS buffer before quantification on the Cytoflex (Beckman Coulter). All data acquisition and fluorescence compensation were performed using CytoFlex (Beckman Coulter, Atlanta, GA). Data analysis was performed using FlowJo software. NK cells were identified through gating on lymphocytes on the forward and side scatter, followed by doublet and dead cell exclusion, and gated on the CD3-CD56+ population. HLA-E expression was then quantified on the CD3-CD56+ NK cell population. Percent blocking was calculated as $100 - ((\text{percent HLA-E positive for anti-CD94 antibody})/(\text{percent HLA-E positive for isotype}) * 100)$.

Antibody competition assay

[0335] Healthy donor PBMCs were seeded in 96-well plates at a density of 100,000 cells per well, incubated with human Fc block (Biolegend) and cell viability dye (Thermo Fisher) for 30 minutes on ice and protected from light. The cells were washed once with FACS buffer (PBS with 2% IgG low FBS). Unconjugated anti-CD94 antibodies at EC80 concentrations, CD3 FITC and CD56 PE antibodies, and APC-labeled anti-CD94 antibodies were incubated with cells for 30 minutes on ice and protected from light. The cells then received a final wash in FACS buffer before quantification on the Cytoflex (Beckman Coulter). All data acquisition and fluorescence compensation were performed using CytoFlex (Beckman Coulter, Atlanta, GA). Data analysis was performed using FlowJo software. NK cells were identified through gating on lymphocytes on the forward and side scatter, followed by doublet and dead cell exclusion, and gated on the CD3-CD56+ population. Anti-CD94 APC was then quantified on the CD3-CD56+ NK cell population. All titration curves and EC50s were generated using Graphpad Prism.

Antibody internalization assay

[0336] Healthy donor PBMCs were seeded in 96-well plates at a density of 100,000 cells per well in RPMI with 10% IgG low FBS, incubated with human Fc block (Biolegend) for 10 minutes at room temperature. Unconjugated anti-CD94 antibodies were incubated with the cells at EC80 concentrations at 4 °C and 37 °C for 30 minutes to 24 hours. The cells were washed once with FACS buffer (PBS with 2% IgG low FBS) and kept on ice for the remaining procedure. Goat anti-mouse Fcγ specific antibodies were incubated with cells for 30 minutes on ice and protected from light. The cells were then washed once and CD94 expression was quantified on the Cytoflex. All data acquisition and fluorescence compensation were performed using CytoFlex (Beckman Coulter, Atlanta, GA). Data analysis was performed using FlowJo software. NK cells were identified through gating on lymphocytes on the forward and side scatter, followed by doublet and dead cell exclusion, and gated on the CD3-CD56+ population. Anti-CD94 APC was then quantified on the CD3-CD56+ NK cell population. Percent decrease in MFI was calculated by computing the difference in MFI between 0.5 and 24 hours at 37 °C and multiplying by 100.

Antibody-dependent cellular cytotoxicity assay

[0337] Approximately 1×10^5 – 2×10^5 fresh or frozen PBMCs were plated in tissue culture-treated 96-well U bottom plates in RPMI with 10% low IgG FBS. The cells were incubated overnight in 10^1 – 10^6 ug/ml in 10-fold dilutions of the human IgG1 isotype control antibody or the 1E4 fucosylated and 18H3-KIF antibody. The cells were then stained with fluorescently labelled antibodies against CD3, CD56 and CD16 to identify the remaining NK cells (see flow cytometry analysis). A minimum of 10,000 events were collected on the flow cytometer in the lymphocyte population. Percent NK/leukemic cell remaining was calculated by normalizing the absolute count by the cell numbers in the isotype treated conditions. The IC50 was determined using GraphPad Prism.

Results

[0338] Anti-CD94 antibodies were generated using a standard hybridoma technique, as described *supra*. Briefly, ATX-Gx Alloy transgenic mice were immunized with C-terminal His-tagged CD94 for five weeks. B cells from mice with the highest serum antibody titer after five weeks were used to generate hybridomas. The hybridomas were screened through ELISA to identify candidates specific towards CD94.

[0339] Positive hits were validated by assessing binding to human NK cells by flow cytometry analysis. Binding of the anti-CD94 antibody clones to primary human NK cells was assessed by flow cytometry analysis. Supernatants from the anti-CD94 hybridomas were used to test binding of the anti-CD94 antibody clones. A commercially available anti-CD94 antibody, HP-3D9, and several IgG isotype controls were also tested for binding on NK cells.

[0340] The affinity of the antibody clones was also assessed by flow cytometry analysis. **FIG. 1** shows the titration curve generated for anti-CD94 antibody clone 18H3. Anti-CD94 antibody 18H3 showed an affinity of 2.6 nM on human primary NK cells. The affinities determined for the other anti-CD94 antibodies are listed in **FIG. 11**. As shown in **FIG. 2**, hybridoma supernatant screening revealed that 18H3, 1M4 and 1E4 bind to human primary NK cells, as measured by flow cytometry.

[0341] The anti-CD94 hybridoma supernatants were also tested for cross-reactivity to cynomolgus CD94. Hybridomas were screened for cross-reactivity to cynomolgus CD94 using cynomolgus CD94-expressing HEK293 cells by flow cytometry. As shown in **FIG. 3A**, this analysis revealed that clones 18H3, 1M4 and 1E4 cross-react with cynomolgus CD94. Supernatant from clone 20F2 did not cross-react with cynomolgus CD94, albeit being reactive to human CD94. The cross-reactivity of commercially available anti-CD94 antibodies was also evaluated. As shown in **FIG. 3B**, none of the commercially available anti-CD94 antibodies tested (HP-3D9, HP-3B1, 131412, 12K45, DX22) exhibited cross-reactivity to cynomolgus CD94.

[0342] These results indicate that anti-CD94 antibodies 18H3, 1M4 and 1E4 bind to an epitope that is not shared with HP-3D9, HP-3B1, 131412, 12K45, DX22, and 20F2 (not commercial) antibodies. The

cross-reactivity of the 18H3, 1M4 and 1E4 antibodies suggests that they could be useful for cynomolgus monkey toxicity studies prior to phase I trials in human subjects.

[0343] Following validation, the VH and VL sequences were determined for the validated antibody clones. **Table A** summarizes the VH and VL sequences for three validated anti-CD94 clones, 18H3, 1M4 and 1E4. The framework and CDR sequences (bolded in **Table A**) were determined using the Kabat numbering scheme.

Table A. Sequences of anti-CD94 antibody clones

Antibody clone	Heavy chain	Light chain
18H3	EVQLVQSGAEVKKPGESLKISCKGSGYRF TSYWIGWVRQMPGKGLEWMGIYPGDS DTRYSPSFQGQ VIISADKSITTAFLQWSSL KASDTAMYYCAR PFDYGGSPGYFDYWG QGTLVTVSS (SEQ ID NO:19)	DIQMTQSPSTLSASVGDRVITITCRAS QSIRSWLAWYQQKPGKAPKLLIYKA SSLESGVPSRFSGSGSGTEFTLTISSLQ PDDFATYYC QQYNTFWTF GGQGTKV EIK (SEQ ID NO:20)
1M4	QLVESGGGLVQPGGSLRLACAASGFTFSN YAMNWVRQAPGKGLEWVSISGSGDTT YCADSVKGRFTISRDNSKNTLHLQLNSLR AEDTAVYYCAK NCYGSGSYNHF FDYWG QGTLVTVSS (SEQ ID NO:21)	EIVMTQSPDSLAVSLGERATINCKSS QSVLYSSNRMN YLAWYQQKPGQPP NLLIY WASTRES GVDPDRFSGSGSGTD FTLTISSLQAEDVAVYYC QQYYSIPL TFGGG GTKVEIK (SEQ ID NO:22)
1E4	QVTLRESGPALVKPTQTLTCTFSGFSL TSDL CVSWIRQPPGKALEWLALIDWNDD KYYSTSLQ TRLTISKDTSKNQVLTMTN MDPVDATYYCARTIA AAGPYDAFDIW GQGTMTVTVSS (SEQ ID NO:23)	DIVMTQSPDSLAVSLGERATINCKSS QSVLYGSNNK NYLAWYQQKPGQPP KLLIY WASTRKS GVDPDRFSGSGSGT DFTLTISSLQAEDVAVYYC QEYYS L RFT FGPGTKVDIK (SEQ ID NO:24)

[0344] The validated anti-CD94 antibodies were further evaluated for their ability (or lack thereof) to block binding by HLA-E. HLA-E is the ligand of CD94/NKG2A heterodimers, and plays a crucial role in the inhibition of NK and CD8+ T cell activity when bound to CD94/NKG2A. Without wishing to be bound to theory, it is thought that the interaction between HLA-E and CD94/NKG2A may result in activation and proliferation of target cells. Thus, it is beneficial that the anti-CD94 antibody candidate does not block the CD94:HLA-E interaction in a diseased setting.

[0345] HLA-E blocking by anti-CD94 antibody clones and commercially available anti-CD94 antibodies was evaluated by flow cytometry. As shown in **FIG. 4**, 18H3 and 1E4 antibodies did not block HLA-E binding. Over 40% HLA-E blocking was observed for commercially available anti-CD94

antibodies, while 0% blocking was observed for the anti-CD94 antibodies. Because expression levels of CD94 varies from dim (~10,000 receptors) to bright (>100,000 receptors), we propose that if an antibody blocks more than 20% of HLA-E binding it can be considered as a ligand blocking antibody. Overall, this HLA-E blocking assay demonstrates that 18H3 and 1E4 antibodies do not block the interaction of CD94 with HLA-E, while commercially available CD94 antibodies block this interaction.

[0346] Competition assays were performed to determine if the newly identified antibodies bound to shared epitopes with themselves and existing antibodies. Anti-CD94 antibodies 18H3, 1M4, and 1E4 were assayed for competition with each other as well as with commercially available antibodies. As shown in **FIGS. 5A-5B**, 18H3 antibody binds to a unique epitope. 18H3 only partially competed with HP-3D9, and did not compete with the DX22, HP-3B1, 131412, 12K45, 1E4 and 1M4 antibodies. Thus, the 18H3 antibody binds to an epitope that is not shared with commercially available antibodies.

[0347] Similarly, 1M4 antibody did not compete with commercially available antibodies. As shown in **FIGS. 6A-6B**, 1M4 competed with 1E4 antibody, but did not compete with DX22, 131412, HP-3D9, 12K45 and HP-3B1.

[0348] The 1E4 antibody did not compete with four out of the five commercially available anti-CD94 antibodies tested. As shown in **FIG. 7**, 1E4 partially competed with 12K45, but did not compete with HP-3D9, DX22, 131412 and HP-3B1.

[0349] An antibody internalization assay was performed to evaluate internalization of CD94 receptors when bound by anti-CD94 antibody. In this assay, a cutoff of above 50% would be considered high degree of internalization. Without wishing to be bound to theory, it is thought that a low level of internalization would be beneficial for antibody-dependent cellular cytotoxicity (ADCC), as CD94 receptor would be retained on the cell surface and maintain a high receptor density for effector cells to execute ADCC. The results depicted in **FIGS. 8A-8B** show that CD94 receptor became internalized when bound to commercial anti-CD94 antibodies, but not when bound to 18H3, 1M4 and 1E4 antibodies. 18H3, 1M4, and 1E4 antibodies did not become internalized above 50% upon binding to CD94. In contrast, a 54%, 56%, 24%, 32%, 18% percent decrease in MFI was observed for HP-3D9, DX22, 18H3, 1M4 and 1E4, respectively, comparing 0.5 hours to 24 hours at 37 °C.

[0350] To test the ability of the anti-CD94 antibodies to induce ADCC of NK cells, an ADCC assay was performed using healthy donor PBMCs. For this assay, 18H3 antibody was produced in Expi-CHO cells cultured in the presence of kifunensine, a potent inhibitor of the mannosidase I enzyme, to produce 18H3-KIF mimicking non-fucosylated antibody. Fucosylated 1E4 antibody was also tested for ADCC. As shown in **FIGS. 9A-9B**, partially non-fucosylated, human IgG1 18H3 and fucosylated 1E4 depleted human NK cells in the PBMC pool of healthy donors in *ex vivo* culture after 24 hours of incubation. The depletion of NK cells by human IgG1 18H3 and 1E4 was concentration-dependent. The IC₅₀ of 18H3-KIF was determined as 0.02 µg/ml, while the IC₅₀ was undetermined for 1E4 antibody.

[0351] Finally, the ability of the 18H3 antibody to induce ADCC of human leukemic cells was evaluated through an ADCC assay using cells from chronic lymphoproliferative disorder of NK cells

(CLPD-NK) patients. For this assay, 18H3 antibody was produced in Expi-CHO cells cultured in the presence of kifunensine to produce 18H3-KIF mimicking non-fucosylated antibody. As shown in **FIG. 10**, partially non-fucosylated, human IgG1 18H3 depleted human CLPD-NK leukemic cells in a PBMC pool of a CLPD-NK patient in *ex vivo* culture after 24 hours of incubation. The 18H3 antibody depleted human CLPD-NK leukemic cells in a concentration dependent manner, with an IC₅₀ of 0.059 µg/ml. This depletion was selective, as no other cell types were affected.

[0352] **FIG. 11** summarizes the characteristics and functional assessment of the anti-CD94 antibodies relative to the commercially available antibodies as described above.

Example 2: Anti-CD94 antibody ATX-130 characterization

[0353] This example describes the characterization of an antibody specific to human CD94.

Materials and methods

[0354] Materials and methods used in this experiment are detailed below. Unless otherwise noted, donor samples and primary cells were prepared as described in Example 1. Unless otherwise noted, antibody affinity assays, HLA-E blocking assay, antibody competition assay, antibody internalization assay, and antibody-dependent cellular cytotoxicity assay were performed as described in Example 1.

Interferon gamma ELISA

[0355] Approximately $1 \times 10^5 - 2 \times 10^5$ fresh or frozen PBMCs were plated in tissue culture-treated 96-well U bottom plates in RPMI with 10% low IgG FBS. The cells were incubated overnight in hATX-130, mATX-130, human IgG1 isotype control and media alone (1, 5, and 10 µg/ml). Cell culture supernatants were collected 24 hours post-incubation and assessed for IFNγ secretion using Human IFN-γ Quantikine ELISA Kit (R&D systems, Minneapolis, MN).

Results

[0356] Four-week old, ATX-Gx Alloy transgenic mice (mice that produce human antibodies) were immunized subcutaneously with C-terminal His-tagged CD94 for five weeks, with one boost of antigen per week. Antibody titers in mouse serum were assessed during pre- and post-boosts via ELISA and flow cytometry. The mice with the highest serum antibody titer were selected for spleen harvest. The B-cells were isolated from the spleen and then the repertoires of manipulated V-genes are cloned into phage library vectors. The phage library was then screened for high affinity binders against immobilized CD94 antigen through 2-3 cycles, followed by elution of phage candidates. The eluted phage was used to infect bacteria and the DNA was sequenced to identify VL and VH sequences. The VL and VH sequences were reformatted on human IgG1 to generate human anti-CD94 antibodies.

[0357] The affinity of the antibody clones was assessed by flow cytometry analysis. ATX-130-KIF mimicking non-fucosylated antibody was produced by culturing Expi-CHO cells cultured in the presence

of kifunensine, a potent inhibitor of the mannosidase I enzyme. **FIG. 12** shows titration curves generated for anti-CD94 antibody clones ATX-130 and ATX-130-KIF. anti-CD94 antibody ATX-130 showed an affinity of 0.6 nM on human primary NK cells. ATX-130-KIF showed an affinity of 1 nM on primary cynomolgus NK cells, 1.4 nM on chronic lymphoproliferative disorder of NK cells (CLPD-NK), and 3 nM on T- large granular lymphocyte leukemia cells (T-LGLL). Thus, ATX-130 and ATX-130-KIF have similar binding affinity on primary human NK cells, cynomolgus NK cells, CLPD-NK cells, and T-LGLL cells.

[0358] The affinity of the antibody clone ATX-130 on CD94 homodimer and heterodimer was also assessed by flow cytometry analysis. **FIG. 13** shows titration curves generated for anti-CD94 antibody clone ATX-130. anti-CD94 antibody clone ATX-130 showed an affinity of 0.3 nM on BaF3 cells overexpressing CD94 homodimer (top panel). anti-CD94 antibody clone ATX-130 showed an affinity of 0.8 nM and 1.8 nM on BaF3 cells overexpressing either CD94/NKG2A heterodimer or CD94/NKG2C, respectively (lower panels). These results show that ATX-130 binds to CD94 homodimer, CD94/NKG2A, and CD94/NKG2C heterodimer BaF3 cells with similar affinity.

[0359] An Interferon gamma ELISA was performed to evaluate ATX-130 agonistic or antagonistic effect on CD94/NKG2A and NKG2C heterodimers. As shown in **FIG. 14**, NK cells did not secrete IFN-gamma in the presence of ATX-130 with mouse inactive Fc (mATX-130), suggesting that binding to CD94 alone in the absence of active human Fc does not activate downstream signaling of NKG2A and NKG2C. Thus, the ATX-130 antibody is not agonist or antagonistic on CD94/NKG2A and NKG2C on NK cells.

[0360] Competition assays were performed to determine if the newly identified antibodies bound to shared epitopes with existing antibodies. Anti-CD94 antibody ATX-130 was assayed for competition with commercially available anti-CD94 antibodies. As shown in **FIG. 15**, ATX-130 binds to a unique epitope. ATX-130 did not compete with HP-3D9, DX22, 131412, 12K45, or HP-3B1. Thus, the ATX-130 antibody binds to an epitope that is not shared with commercially available antibodies.

[0361] Following validation, the VH and VL sequences were determined for the validated antibody clones. Table 2 summarizes the VH and VL sequences for the validated anti-CD94 clone, ATX-130. The framework and CDR sequences (*see* Table 1) were determined using the Kabat numbering scheme.

[0362] The validated anti-CD94 antibody was further evaluated for its ability (or lack thereof) to block binding by HLA-E, as described in Example 1. HLA-E blocking by anti-CD94 antibody ATX-130-KIF and an isotype control were evaluated by flow cytometry. As shown in **FIG. 16**, saturating concentrations of ATX-130-KIF did not block HLA-E binding.

[0363] An antibody internalization assay was performed to evaluate internalization of CD94 receptors when bound by anti-CD94 antibody, as described in Example 1. As shown in **FIG. 17**, CD94 receptor did not become internalized for up to 24 hours at 37°C when bound to unconjugated ATX-130.

[0364] KIF-treated (ATX-130-KIF) non-fucosylated antibody binding selectivity was assessed by flow cytometry analysis on healthy human, cynomolgus, and LGLL patient immune cells. As shown in **FIG.**

18, ATX-130-KIF did not bind on monocytes, CD4+ T cells, or B cells in normal human and cynomolgus PBMCs, and LGL leukemia patient PBMCs. Small subsets of CD8+ T cells were recognized by ATX-130-KIF in all three sample types. Thus, ATX-130-KIF selectively binds to normal and LGLL NK cells from all three sample types.

[0365] To test the ability of the anti-CD94 antibodies to induce ADCC of NK cells, an ADCC assay was performed using human healthy donor PBMCs. For this assay, anti-CD94 non-fucosylated antibody (ATX-130-KIF) was tested for ADCC in human NK cells, B cells, T cells, and monocytes. As shown in **FIG. 19**, ATX-130-KIF depleted human NK cells in the PBMC pool of healthy donors in *ex vivo* culture after 24 hours of incubation, whereas human B cells, T cells, and monocytes were unaffected. The depletion of NK cells by ATX-130-KIF was concentration-dependent. The IC₅₀ of ATX-130-KIF was determined as 0.8 ng/ml. Depletion of over 50% of NK cells was observed at the highest concentration *ex vivo*. ATX-130 potency on NK cells and preservation of other immune cells suggests that this molecule can exhibit high efficacy and favorable toxicity profile *in vivo*.

[0366] Next, to test the ability of the anti-CD94 antibodies to induce ADCC of NK cells, an ADCC assay was performed using cynomolgus PBMCs. For this assay, anti-CD94 non-fucosylated antibody (ATX-130-KIF) was tested for ADCC in cynomolgus NK cells, B cells, T cells, and monocytes. As shown in **FIG. 20**, ATX-130-KIF depleted cynomolgus NK cells in the cynomolgus PBMC pool in *ex vivo* culture after 24 hours of incubation, whereas cynomolgus B cells, T cells, and monocytes were unaffected. The depletion of NK cells by ATX-130-KIF was concentration-dependent. The IC₅₀ of ATX-130-KIF was determined as 0.3 ng/ml. Depletion of over 50% of NK cells was observed at the highest concentration *ex vivo*. ATX-130 potency on NK cells and preservation of other immune cells suggested that this molecule can exhibit high efficacy and favorable toxicity profile *in vivo*.

[0367] Finally, the ability of the ATX-130-KIF antibody to induce ADCC of human leukemic cells was evaluated through an ADCC assay using cells from chronic lymphoproliferative disorder of NK cells (CLPD-NK) and T-large granular lymphocyte leukemia (T-LGLL) patients. As shown in **FIG. 21**, the ATX-130-KIF antibody depleted human T-LGLL and CLPD-NK leukemic cells in a concentration dependent manner, with an IC₅₀ of 0.2 ng/ml and 0.6 ng/ml, respectively. Depletion of over 30% and 50% of T-LGLL and CLPD-NK leukemic cells, was observed at the highest concentration *ex vivo*, respectively. This depletion was selective, as no other cell types were affected.

Example 4: Anti-CD94 antibody ATX-130-KIF study in non-human primates

[0368] This example describes an exploratory pharmacodynamic (PD) in cynomolgus macaques to evaluate the efficacy of ATX-130-KIF *in vivo*.

Materials and methods

In vivo non-human primate exploratory study

[0369] Two healthy male cynomolgus monkeys, ages 6.5 and 9.2 years and weighing 6.54 and 7.18 kg, respectively, naïve to all compounds prior to study commencement and with no prior history of illness were selected for the study. As shown in **FIG. 24A**, two doses of ATX-130-KIF (2 mg/kg) were administered to Cyno #1 through intravenous (IV) infusion at a rate of approximately 0.25 mL/min over 60 minutes on Week 0 and 8. Two doses of ATX-130-KIF (2 mg/kg) were administered to Cyno #2 through IV infusion at a rate of approximately 0.25 mL/min over 60 minutes on Week 0 and 16. Blood, serum and PBMCs were collected at various time intervals at pre- and post-dose as shown in **FIG. 24A**. PD was determined via target cell depletion by flow cytometry analysis. The study endpoint was projected at 22 weeks.

Results

[0370] To evaluate the efficacy of ATX-130-KIF *in vivo*, a PD study was completed in non-human primates (NHP). Two healthy male cynomolgus monkeys, ages 6.5 and 9.2 years and weighing 6.54 and 7.18 kg (Cyno #1 and Cyno #2), respectively, naïve to all compounds prior to study commencement and with no prior history of illness were selected for the study. Pharmacodynamic (PD) activity was determined via target cell depletion by flow cytometry analysis. All bioanalytical data were presented up to 18 weeks, with the study endpoint projected at 22 weeks.

[0371] The ability (or lack thereof) of ATX-130-KIF to deplete cynomolgus NK cells in blood was assessed by flow cytometry analysis. As shown in **FIG. 24B**, the composition of NK cells in total PBMCs in Cyno #1 (left panel) and Cyno #2 (right panel) were 20% and 25% at baseline, respectively. For each dose, depletion of targets cells (NK cells) to <5% of PBMCs was detected in both animals 6 hours post-administration of ATX-130-KIF. In Cyno #1, a steady increase in percent NK cells was observed from 6 hours to 336 hours, which then stabilized at 50% of baseline up to administration of the second dose at 1008 hours. Stabilization of NK cell count at 50% of baseline was observed after 168 hours following the 2nd dose. In Cyno #2, NK cell recovery was slower than in Cyno #1. NK cell count remained at low levels 6 weeks following dose 1, with an increase over Weeks 8 to 14. Administration of ATX-130-KIF at Week 16 reduced NK cell levels 6 hours post-dose and remained low up to the latest sample collection. Overall, the current results show that ATX-130-KIF can demonstrate efficacy *in vivo* in cynomolgus macaques.

[0372] The ability (or lack thereof) of ATX-130-KIF to deplete cynomolgus CD4 T, CD8 T, and B cells in blood was assessed by flow cytometry analysis. As shown in **FIG. 25A**, the composition of CD4+ T cells, CD8+ T cells, and B cells of total PBMCs in Cyno #1 was 27%, 40%, and 4% at baseline, respectively. As shown in **FIG. 25B**, the composition of CD4+ T cells, CD8+ T cells, and B cells of total PBMCs in Cyno #2 was 26%, 40%, and 5% at baseline, respectively. Depletion of T and B cells was detected in both animals 6 hours post-administration of ATX-130-KIF. However, these immune cell populations returned to baseline levels 24 hours post-dose. The results from this study show that ATX-130-KIF only transiently depletes other immune cells, without depletion of non-CD94 expressing cells.

[0373] Cynomolgus monocyte depletion was assessed by flow cytometry. As shown in **FIG. 26**, elevation of monocytes was observed 6 hours post-dose, but returned to baseline levels after 7 days. The results from the study show that ATX-130-KIF transiently elevates monocytes, suggesting that ATX-130-KIF can engage monocytes to perform ADCC and contribute to targeted depletion of NK cells.

[0374] Cynomolgus CD16 expression on monocytes was assessed by flow cytometry. As shown in **FIG. 27**, elevation of CD16 on monocytes was observed 24 hours post-dose, but returned to baseline levels after 7 days. The results from the study show that ATX-130-KIF transiently elevates CD16 on monocytes, suggesting that ATX-130-KIF engages monocytes to perform ADCC and contribute to targeted depletion of NK cells.

Example 3: Anti-CD94 antibody ATX-130 in vivo mouse study

[0375] This example describes the characterization of antibodies specific to human CD94 using *in vivo* mouse studies.

Materials and methods

In vivo humanized IL-15 transgenic mouse studies

[0376] The humanized NSGTM-IL-15 transgenic mouse was obtained from the Jackson Lab. Mice are engrafted with healthy donor and LGLL donor PBMCs for 3 and 28 days, respectively. One dose of human IgG1 isotype control or ATX-130 (5 mg/kg) was injected into mice, and depletion of normal NK cells, normal CD8 T cells and CD8 T leukemic cells in the blood, spleen, bone marrow and liver were assessed by flow cytometry 48 hours post-dose (**FIG. 22A**).

Results

[0377] The ability (or lack thereof) of ATX-130 to deplete human NK and CD8 T cells was assessed in IL-15 transgenic mice (NSGTM-IL-15). The humanized NSGTM-IL-15 transgenic mouse is a mouse strain with a complete absence of the mouse IL-2R gamma gene, resulting in defective adaptive and innate immune systems. Expression of human IL-15 enables efficient engraftment of human immune cells, particularly cytotoxic immune cells, from healthy donors and leukemic patients. As shown in **FIG. 22B**, complete NK cell depletion was observed with ATX-130 treatment (5 mg/kg) relative to isotype control. Partial depletion (~50%) of CD8 T cells was observed. The remaining CD8 T cells were CD94-negative, and thus were not depleted. Overall, ATX-130 depletes CD94+ cells, which includes all human NK cells, and 50% of CD8 T cells.

[0378] The ability (or lack thereof) of ATX-130-KIF to deplete LGLL in blood, spleen, bone marrow, and liver was assessed in IL-15 transgenic mice (NSGTM-IL-15). As shown in **FIG. 23**, more than 50% LGLL cell depletion was observed with ATX-130 treatment (5 mg/kg) relative to isotype control. The remaining LGLL cells were CD94-negative, and thus were not depleted. Overall, ATX-130 efficiently depletes CD94+ LGLL cells in mice *in vivo*.

Example 5: Anti-CD94 antibody ATX-130 non-GLP study in non-human primates

[0379] This example describes a second pharmacodynamic (PD) in cynomolgus macaques to evaluate the efficacy of ATX-130 *in vivo*.

Materials and methods***In vivo non-human primate non-GLP study***

[0380] A second non-GLP pharmacodynamic (PD) study of 14 healthy cynomolgus monkeys naïve to all compounds prior to study commencement and with no prior history of illness were selected for the study. Five doses of ATX-130 (0-100 mg/kg) were administered through intravenous (IV) infusion at a rate of approximately 0.25 mL/min over 60 minutes weekly. PBMCs were collected at various time intervals at pre- and post-dose. PD was determined via NK cell depletion (CD3-CD16+) and CD8 T cell depletion (CD3+CD8+NKG2A+) in blood by flow cytometry analysis. Depletion of the same target cells was determined in tissues that were harvested at the time of necropsy.

Results

[0381] To evaluate the efficacy of ATX-130 *in vivo*, a second pharmacodynamic (PD) study was completed in NHP (cynomolgus macaques; **FIG. 28A**). To demonstrate *in vivo* activity of ATX-130 in NHP, ATX-130 was used as the test article. Fourteen healthy cynomolgus macaques naïve to all compounds prior to study commencement and with no prior history of illness were selected for the study.

[0382] The ability (or lack thereof) of ATX-130 to deplete cynomolgus NK cells in blood was assessed by flow cytometry analysis. As shown in **FIG. 28B**, depletion of targets cells (NK cells) to <5% of PBMCs was detected in all animals 6 hours post-administration of ATX-130 at each dose. Overall, the current results show that ATX-130 can demonstrate efficacy *in vivo* in cynomolgus macaques at 5, 50, and 100mg/kg.

[0383] The ability (or lack thereof) of ATX-130 to deplete cynomolgus CD94+CD8+NKG2A+ cells in blood at 5, 50, and 100mg/kg was assessed by flow cytometry. As shown in **FIG. 29**, depletion of targets cells (CD8 T cells) to <50% of PBMCs was detected in all animals 8 days post-administration of ATX-130 at each dose. Overall, the current results showed that ATX-130 can demonstrate efficacy *in vivo* on CD94+ CD8 T cells in cynomolgus macaques at 5, 50, and 100 mg/kg.

[0384] The ability (or lack thereof) of ATX-130 to deplete cynomolgus NK and CD8+NKG2A+ T cells in tissue was assessed by flow. As shown in **FIG. 30**, depletion of targets cells (NK and CD8 T cells) to <50% of total cells in animals treated with 5, 50, and 100 mg/kg of ATX-130 relative to 0 mg/kg was detected at the end of study. Overall, the current results showed that ATX-130 can demonstrate efficacy *in vivo* on NK and CD94+ CD8 T cells in cynomolgus macaque tissue.

Example 6: Characterization of additional anti-CD94 antibodies

[0385] This example describes characterization of additional ATX anti-CD94 antibodies with respect to binding cells expressing CD94 and CD94 ligand blocking.

[0386] First, cell binding affinity of anti-CD94 antibodies ATX-122, -123, -124, -125, -126, -127, -128, -129, and -130 was examined. For human NK cell binding, PBMCs were freshly isolated from healthy donors and incubated with unconjugated antibodies in a dilution series from 100 nM to 0.046 nM. Secondary anti-human antibody labeled with Alexa Fluor 647 was used to detect binding on CD3-CD56bright NK cells. For cynomolgus CD94 binding, HEK293 cells overexpressing cynomolgus CD94 were incubated with unconjugated antibodies in a dilution series from 100 nM to 0.046 nM. Secondary anti-human antibody labeled with Alexa Fluor 647 was used to detect binding on the cells.

[0387] The results demonstrated that the ATX series anti-CD94 antibodies bound human NK cells (**FIG. 31A**) and cells overexpressing cynomolgus CD94 (mimicking cynomolgus NK cells; **FIG. 31B**). In freshly isolated PBMCs from healthy donors and HEK293 cells expressing cynomolgus CD94, ATX anti-CD94 antibodies bound with affinities (EC50) ranging from 0.3 to 27nM.

[0388] Second, anti-CD94 antibodies ATX-122, -123, -124, -125, -126, -127, -128, -129, and -130 were characterized in HLA-E tetramer blocking assays to determine whether they block HLA-E binding. Healthy donor PBMCs were incubated with anti-CD94 antibodies. PE labeled HLA-E tetramer was then incubated with cells and antibody mixture and detected by flow cytometry.

[0389] The results demonstrated that most anti-CD94 antibodies did not block HLA-E binding (**FIGS. 32A-32I**). Percent blocking was calculated as $100 - ((\text{percent HLA-E positive for anti-CD94 antibody}) / (\text{percent HLA-E positive for isotype}) * 100)$. If an antibody blocked more than 20% of HLA-E binding, it was considered a ligand-blocking antibody. Overall, 6 out of 9 ATX series anti-CD94 antibodies did not block HLA-E binding, whereas commercially available anti-CD94 antibodies block this interaction (*see* Example 1). A summary of ATX series anti-CD94 antibody characteristics is provided in Table 3.

Table 3. Summary of ATX series anti-CD94 antibody characteristics.

Antibody	Affinity on human NK cells (nM)	Cyno CD94 cross-reactivity	HLA-E blocking
ATX-122	27.04	No	0%
ATX-123	1.12	Yes	39%
ATX-124	10.03	No	18%
ATX-125	4.63	Yes	11%
ATX-126	2.52	Yes	0%

ATX-127	0.31	Yes	77%
ATX-128	0.32	No	10%
ATX-129	2.8	Yes	96%
ATX-130	0.6	Yes	0%

[0390] Although the present disclosure has been described in some detail by way of illustration and example for purposes of clarity of understanding, the descriptions and examples should not be construed as limiting the scope of the present disclosure. The disclosures of all patent and scientific literature cited herein are expressly incorporated in the entirety by reference.

CLAIMS

What is claimed is:

1. A human or humanized antibody that binds to human CD94, wherein binding of the antibody to human CD94 does not block binding between human CD94 and human HLA-E.
2. The antibody of claim 1, wherein the antibody binds human CD94 expressed on the surface of a cell.
3. The antibody of claim 2, wherein the cell is a human natural killer (NK) cell.
4. A human or humanized antibody that binds to human CD94 and cynomolgus CD94.
5. The antibody of claim 4, wherein the antibody binds human CD94 expressed on the surface of a cell.
6. The antibody of claim 5, wherein the cell is a human natural killer (NK) cell.
7. The antibody of any one of claims 4-6, wherein binding of the antibody to human CD94 does not block binding between human CD94 and human HLA-E.
8. The antibody of any one of claims 1-3 and 7, wherein binding of the antibody to cells expressing human CD94 blocks less than 20% of HLA-E binding to the human CD94.
9. The antibody of any one of claims 1-8, wherein incubating the antibody with a cell expressing human CD94 on its surface for 24 hours at 37°C results in a decrease in surface antibody staining of less than 50% due to internalization.
10. The antibody of any one of claims 1-9, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:6.
11. The antibody of any one of claims 1-9, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1

comprising the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6.

12. The antibody of claim 10 or claim 11, wherein the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:19, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:20.

13. The antibody of claim 12, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:19, and the VL domain comprises the amino acid sequence of SEQ ID NO:20.

14. The antibody of any one of claims 1-9, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:7, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:8, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:9; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:10, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:11, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:12.

15. The antibody of any one of claims 1-9, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:7, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:8, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:9; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:10, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:11, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:12.

16. The antibody of claim 14 or claim 15, wherein the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:21, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:22.

17. The antibody of claim 16, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:21, and the VL domain comprises the amino acid sequence of SEQ ID NO:22.

18. The antibody of any one of claims 1-9, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:18.

19. The antibody of any one of claims 1-9, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18.

20. The antibody of claim 18 or claim 19, wherein the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:23, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:24.

21. The antibody of claim 20, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:23, and the VL domain comprises the amino acid sequence of SEQ ID NO:24.

22. The antibody of any one of claims 1-9, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein:

(a) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:30, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:31, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:32; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:35;

(f) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:62; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:63, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:64.

23. The antibody of any one of claims 4-6, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein:

(a) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:37, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:38; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:35;

(b) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:54, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:55; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:56; or

(c) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:83, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:84, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:85; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:86, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid

sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:61.

24. The antibody of any one of claims 1-9, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein:

- (a) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:30, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:31, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:32; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35;
 - (b) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:39, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:40; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35;
 - (c) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:41, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:42, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:43; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:44, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:46;
 - (d) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:49; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:51, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:52;
 - (e) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:57, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:58, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:59; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:60, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61;
- or
- (f) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:62; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:63, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:64.

25. The antibody of any one of claims 1-9, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein:

(a) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:88, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:89; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35;

(b) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:92, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:94; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35;

(c) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:95, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:96, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:97; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:98, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:99, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:100;

(d) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:109, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:110, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:114; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:115, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:99, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:52;

(e) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:101, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:102, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:103; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:104, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61;

or

(f) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:109, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:110, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:111; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:112, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:113, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:64.

26. The antibody of any one of claims 4-6, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein:

(a) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:37, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:38; and wherein the VL domain comprises a CDR-L1

comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35;
 (b) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:54, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:55; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:56;
 or

(c) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:83, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:84, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:85; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:86, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61.

27. The antibody of any one of claims 4-6, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein:

(a) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:92, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:93; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35;

(b) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:116, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:117, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:118; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:115, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:99, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:56;
 or

(c) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:105, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:106, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:107; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:108, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61.

28. The antibody of any one of claims 1-9, 22, 24, and 25, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein:

(a) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:65, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:66;

- (b) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:69, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:70;
 - (c) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:71, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:72;
 - (d) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:73, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:74;
 - (e) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:77, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:78; or
 - (f) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:81, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:82.
29. The antibody of claim 28, wherein:
- (a) the VH domain comprises the amino acid sequence of SEQ ID NO:65, and the VL domain comprises the amino acid sequence of SEQ ID NO:66;
 - (b) the VH domain comprises the amino acid sequence of SEQ ID NO:69, and the VL domain comprises the amino acid sequence of SEQ ID NO:70;
 - (c) the VH domain comprises the amino acid sequence of SEQ ID NO:71, and the VL domain comprises the amino acid sequence of SEQ ID NO:72;
 - (d) the VH domain comprises the amino acid sequence of SEQ ID NO:73, and the VL domain comprises the amino acid sequence of SEQ ID NO:74;
 - (e) the VH domain comprises the amino acid sequence of SEQ ID NO:77, and the VL domain comprises the amino acid sequence of SEQ ID NO:78; or
 - (f) the VH domain comprises the amino acid sequence of SEQ ID NO:81, and the VL domain comprises the amino acid sequence of SEQ ID NO:82.
30. The antibody of any one of claims 4-6, 23, 26, and 27, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein:
- (a) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:67, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:68;
 - (b) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:75, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:76; or

(c) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:79, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:80.

31. The antibody of claim 30, wherein:

- (a) the VH domain comprises the amino acid sequence of SEQ ID NO:67, and the VL domain comprises the amino acid sequence of SEQ ID NO:68;
- (b) the VH domain comprises the amino acid sequence of SEQ ID NO:75, and the VL domain comprises the amino acid sequence of SEQ ID NO:76; or
- (c) the VH domain comprises the amino acid sequence of SEQ ID NO:79, and the VL domain comprises the amino acid sequence of SEQ ID NO:80.

32. An antibody that binds to human CD94, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:6.

33. The antibody of claim 32, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6.

34. The antibody of claim 32 or claim 33, wherein the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:19, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:20.

35. The antibody of claim 34, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:19, and the VL domain comprises the amino acid sequence of SEQ ID NO:20.

36. An antibody that binds to human CD94, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of

SEQ ID NO:7, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:8, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:9; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:10, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:11, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:12.

37. The antibody of claim 36, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:7, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:8, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:9; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:10, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:11, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:12.

38. The antibody of claim 36 or claim 37, wherein the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:21, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:22.

39. The antibody of claim 38, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:21, and the VL domain comprises the amino acid sequence of SEQ ID NO:22.

40. An antibody that binds to human CD94, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:18.

41. The antibody of claim 40, wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18.

42. The antibody of claim 40 or claim 41, wherein the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:23, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:24.
43. The antibody of claim 42, wherein the VH domain comprises the amino acid sequence of SEQ ID NO:23, and the VL domain comprises the amino acid sequence of SEQ ID NO:24.
44. An antibody that binds to human CD94, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein:
- (a) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:30, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:31, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:32; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:35;
 - (b) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:37, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:38; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:35;
 - (c) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:39, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:40; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:35;

(h) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:83, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:84, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:85; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:86, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:61; or

(i) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:62; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:63, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:64.

45. An antibody that binds to human CD94, wherein the antibody comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein:

(a) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:88, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:89; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:35;

(b) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:92, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:93; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid

sequence of SEQ ID NO:99, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:56;

(g) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:101, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:102, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:103; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:104, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:61;

(h) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:105, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:106, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:107; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:108, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:61; or

(i) the VH domain comprises a CDR-H1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:109, a CDR-H2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:110, and a CDR-H3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:111; and wherein the VL domain comprises a CDR-L1 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:112, a CDR-L2 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:113, and a CDR-L3 comprising an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:64.

46. The antibody of claim 44, wherein:

- (a) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:30, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:31, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:32; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35;
- (b) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:37, and a CDR-H3 comprising the

amino acid sequence of SEQ ID NO:38; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35;

(c) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:36, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:39, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:40; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:33, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35;

(d) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:41, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:42, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:43; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:44, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:46;

(e) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:49; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:51, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:52;

(f) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:54, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:55; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:50, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:45, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:56;

(g) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:57, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:58, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:59; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:60, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61;

(h) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:83, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:84, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:85; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:86, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61;

or

(i) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:47, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:48, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:62; and wherein the VL domain comprises a CDR-L1

comprising the amino acid sequence of SEQ ID NO:63, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:34, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:64.

47. The antibody of claim 45, wherein:

- (a) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:88, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:89; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35;
- (b) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:92, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:93; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35;
- (c) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:92, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:94; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:90, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:35;
- (d) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:95, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:96, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:97; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:98, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:99, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:100;
- (e) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:109, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:110, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:114; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:115, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:99, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:52;
- (f) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:116, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:117, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:118; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:115, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:99, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:56;
- (g) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:101, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:102, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:103; and wherein the VL domain comprises a CDR-L1

comprising the amino acid sequence of SEQ ID NO:104, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61;
(h) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:105, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:106, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:107; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:108, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:91, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:61;
or

(i) the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:109, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:110, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:111; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:112, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:113, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:64.

48. The antibody of any one of claims 44-47, wherein:

- (a) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:65, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:66;
- (b) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:67, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:68;
- (c) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:69, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:70;
- (d) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:71, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:72;
- (e) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:73, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:74;
- (f) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:75, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:76;
- (g) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:77, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:78;

- (h) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:79, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:80; or
 - (i) the VH domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:81, and the VL domain comprises an amino acid sequence with at least 80% sequence identity to the amino acid sequence of SEQ ID NO:82.
49. The antibody of claim 48, wherein:
- (a) the VH domain comprises the amino acid sequence of SEQ ID NO:65, and the VL domain comprises the amino acid sequence of SEQ ID NO:66;
 - (b) the VH domain comprises the amino acid sequence of SEQ ID NO:67, and the VL domain comprises the amino acid sequence of SEQ ID NO:68;
 - (c) the VH domain comprises the amino acid sequence of SEQ ID NO:69, and the VL domain comprises the amino acid sequence of SEQ ID NO:70;
 - (d) the VH domain comprises the amino acid sequence of SEQ ID NO:71, and the VL domain comprises the amino acid sequence of SEQ ID NO:72;
 - (e) the VH domain comprises the amino acid sequence of SEQ ID NO:73, and the VL domain comprises the amino acid sequence of SEQ ID NO:74;
 - (f) the VH domain comprises the amino acid sequence of SEQ ID NO:75, and the VL domain comprises the amino acid sequence of SEQ ID NO:76;
 - (g) the VH domain comprises the amino acid sequence of SEQ ID NO:77, and the VL domain comprises the amino acid sequence of SEQ ID NO:78;
 - (h) the VH domain comprises the amino acid sequence of SEQ ID NO:79, and the VL domain comprises the amino acid sequence of SEQ ID NO:80; or
 - (i) the VH domain comprises the amino acid sequence of SEQ ID NO:81, and the VL domain comprises the amino acid sequence of SEQ ID NO:82.
50. The antibody of any one of claims 32-49, wherein the antibody is a human antibody.
51. An antibody that binds the same epitope as the antibody of any one of claims 10-50.
52. An antibody that competes with the antibody of any one of claims 10-51 for binding to human CD94.
53. The antibody of any one of claims 1-52, wherein the antibody is an antigen-binding antibody fragment or single chain antibody.
54. The antibody of any one of claims 1-52, wherein the antibody further comprises an Fc region.
55. The antibody of claim 54, wherein the Fc region is a human IgG1 Fc region.

56. The antibody of claim 54 or claim 55, wherein the antibody comprises a human Fc region that is non-fucosylated.
57. The antibody of any one of claims 54-56, wherein the antibody binds to a human cellular Fc gamma receptor IIIA to a greater extent than an antibody comprising a wild type human IgG1 Fc region.
58. The antibody of any one of claims 54-57, wherein the antibody is capable of inducing antibody-dependent cellular cytotoxicity (ADCC) against a cell expressing human CD94 on its surface.
59. A polynucleotide encoding the antibody of any one of claims 1-58.
60. A vector comprising the polynucleotide of claim 59.
61. The vector of claim 60, wherein the vector is an expression vector.
62. An isolated host cell comprising the polynucleotide of claim 59 or the vector of claim 60 or claim 61.
63. A method of producing an antibody, comprising culturing the host cell of claim 62 under conditions suitable for production of the antibody.
64. The method of claim 63, further comprising recovering the antibody from the host cell.
65. A pharmaceutical composition comprising the antibody of any one of claims 1-58 and a pharmaceutically acceptable carrier.
66. A method for treating a disease or disorder in a subject, comprising administering to the subject an effective amount of the antibody of any one of claims 1-58 or the composition of claim 65.
67. The method of claim 66, wherein administration of the antibody results in a reduction in the number of peripheral blood LGL or NK cells in the subject.
68. The method of claim 66, wherein the disease or disorder is Felty's syndrome, and wherein administration of the antibody to the subject results in a reduction of one or more Felty's syndrome symptoms in the subject.
69. The method of claim 66, wherein the disease or disorder is inclusion body myositis, and wherein administration of the antibody to the subject results in a reduction of one or more inclusion body myositis symptoms in the subject.
70. The method of claim 66, wherein the disease or disorder is aggressive NK leukemia, and wherein administration of the antibody to the subject results in a reduction of one or more aggressive NK leukemia symptoms in the subject.

71. The method of claim 66, wherein the disease or disorder is rheumatoid arthritis, and wherein administration of the antibody to the subject results in a reduction of one or more rheumatoid arthritis symptoms in the subject.
72. The method of claim 66, wherein the disease or disorder is LGL leukemia, and wherein administration of the antibody to the subject results in a reduction of one or more LGL leukemia symptoms in the subject.
73. The method of claim 66, wherein the disease or disorder is CLPD-NK, and wherein administration of the antibody to the subject results in a reduction of one or more CLPD-NK symptoms in the subject.
74. The method of claim 66, wherein the disease or disorder is natural killer (NK) cell or T-cell lymphoma, and wherein administration of the antibody to the subject results in a reduction of one or more lymphoma symptoms in the subject.
75. The method of claim 66, wherein the disease or disorder is microscopic colitis, and wherein administration of the antibody to the subject results in a reduction of one or more microscopic colitis symptoms in the subject.
76. A method for reducing the number of peripheral blood LGL and/or NK cells in a subject, comprising administering to the subject an effective amount of the antibody of any one of claims 1-58 or the composition of claim 65.
77. A method for inducing ADCC activity in a subject, comprising administering to the subject an effective amount of the antibody of any one of claims 1-58 or the composition of claim 65.
78. A method for treating CLPD-NK in a human subject in need thereof, comprising administering to the subject an effective amount of the antibody of any one of claims 1-58 or the composition of claim 65.
79. The method of claim 78, wherein administration of the antibody results in an improvement of one or more CLPD-NK symptoms in the subject.
80. A method of treating natural killer (NK) cell or T-cell lymphoma, comprising administering to a subject in need thereof an effective amount of an antibody that binds human CD94.
81. The method of claim 80, wherein the antibody does not bind to the same epitope on human CD94 as anti-CD94 antibody clones HP-3D9, DX22, 131412, or 12K45.
82. The method of claim 80, wherein the antibody binds to human CD94 with a greater affinity than anti-CD94 antibody clones HP-3D9, DX22, 131412, and 12K45.

83. The method of any one of claims 74 and 80-82, wherein the NK cell or T-cell lymphoma is extranodal NK/T cell lymphoma, hepatosplenic T cell lymphoma (TCL), enteropathy-associated TCL, cutaneous TCL, anaplastic large cell lymphoma (ALK+), anaplastic large cell lymphoma (ALK-), peripheral TCL, angioimmunoblastic TCL, adult TCL, monomorphic epitheliotropic intestinal TCL, epidermotropic CD8+ cutaneous TCL, primary cutaneous gamma/delta TCL, or subcutaneous panniculitis TCL.
84. The method of claim 83, wherein the NK cell or T-cell lymphoma is extranodal NK/T cell lymphoma, hepatosplenic TCL, or enteropathy-associated TCL.
85. A method for enhancing chimeric antigen receptor T cell (CAR-T) therapy in a human subject in need thereof, comprising administering to the subject an effective amount of the antibody of any one of claims 1-58 or the composition of claim 65 prior to administration of a CAR-T treatment to the subject.
86. The method of claim 85, wherein the administration of the antibody or composition results in depletion of NK cells in the subject prior to administration of the CAR-T treatment.
87. A method for depleting CD8+ CD94+ T cells in a human subject in need thereof, comprising administering to the subject an effective amount of the antibody of any one of claims 1-58 or the composition of claim 65.
88. The method of any one of claims 66-87, further comprising administering an IL-2 polypeptide to the subject.
89. The method of any one of claims 66-88, wherein the subject is a human.

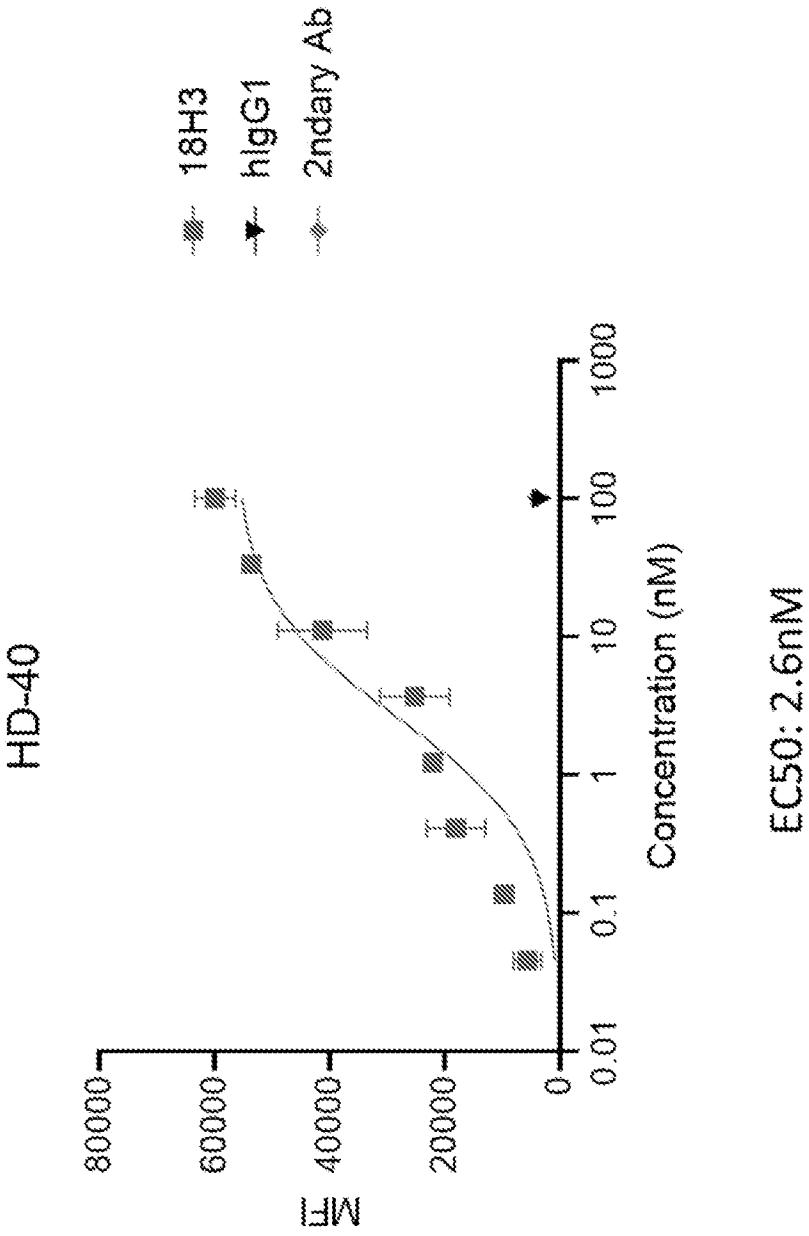


FIG. 1

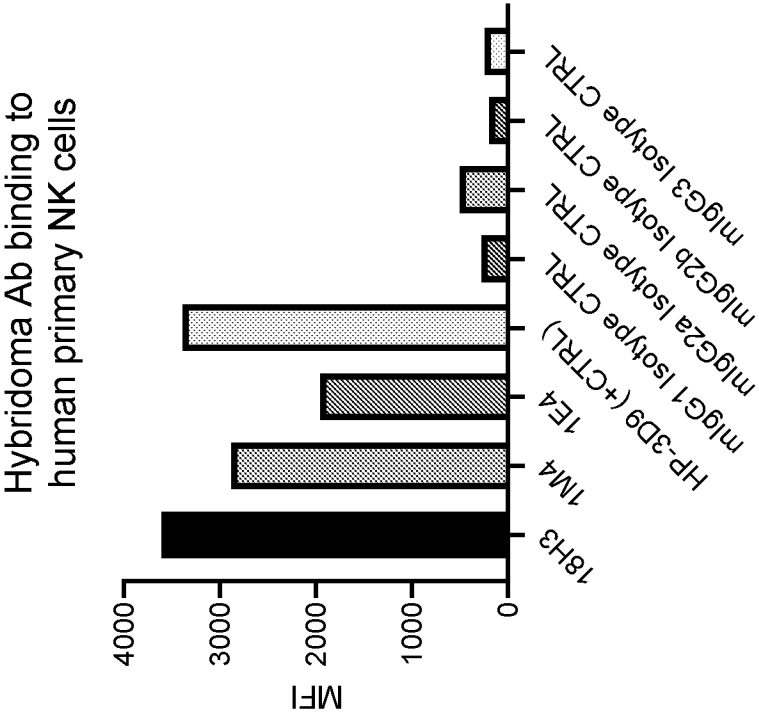


FIG. 2

Hybridoma Ab cross-reactivity
with cyno CD94

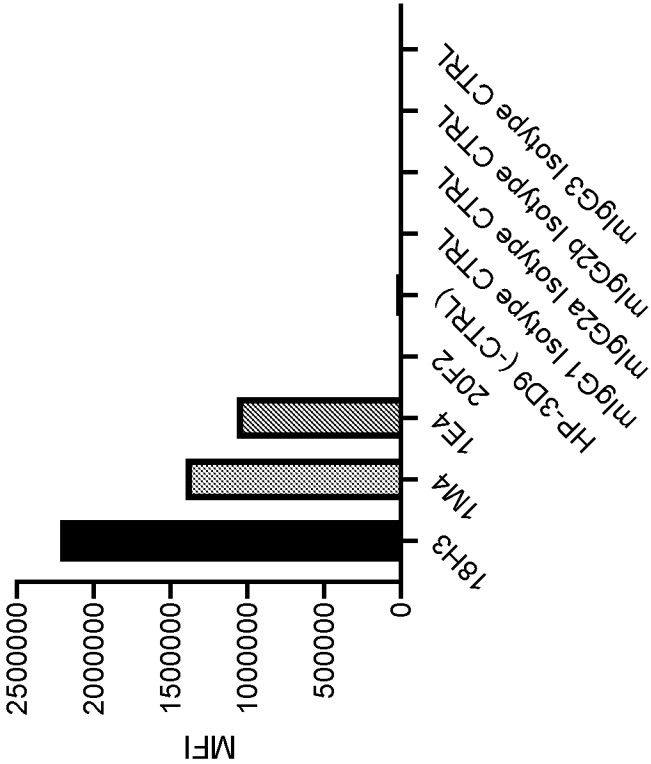


FIG. 3A

Commercial CD94 antibody
binding to Cyno CD94

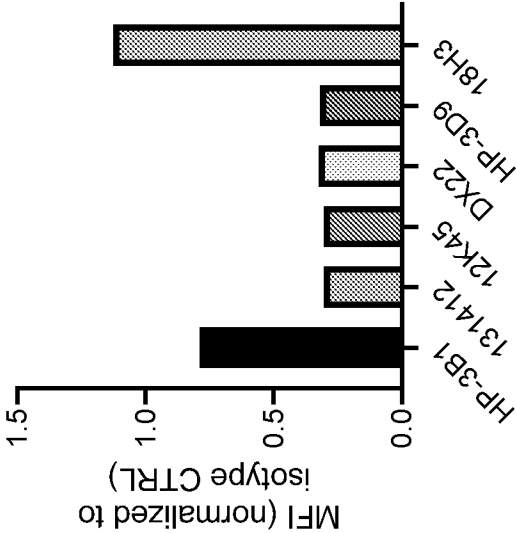


FIG. 3B

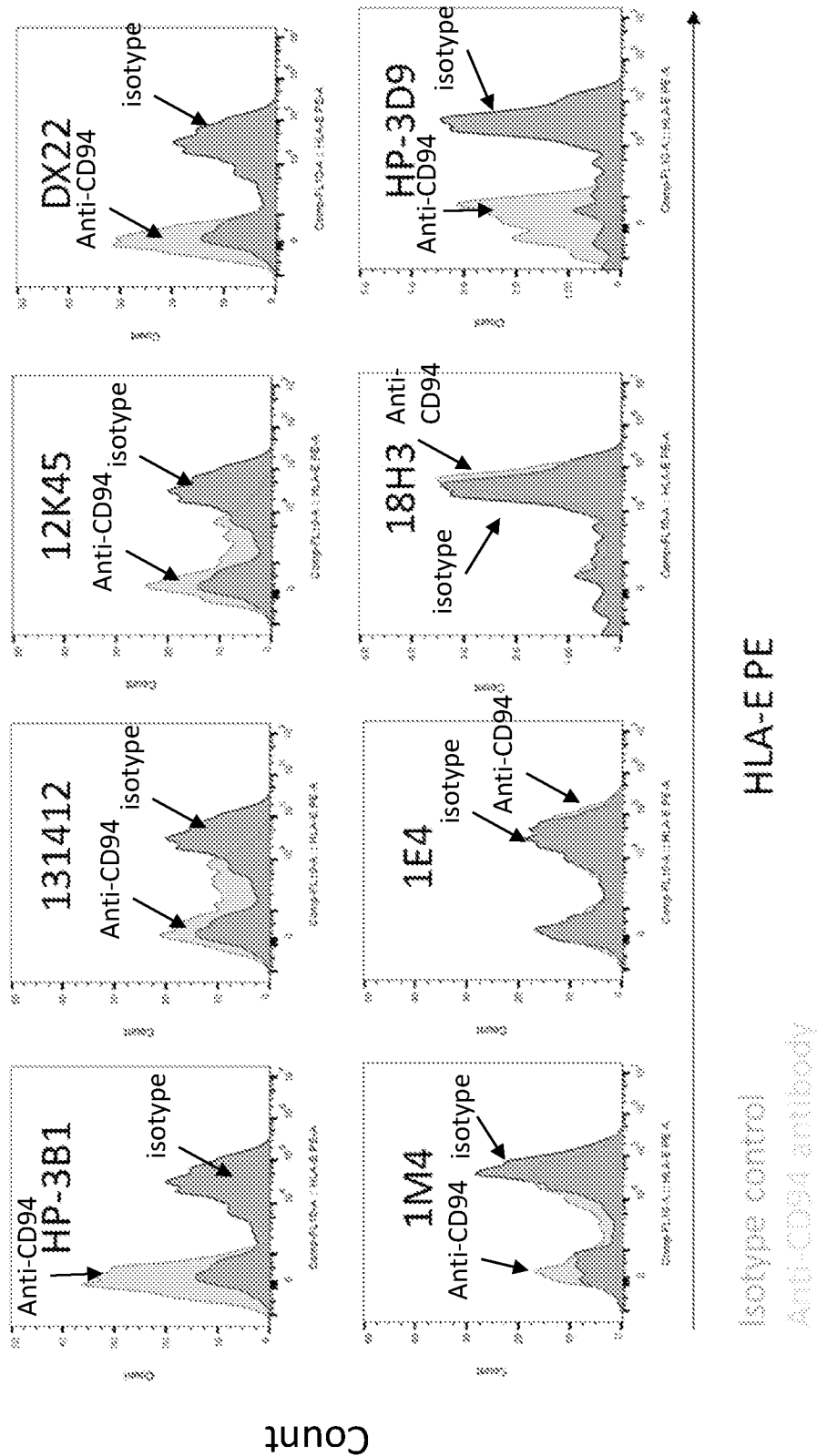


FIG. 4

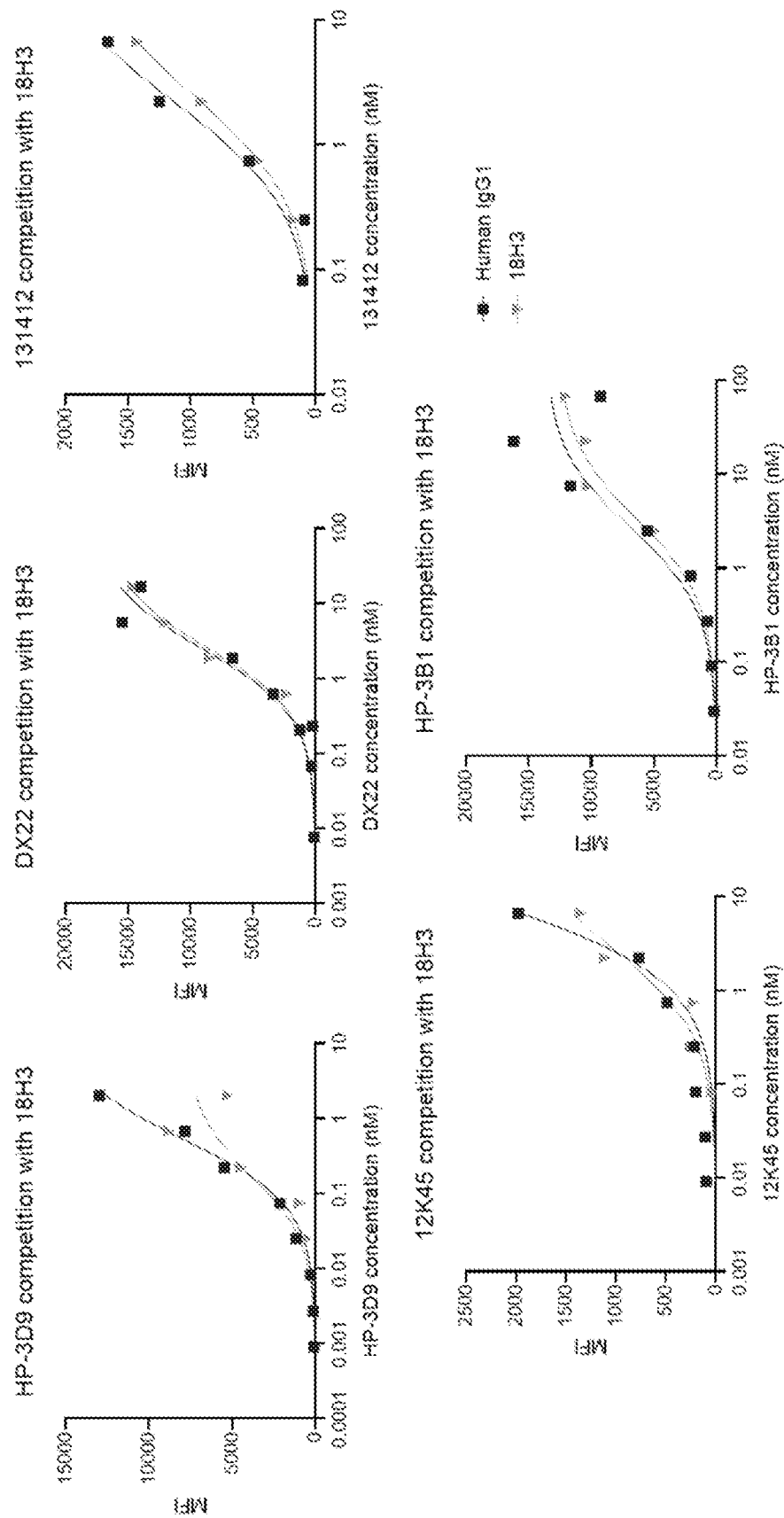


FIG. 5A

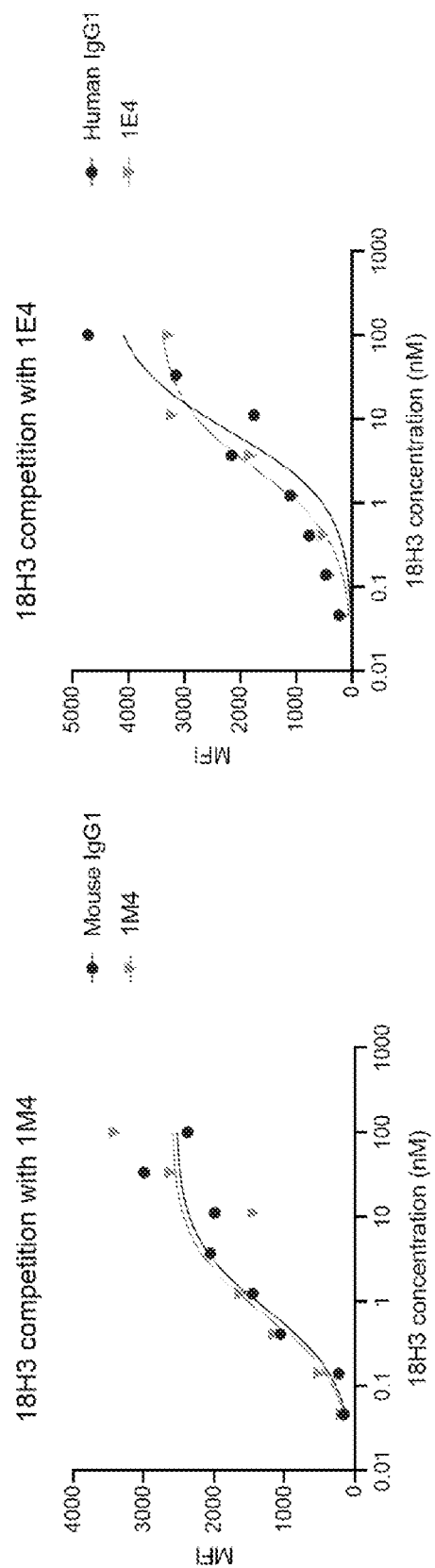


FIG. 5B

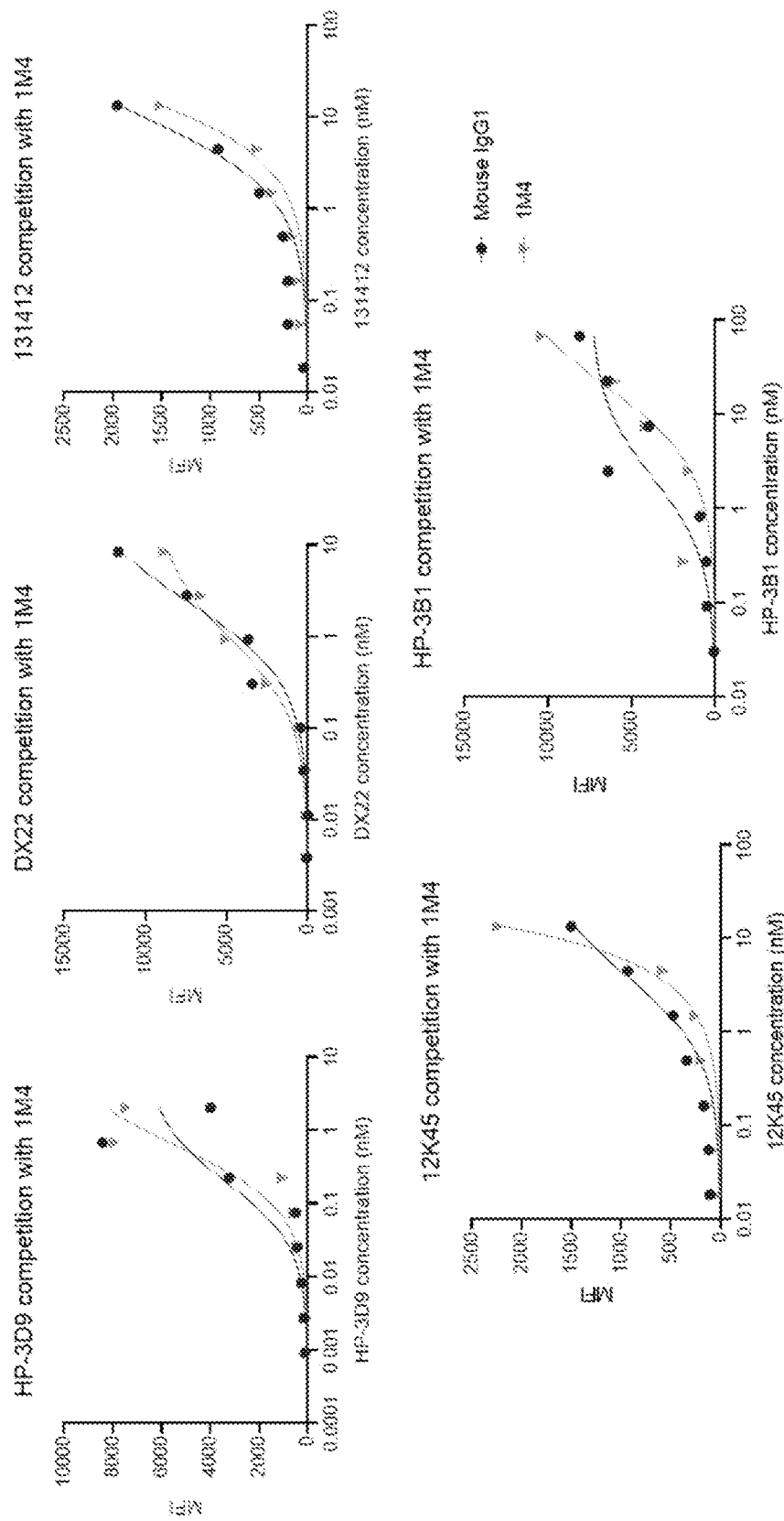


FIG. 6A

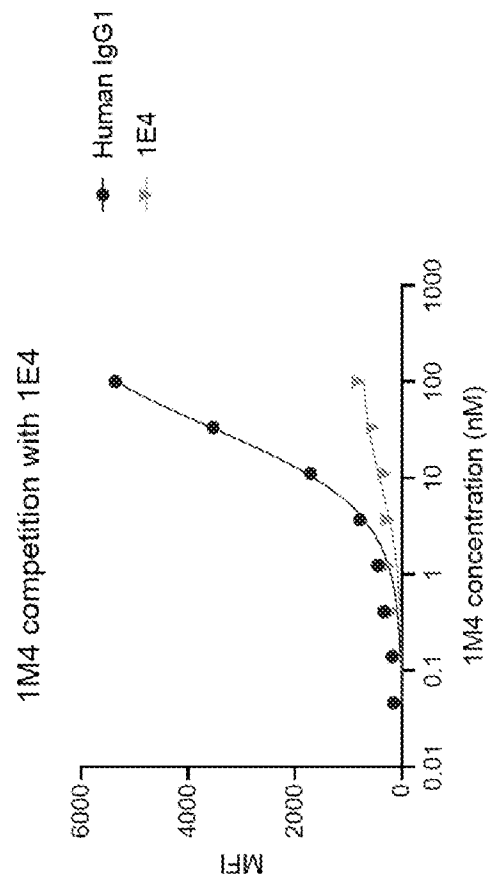


FIG. 6B

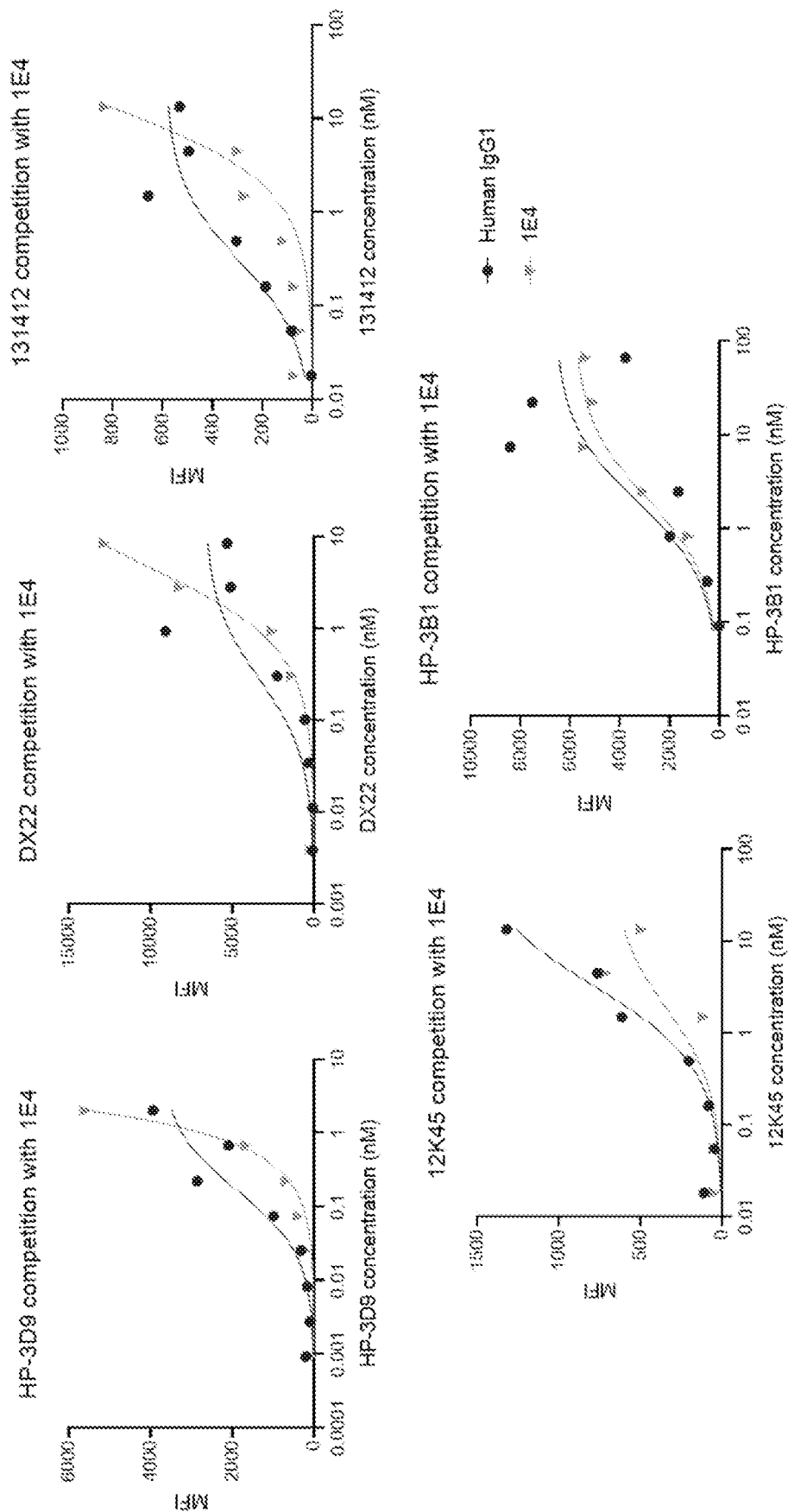


FIG. 7

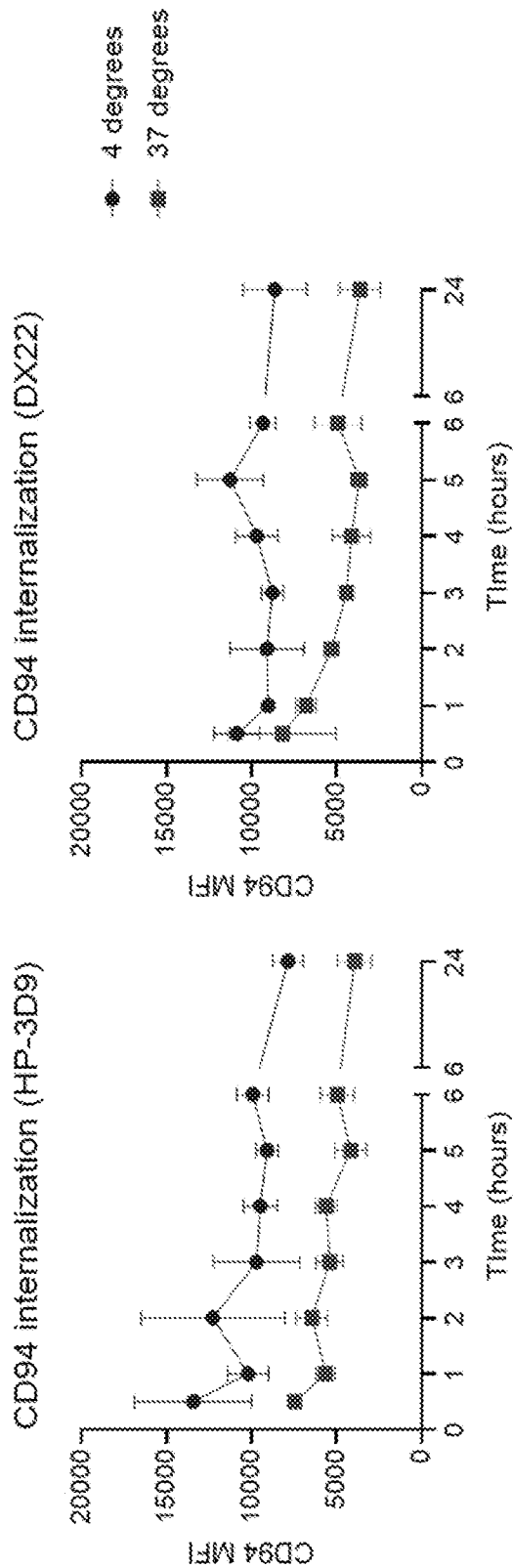


FIG. 8A

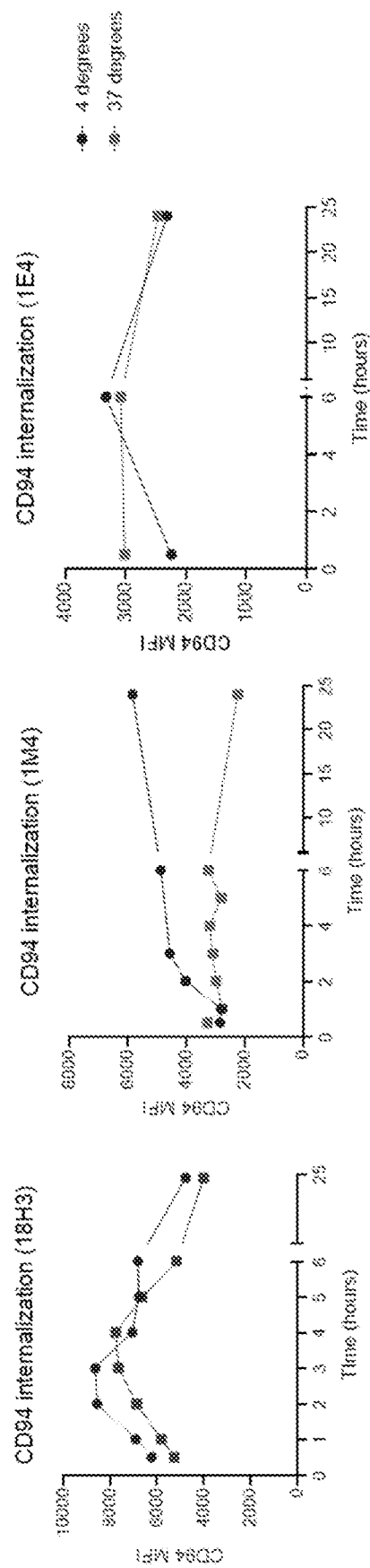


FIG. 8B

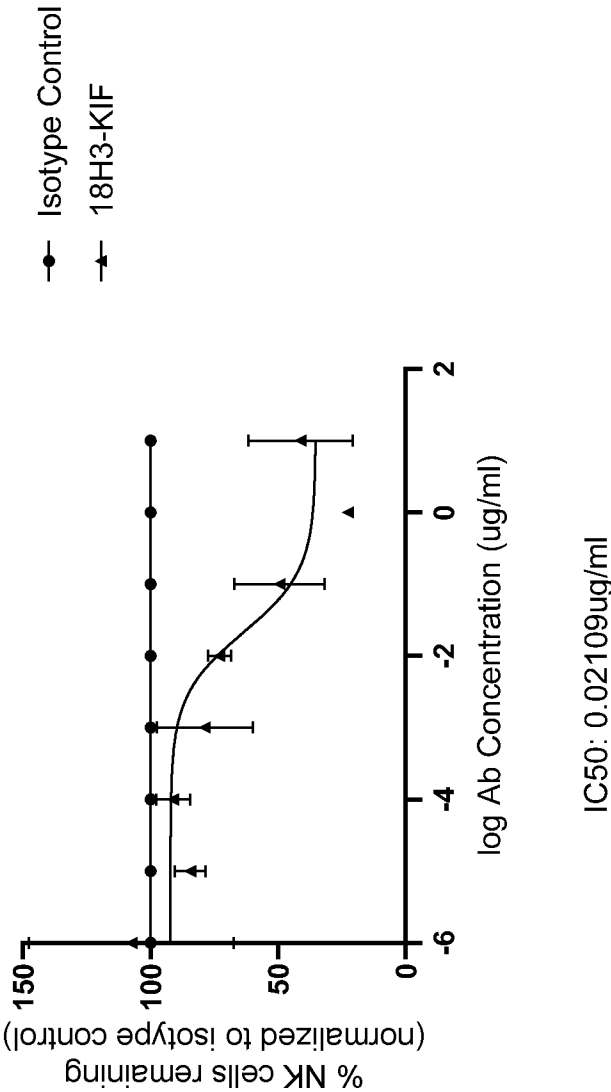


FIG. 9A

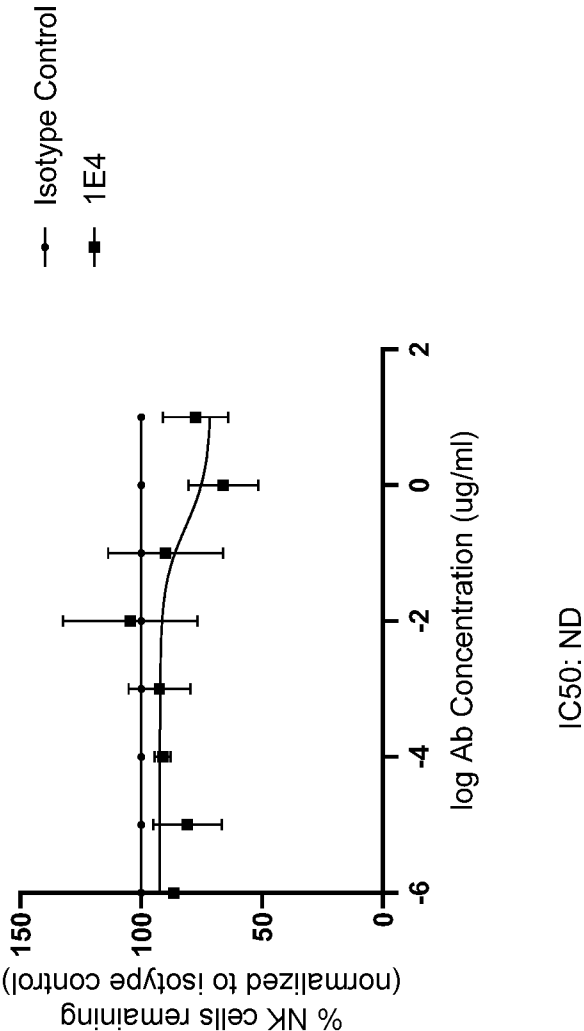


FIG. 9B

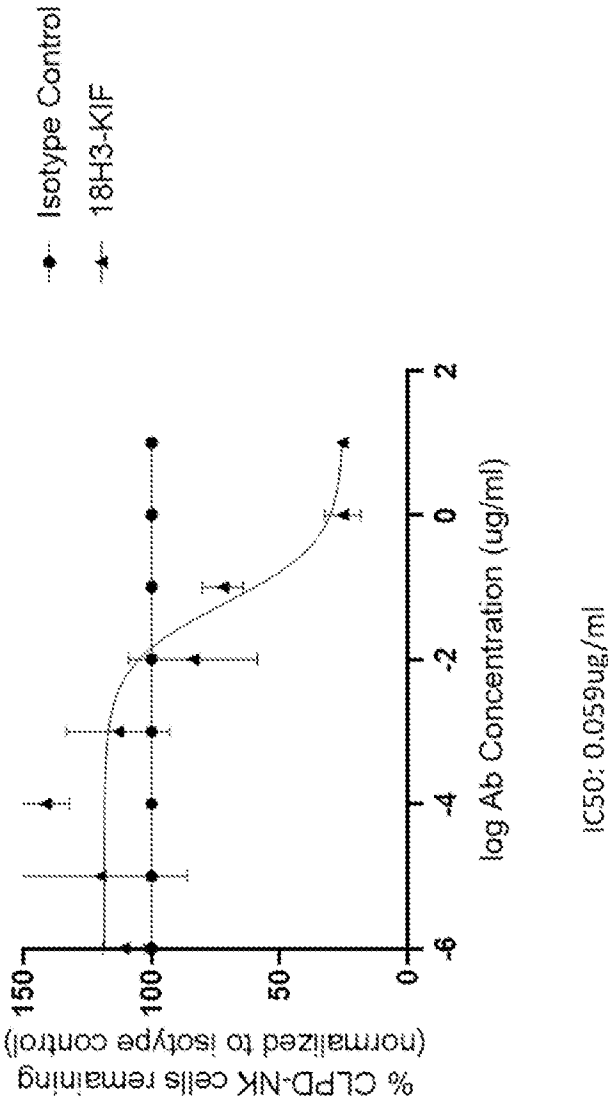


FIG. 10

Antibody	Affinity on human NK cells	Cyno CD94 cross-reactivity	HLA-E blocking	Antibody competition	Antibody internalization from 0.5-24 hours at 37 °C	ADCC activity in normal NK cells	ADCC activity in normal non-targeted cells	ADCC activity in LGL	ADCC activity in LGL non-targeted cells
HP-3D9	0.07nM	No	99%	Partially with 18H3	53%	N/A	N/A	N/A	N/A
DX22	0.15nM	No	99%	None	56%	N/A	N/A	N/A	N/A
HP-3B1	3nM	No	99.8%	None	N/A	N/A	N/A	N/A	N/A
131412	11nM	No	40%	None	N/A	N/A	N/A	N/A	N/A
12K45	7nM	No	47%	Partially with 1E4	N/A	N/A	N/A	N/A	N/A
18H3	2.6nM	Yes	0%	Partially with HP-3D9	24%	IC50: 0.02ug/ml	None	IC50: 0.05ug/ml	None
1M4	7nM	Yes	0%	1E4	32%	N/A	N/A	N/A	N/A
1E4	75nM	Yes	0%	1M4; Partially with 12K45	18%	Depletion observed; IC50 ND	None	N/A	None

FIG. 11

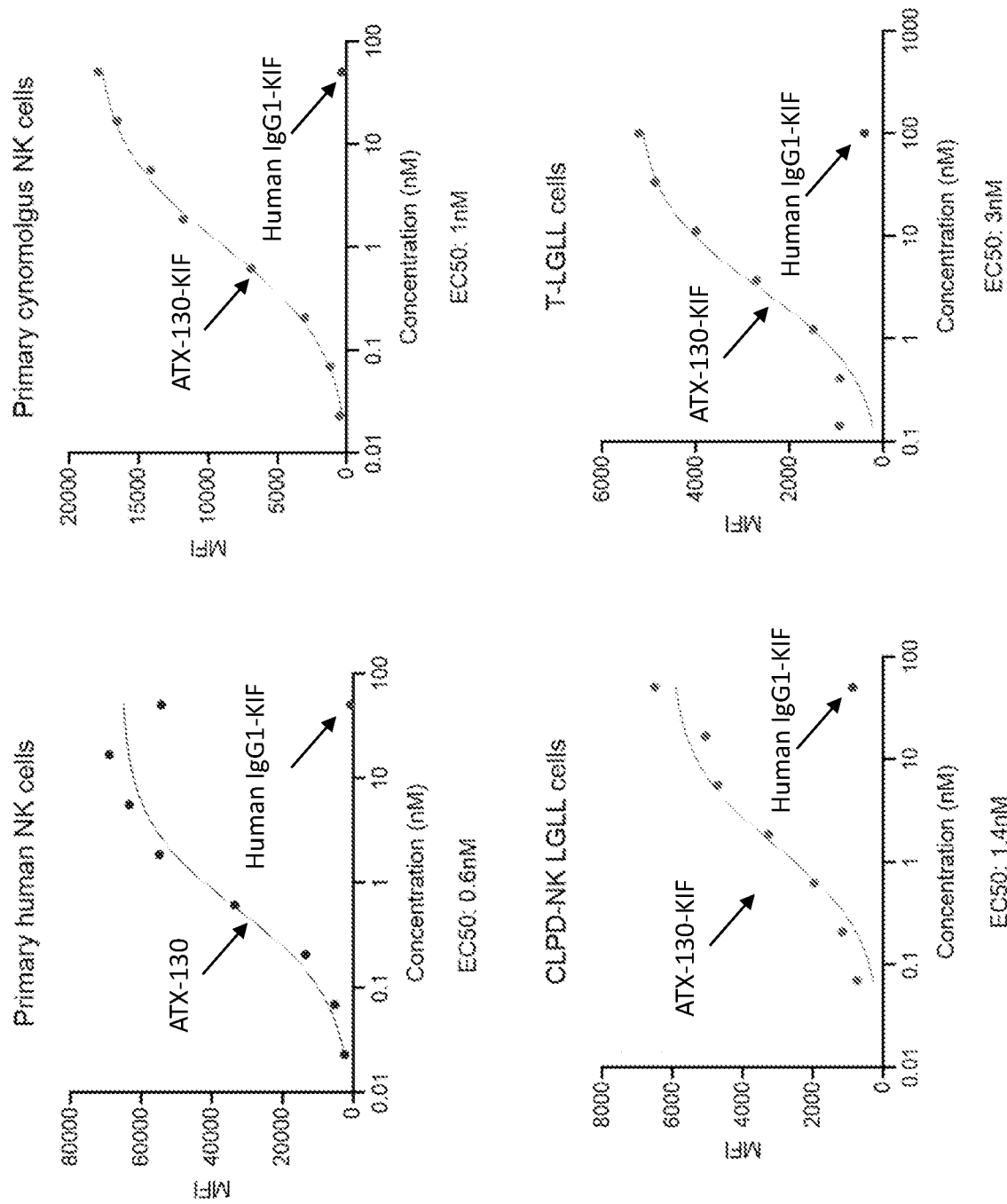


FIG. 12

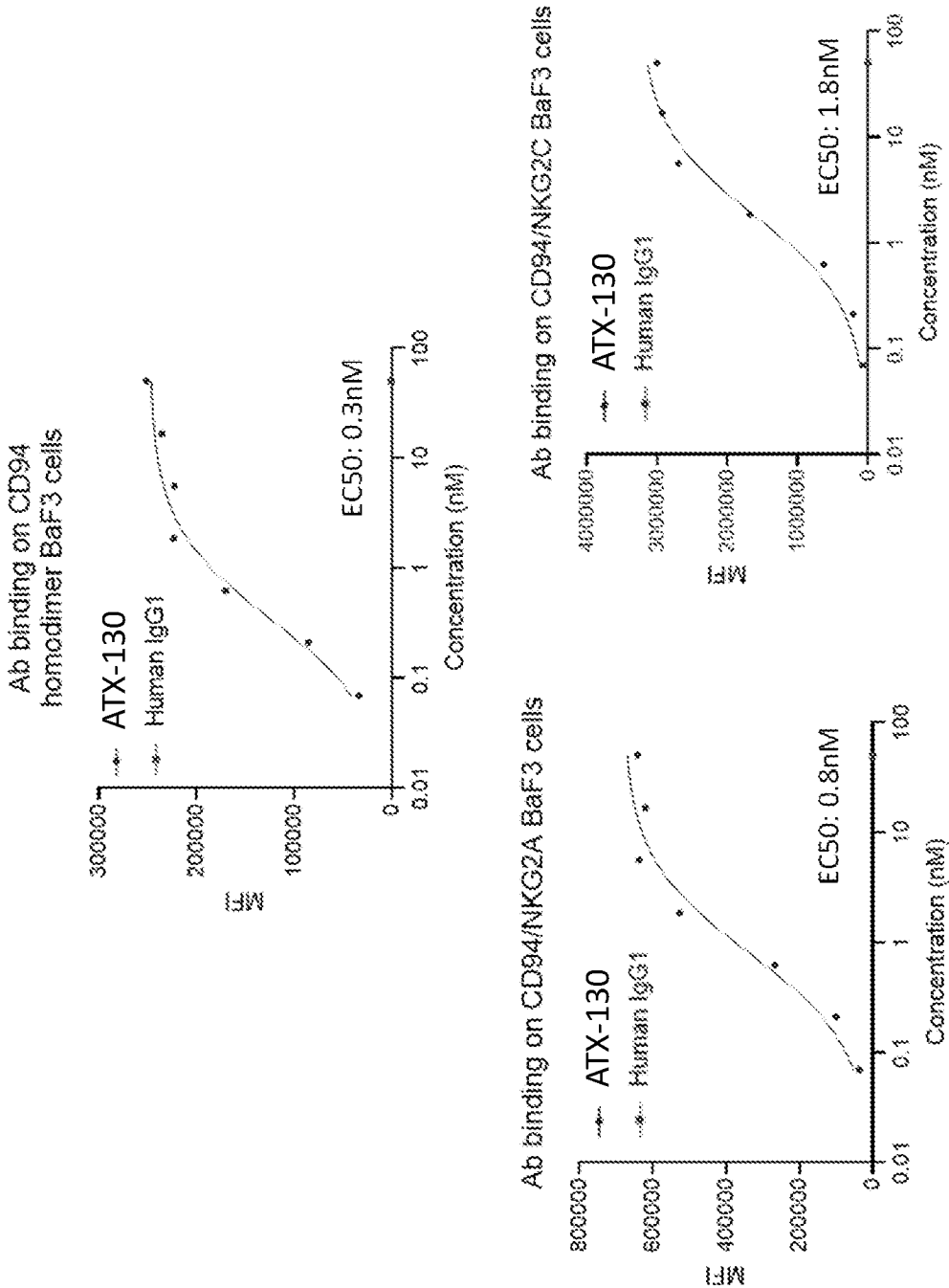


FIG. 13

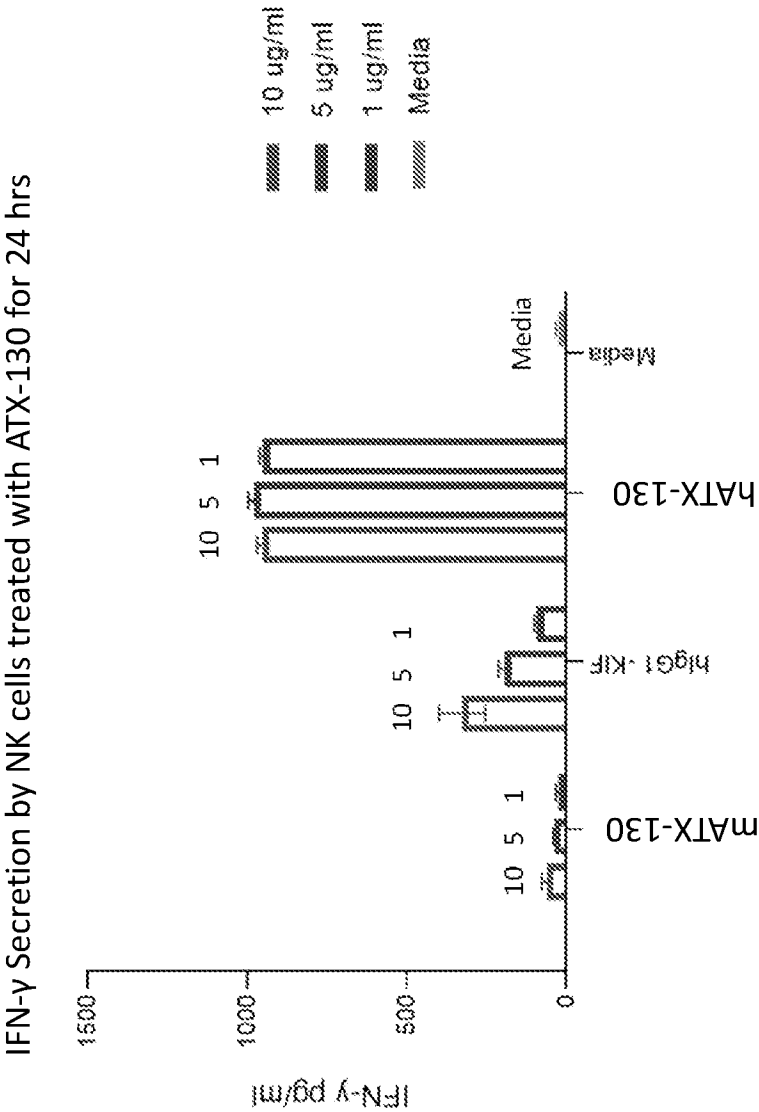


FIG. 14

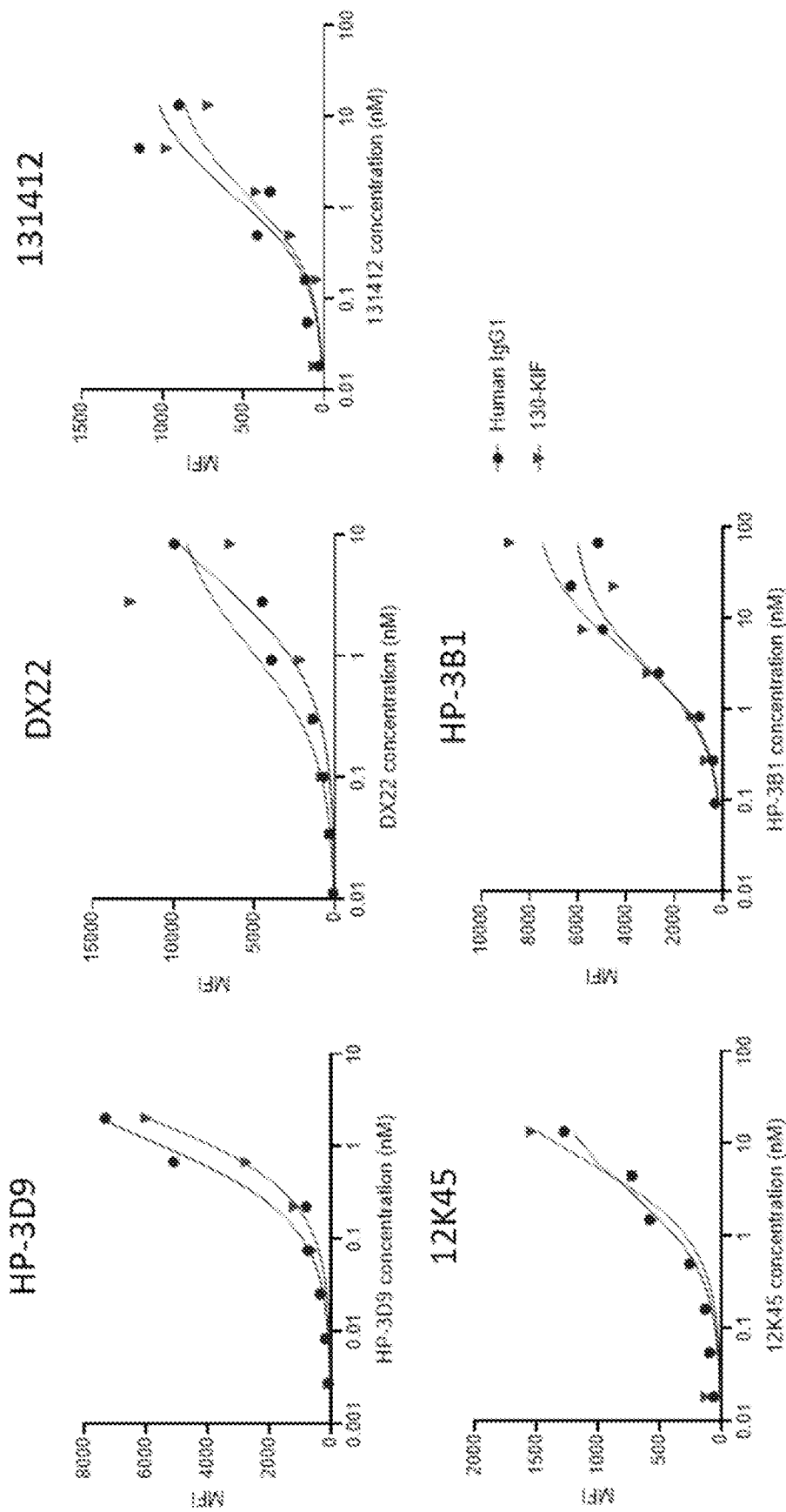


FIG. 15

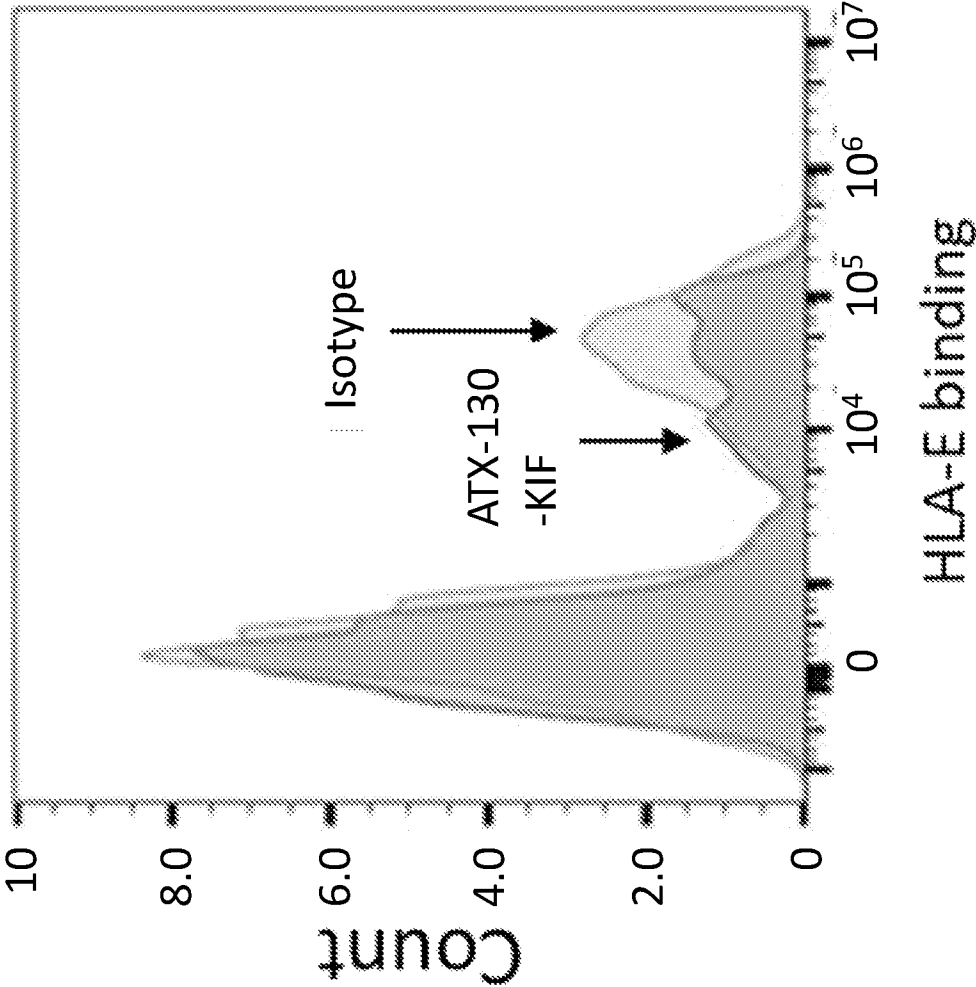


FIG. 16

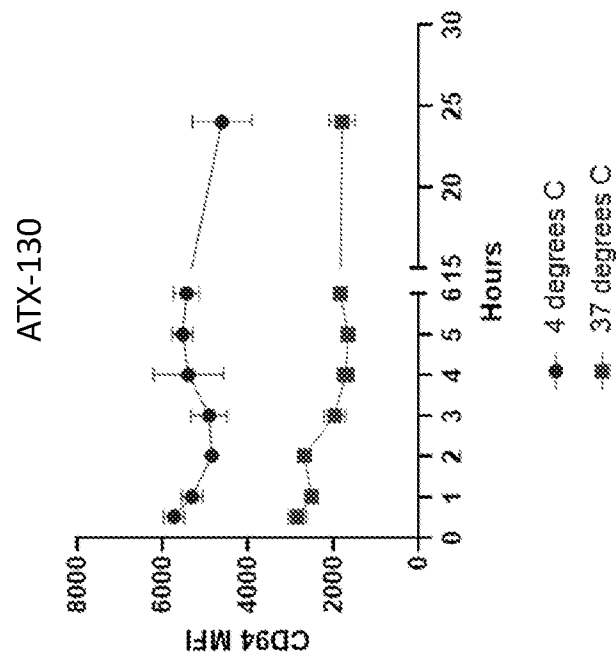


FIG. 17

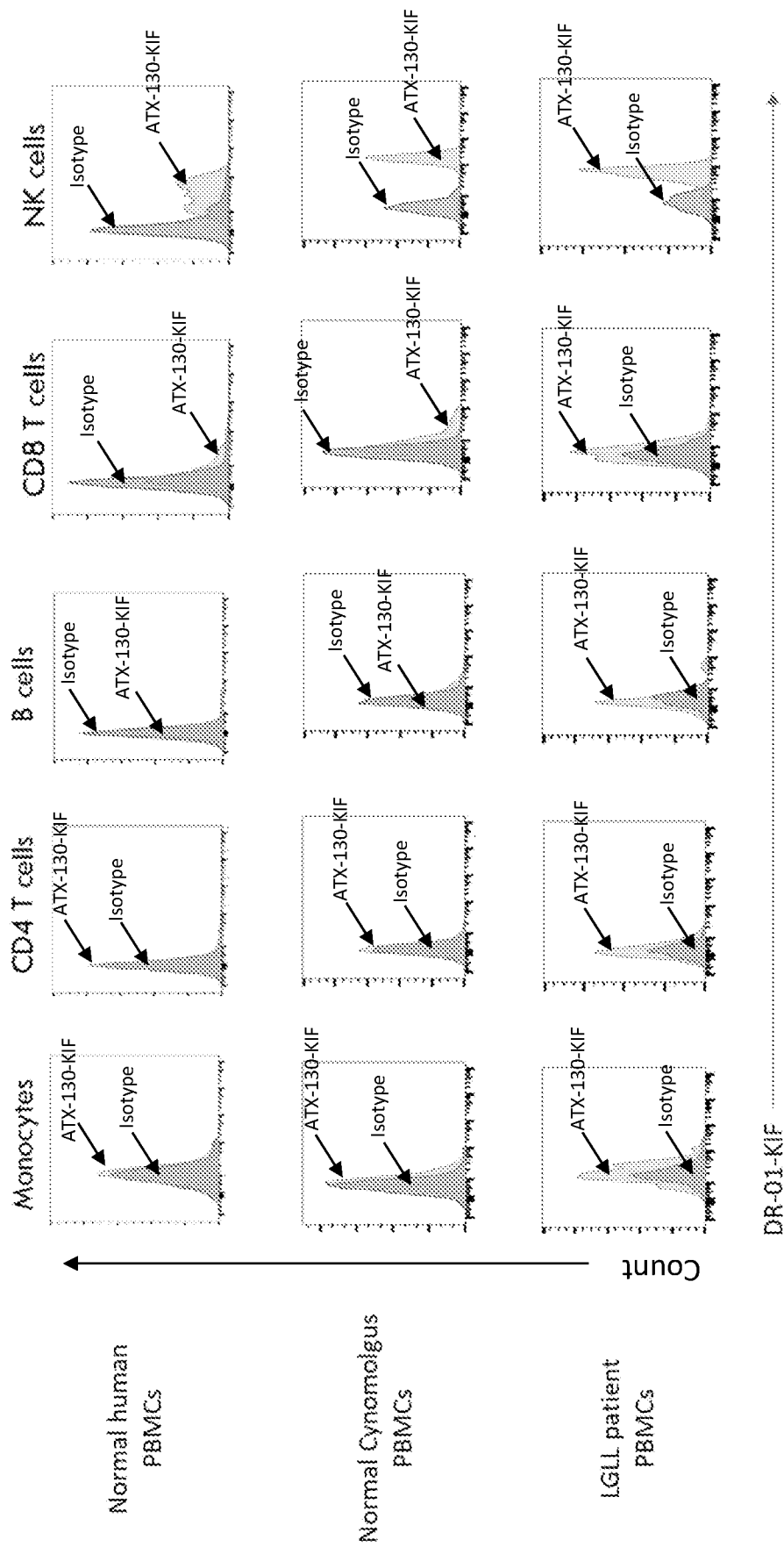


FIG. 18

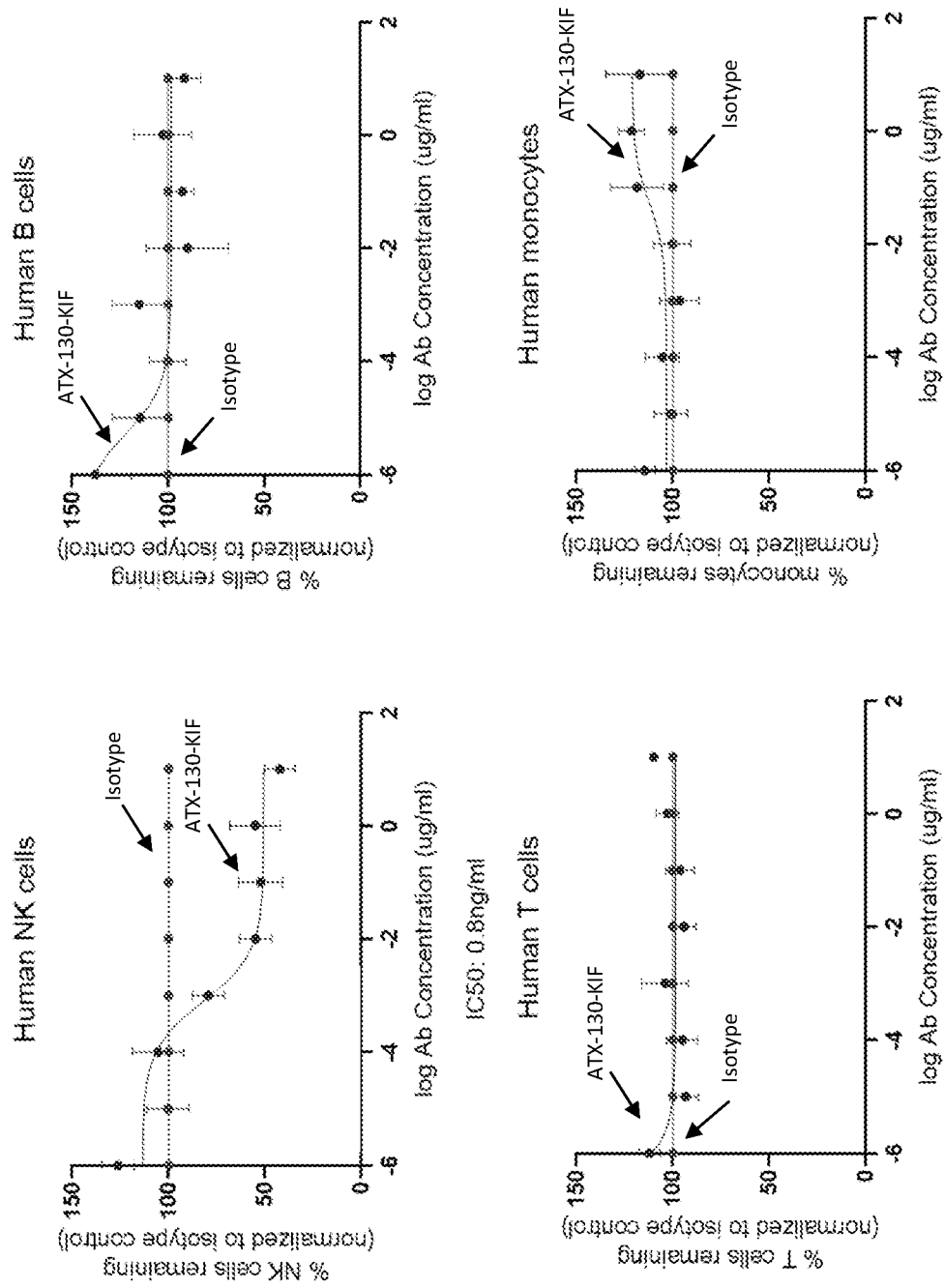


FIG. 19

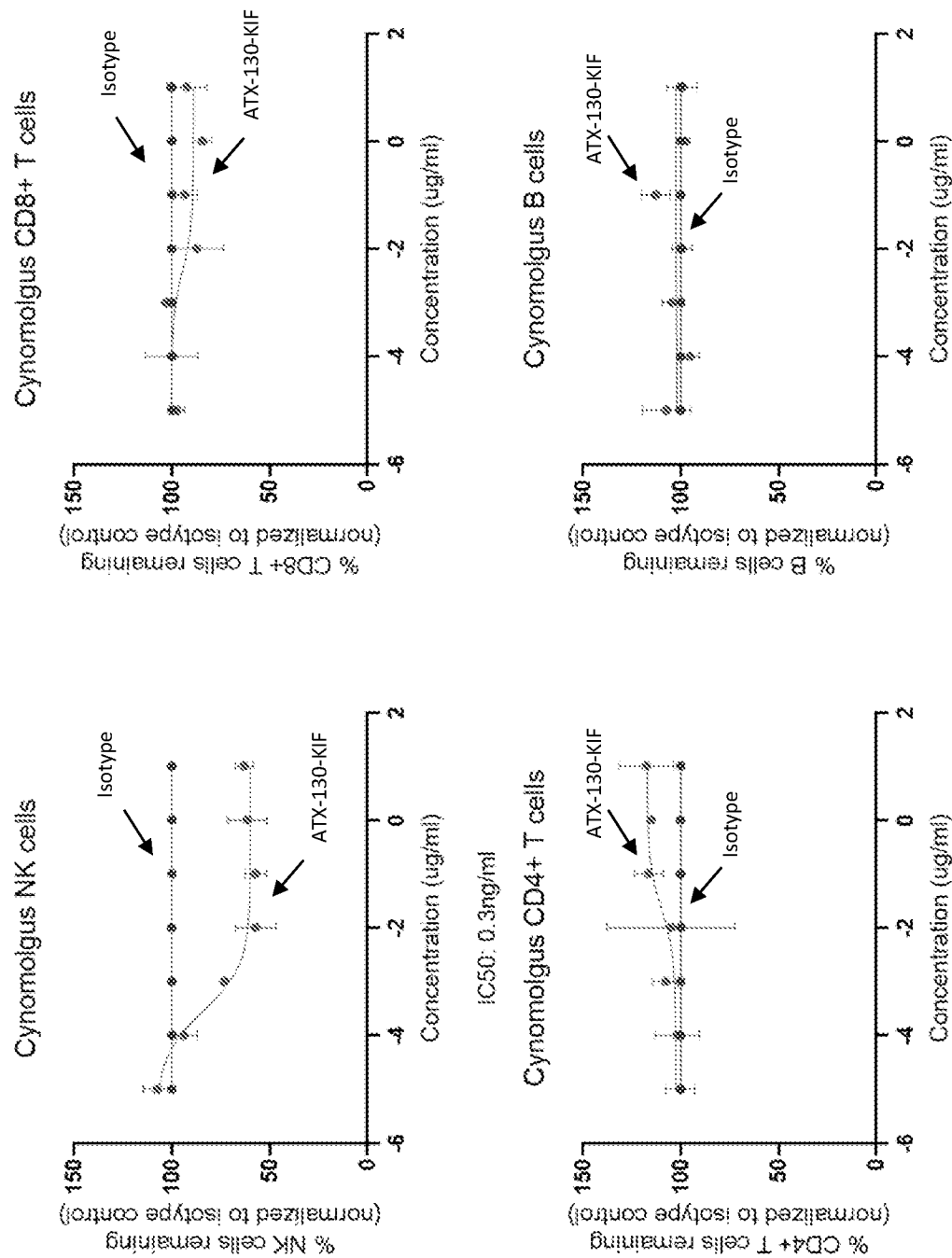


FIG. 20

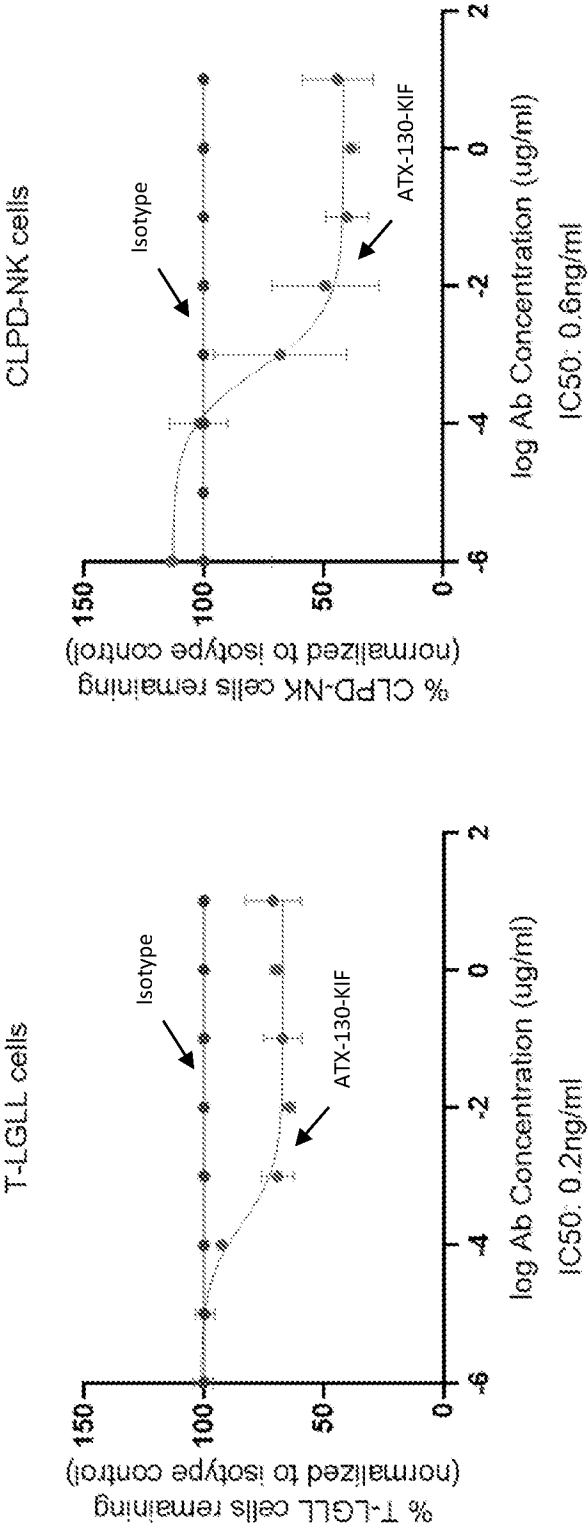


FIG. 21

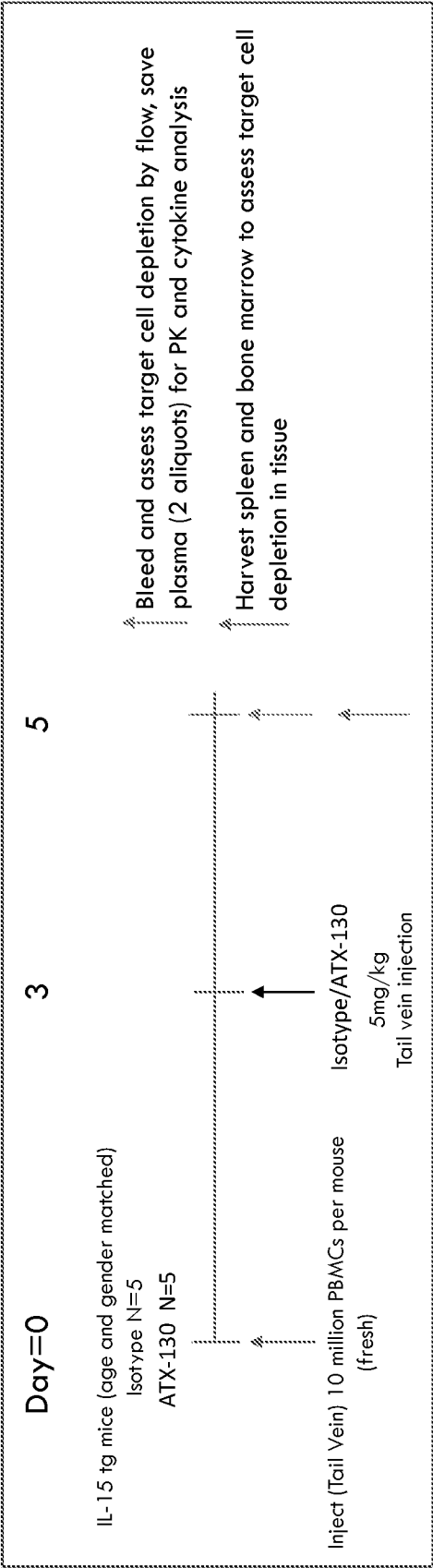


FIG. 22A

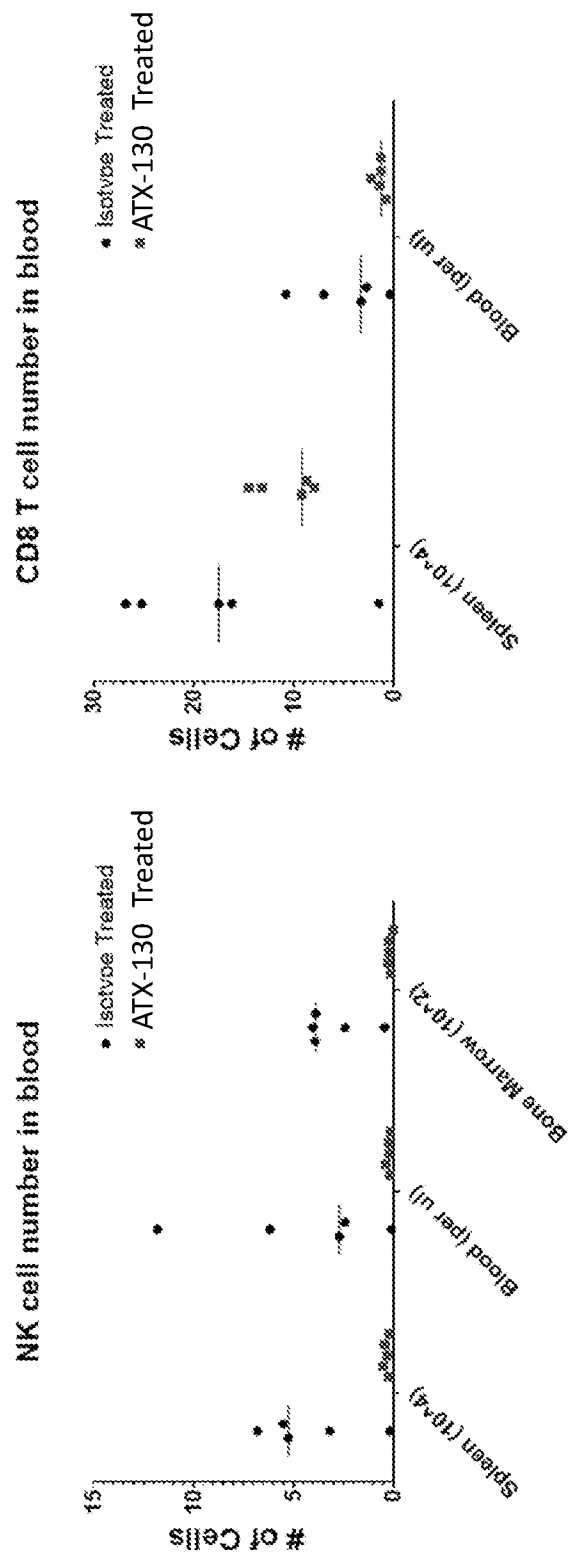


FIG. 22B

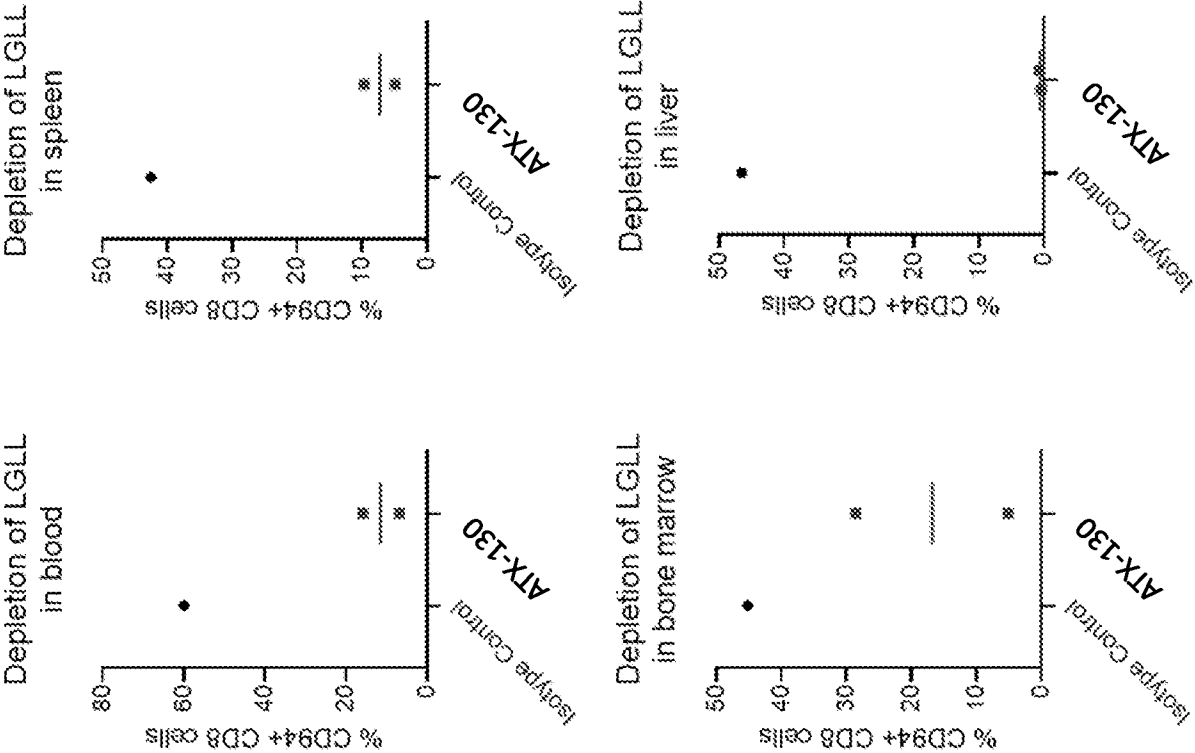


FIG. 23

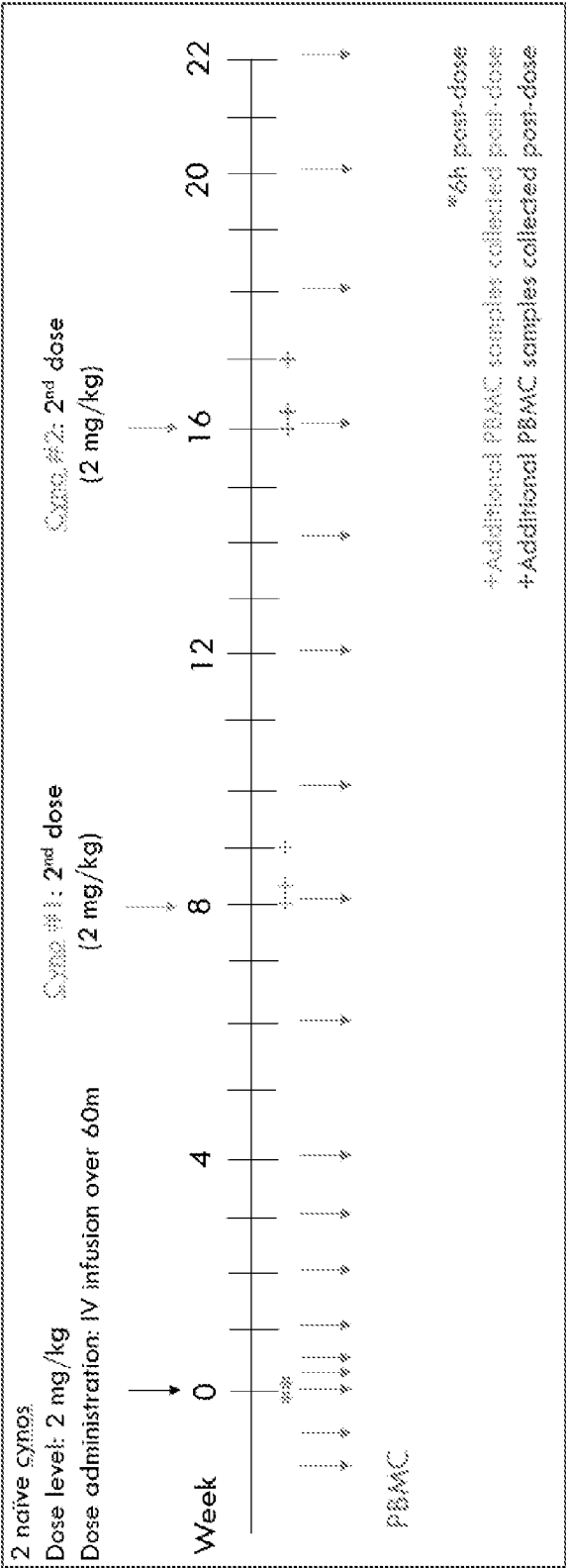
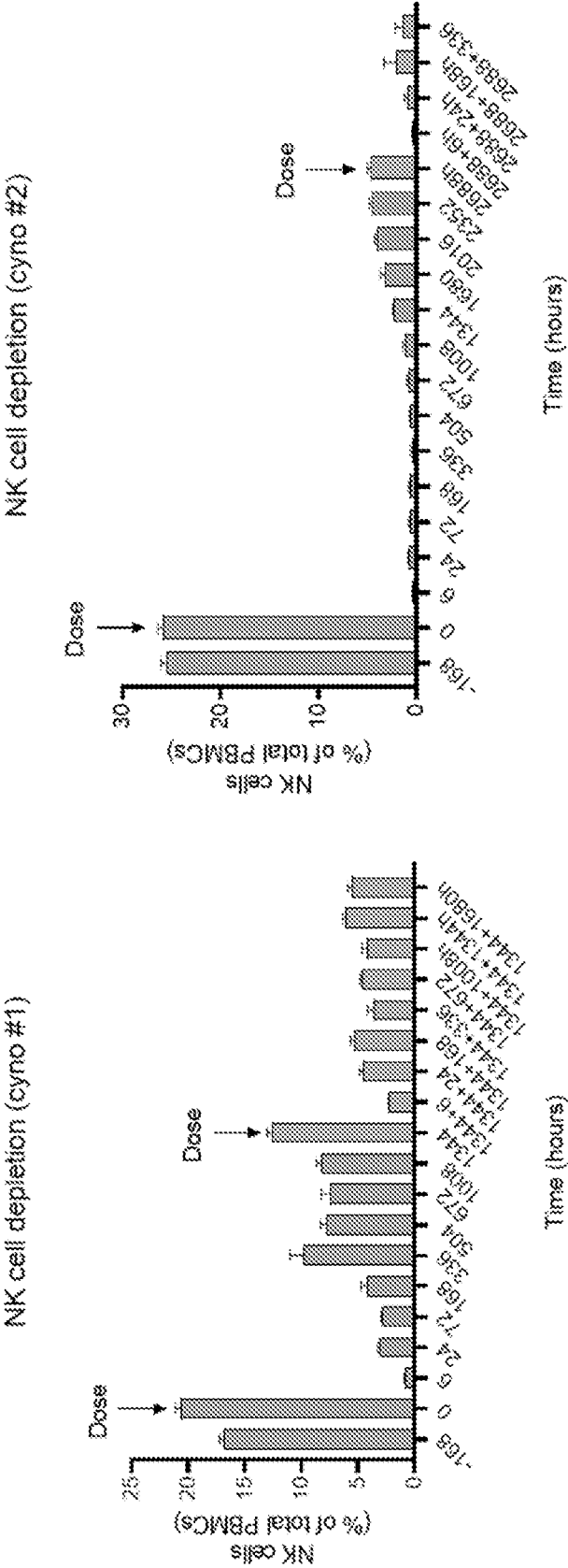
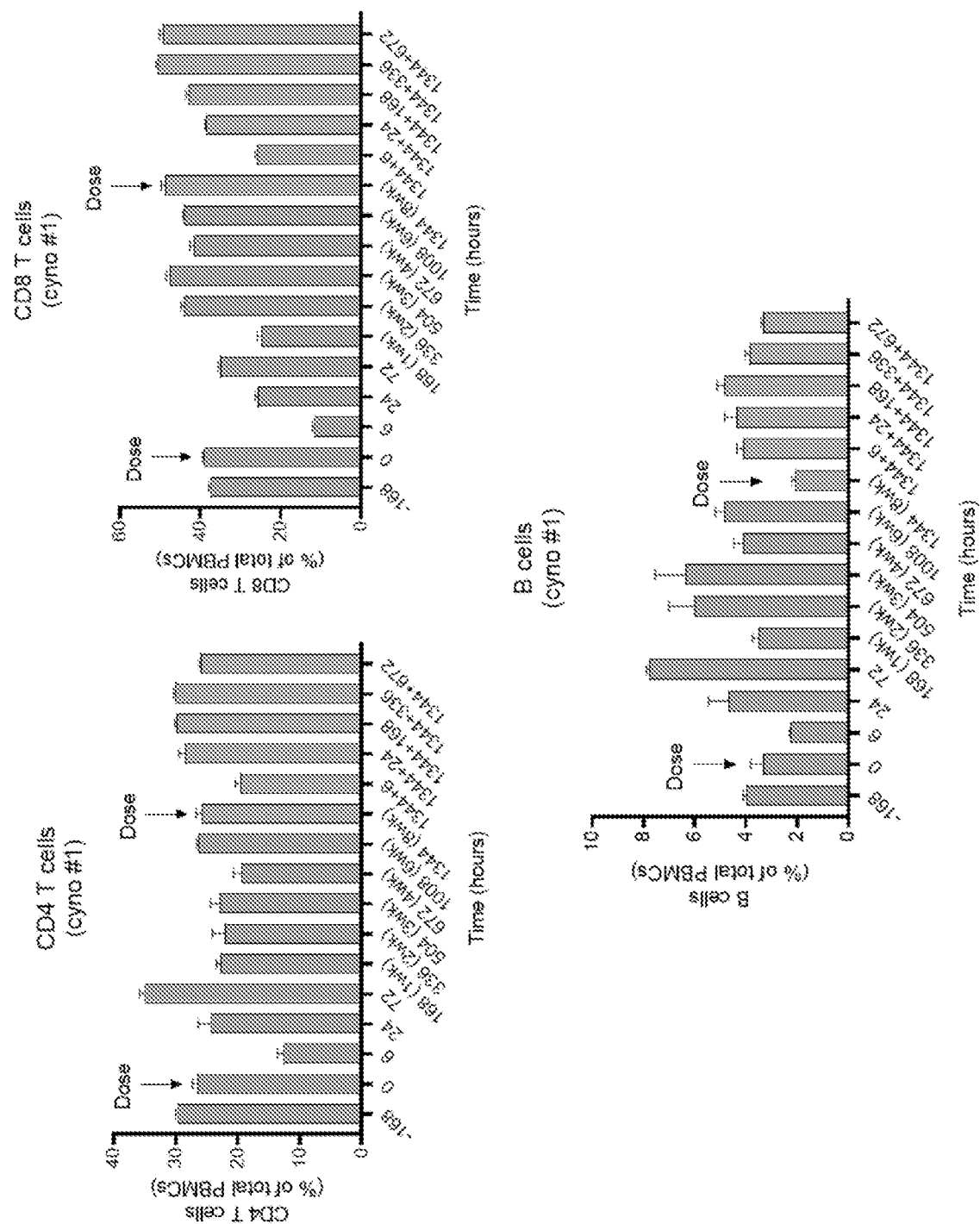


FIG. 24A





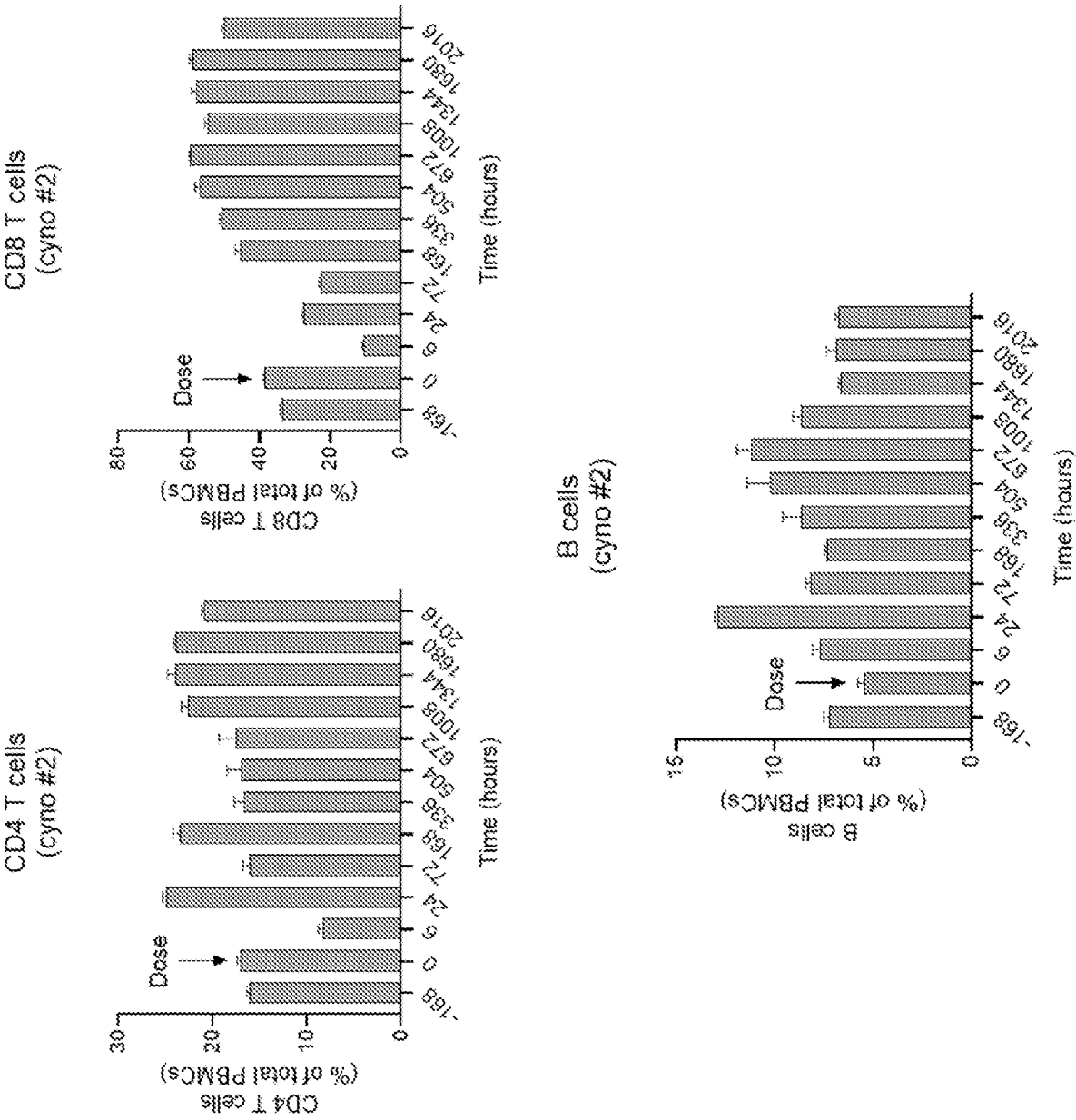


FIG. 25B

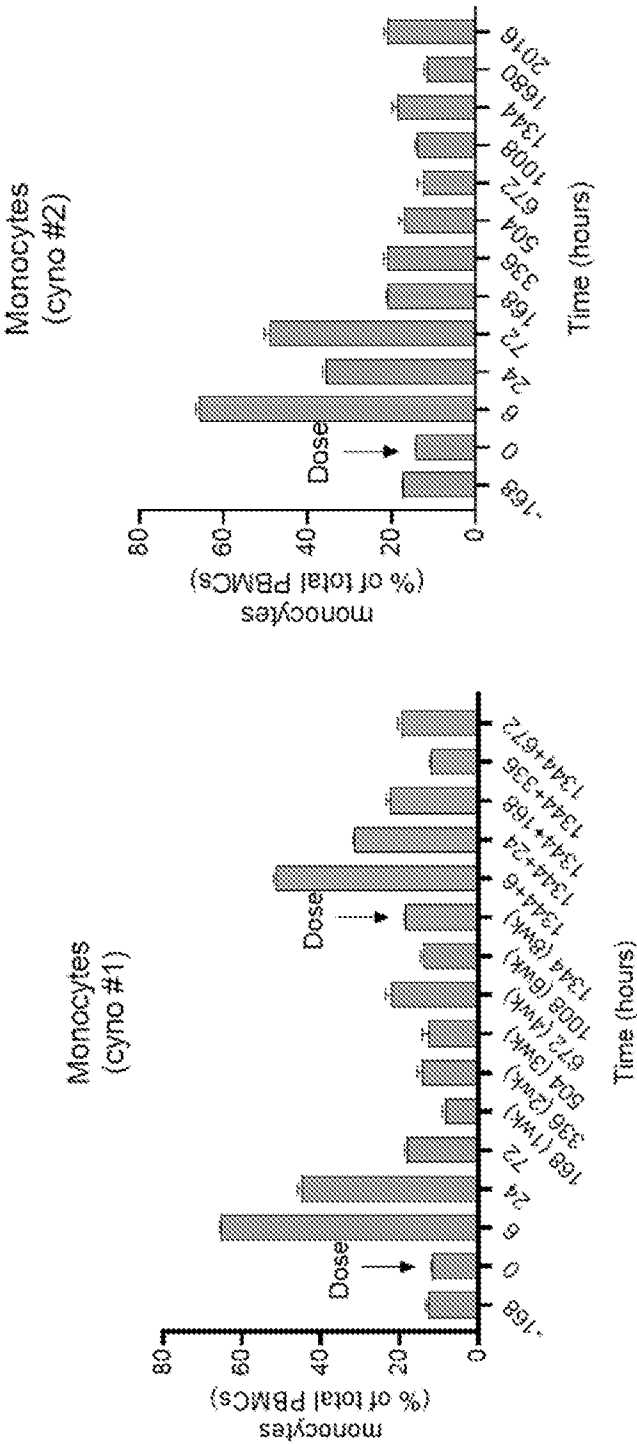


FIG. 26

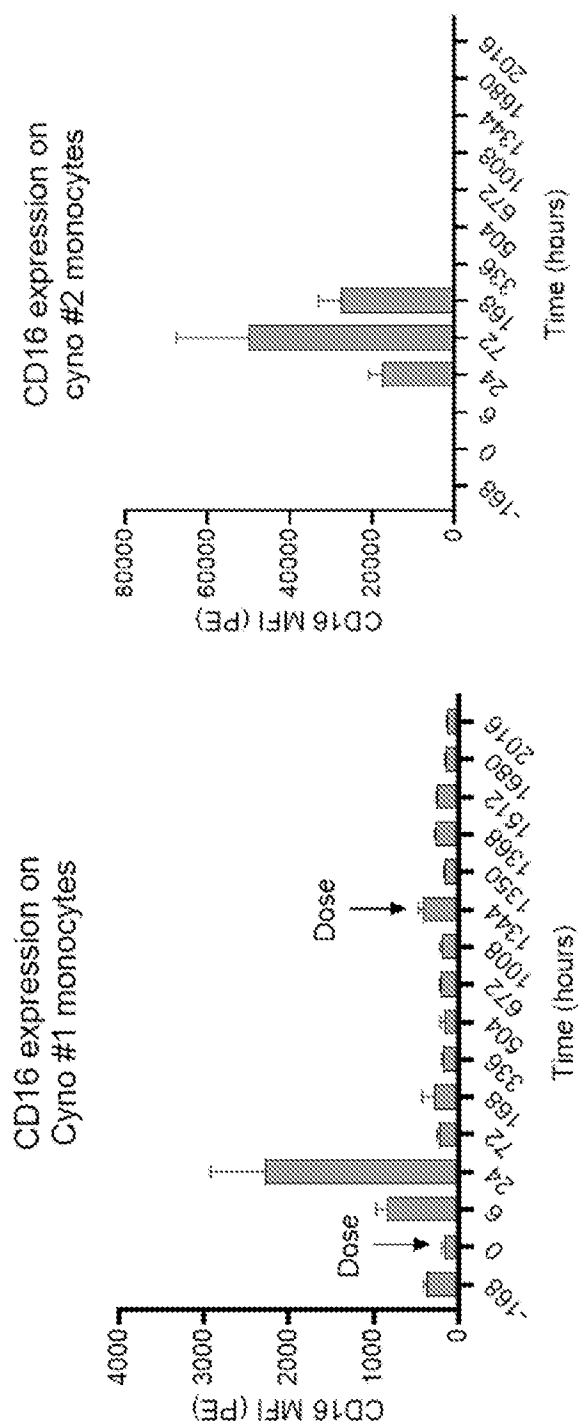


FIG. 27

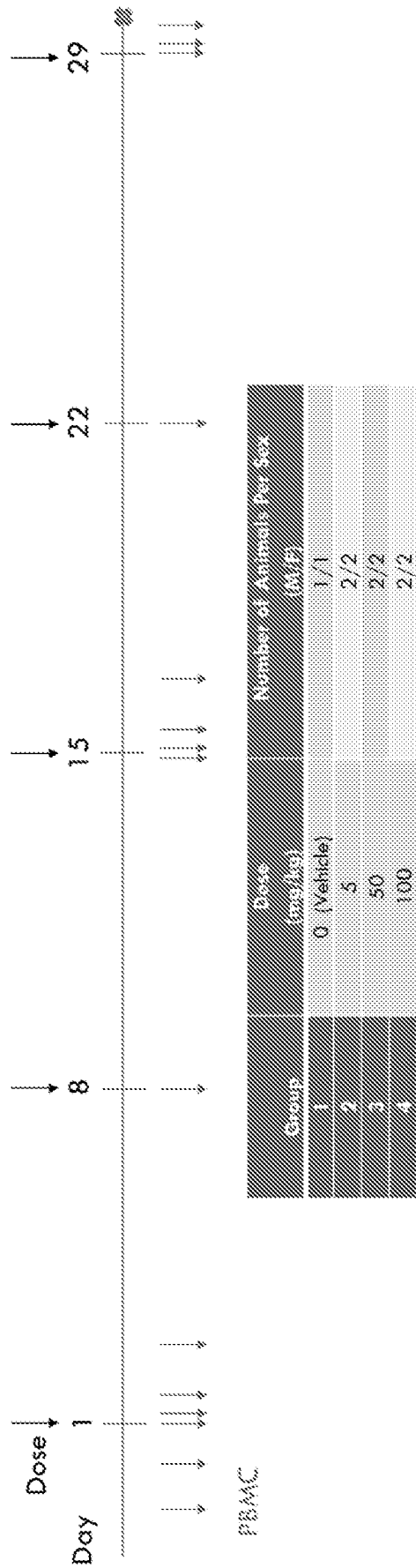


FIG. 28A

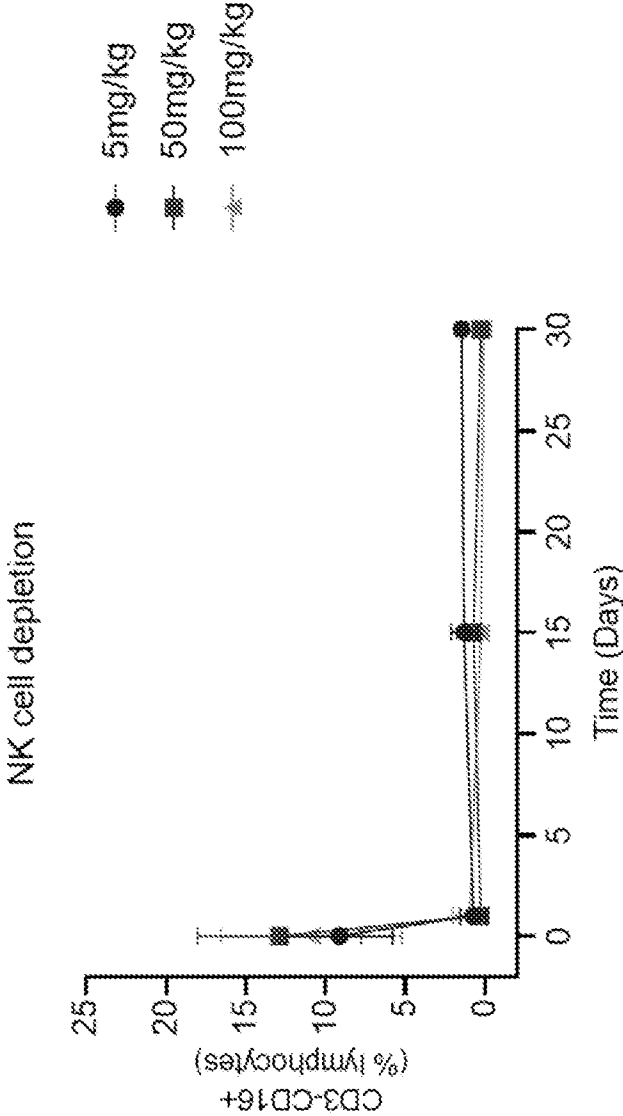


FIG. 28B

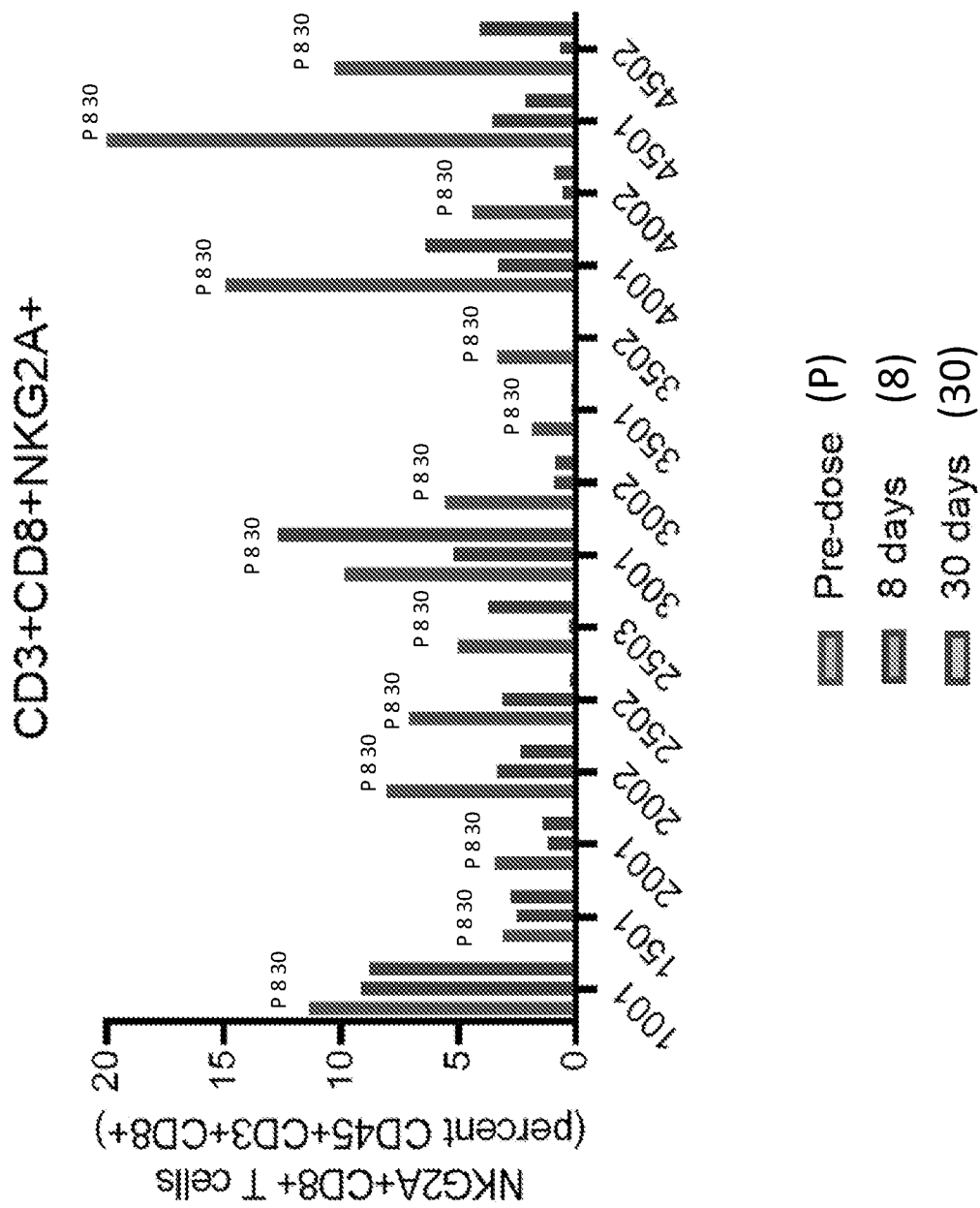


FIG. 29

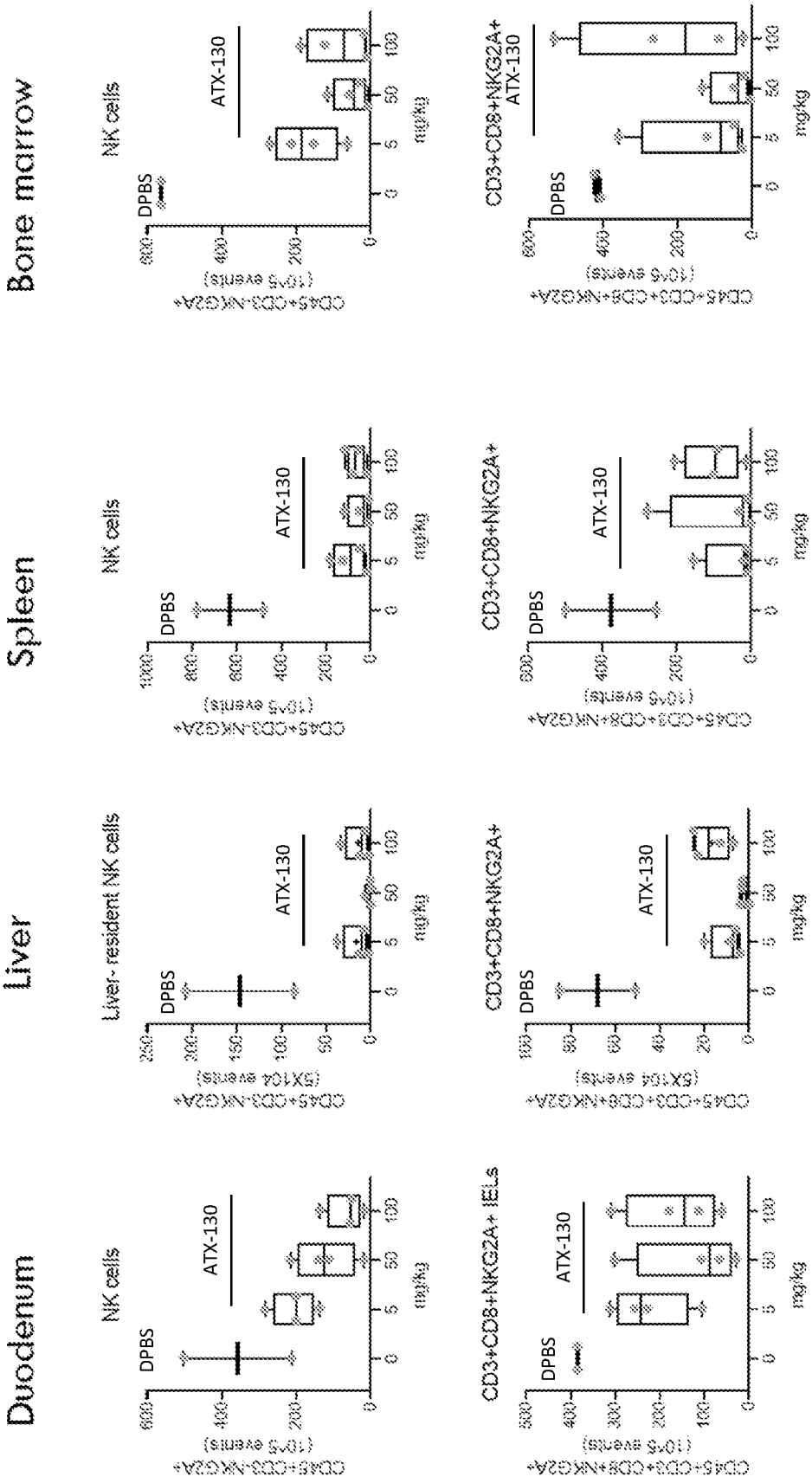


FIG. 30

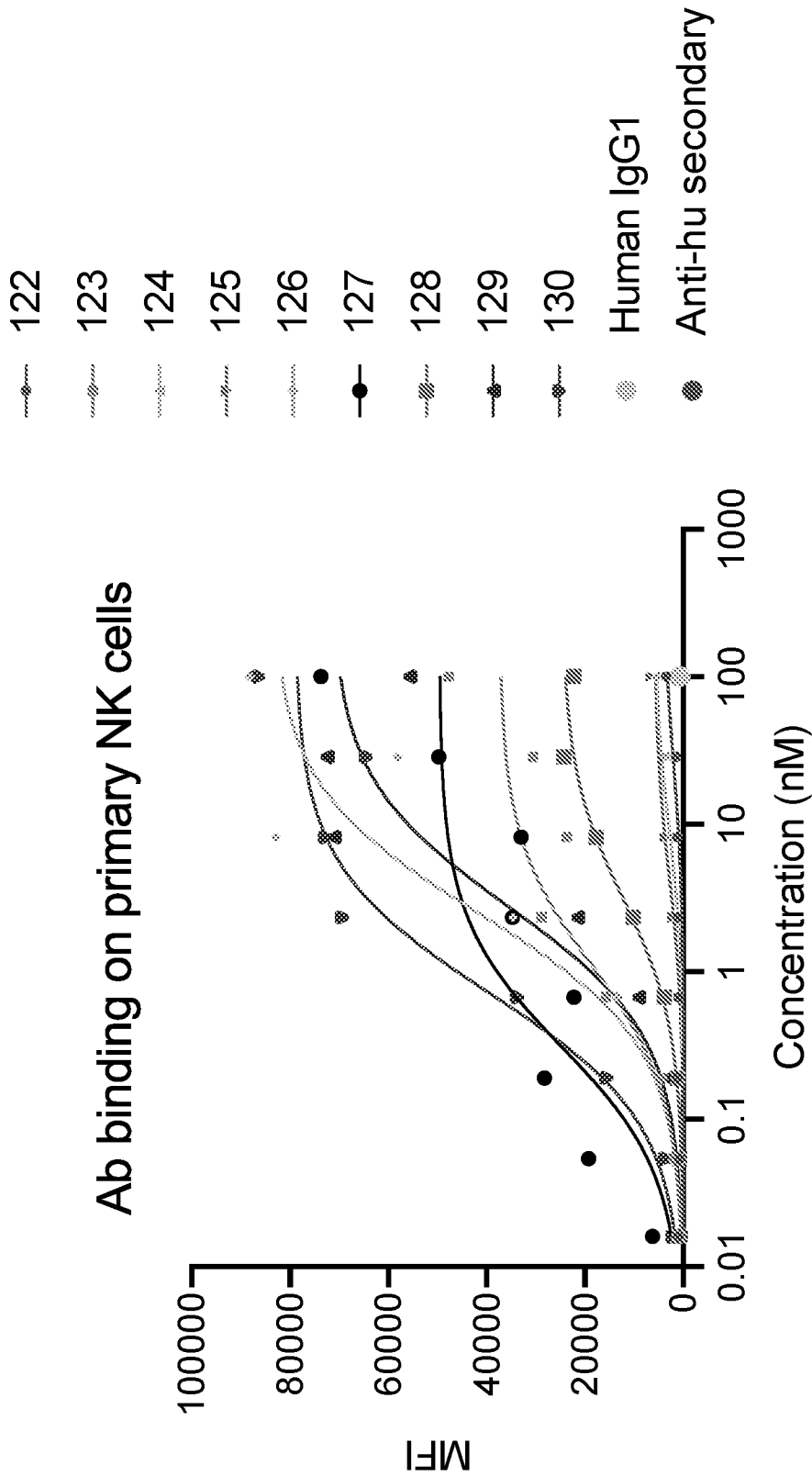


FIG. 31A

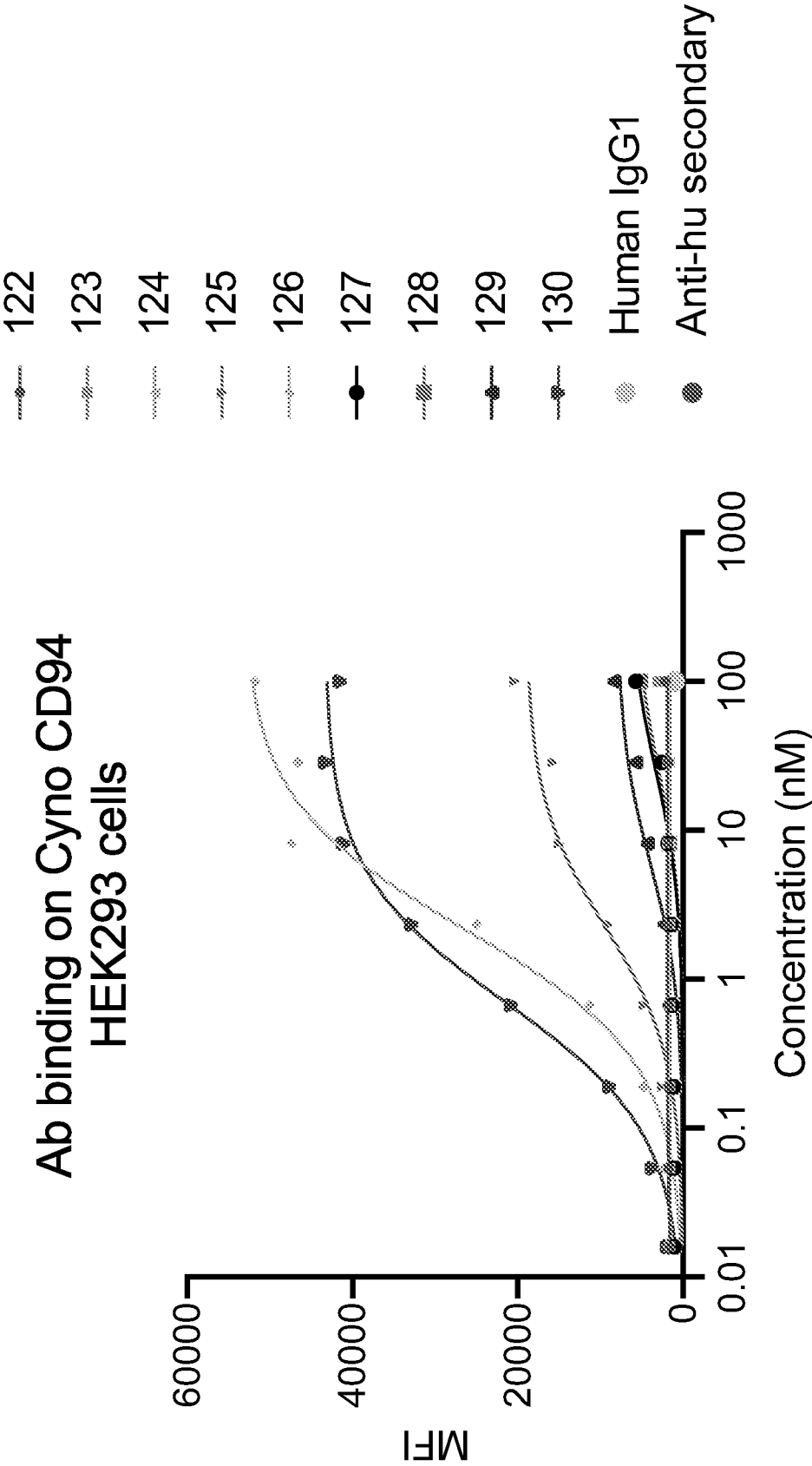


FIG. 31B

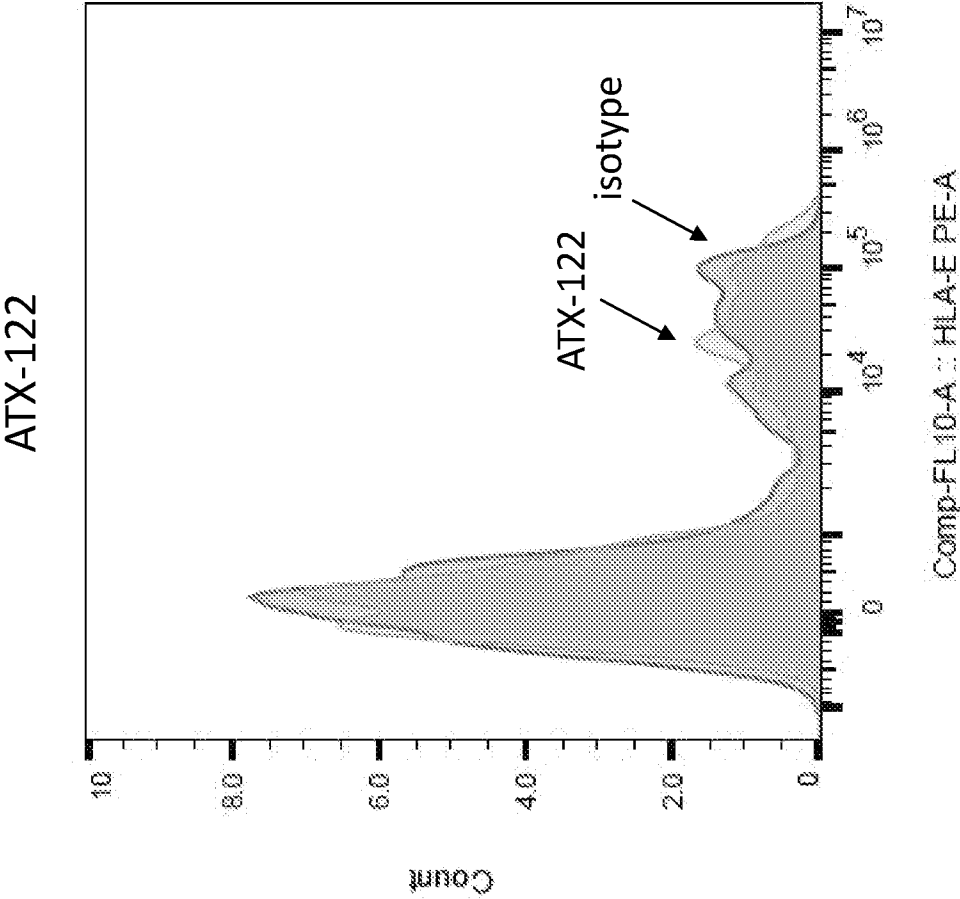


FIG. 32A

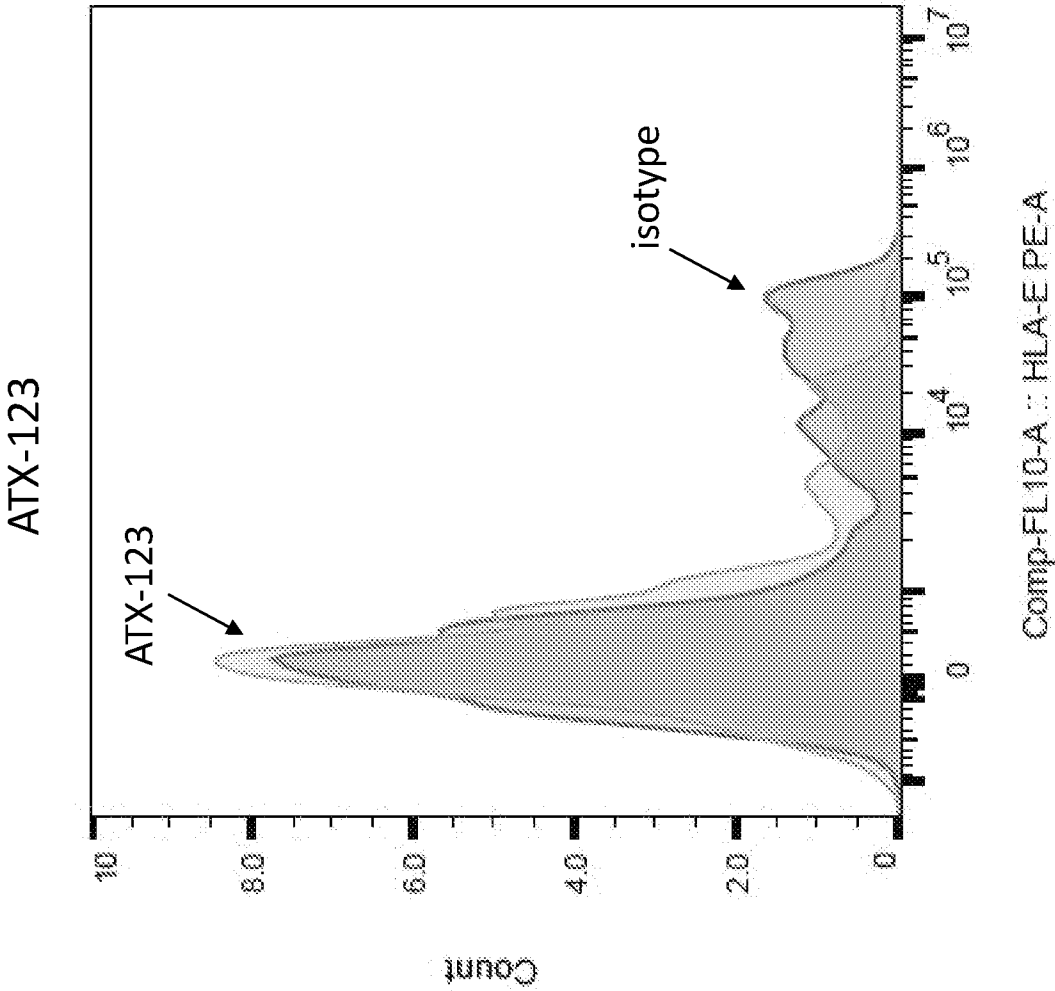


FIG. 32B

ATX-124

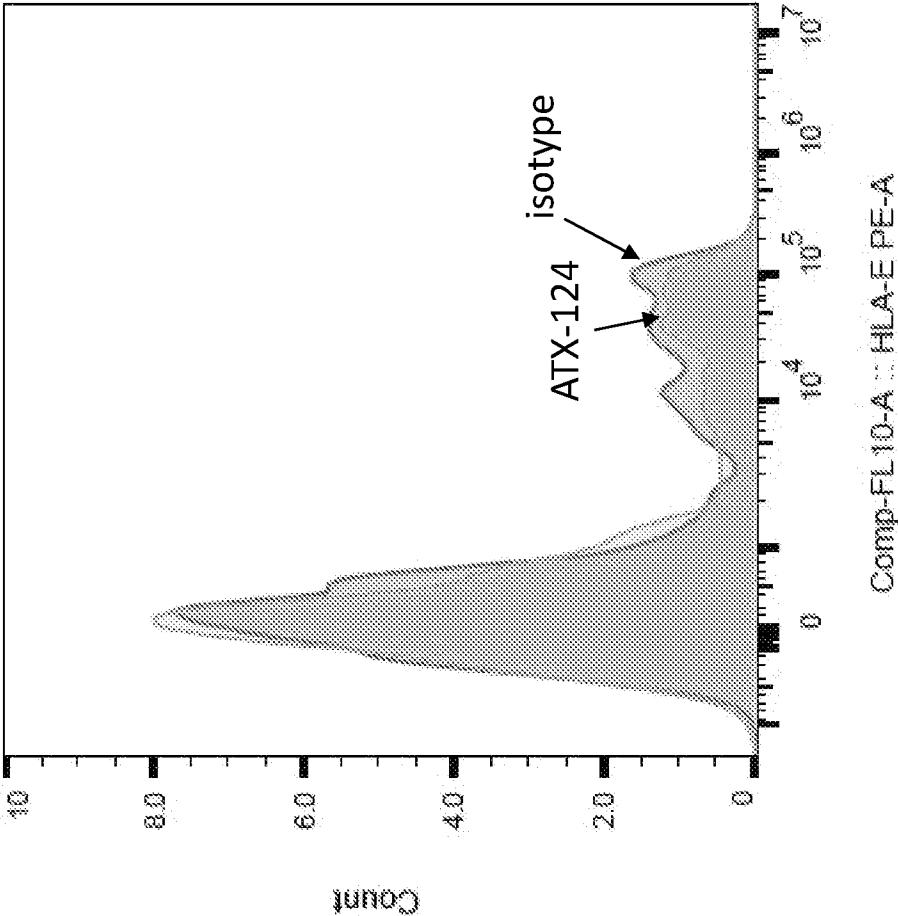


FIG. 32C

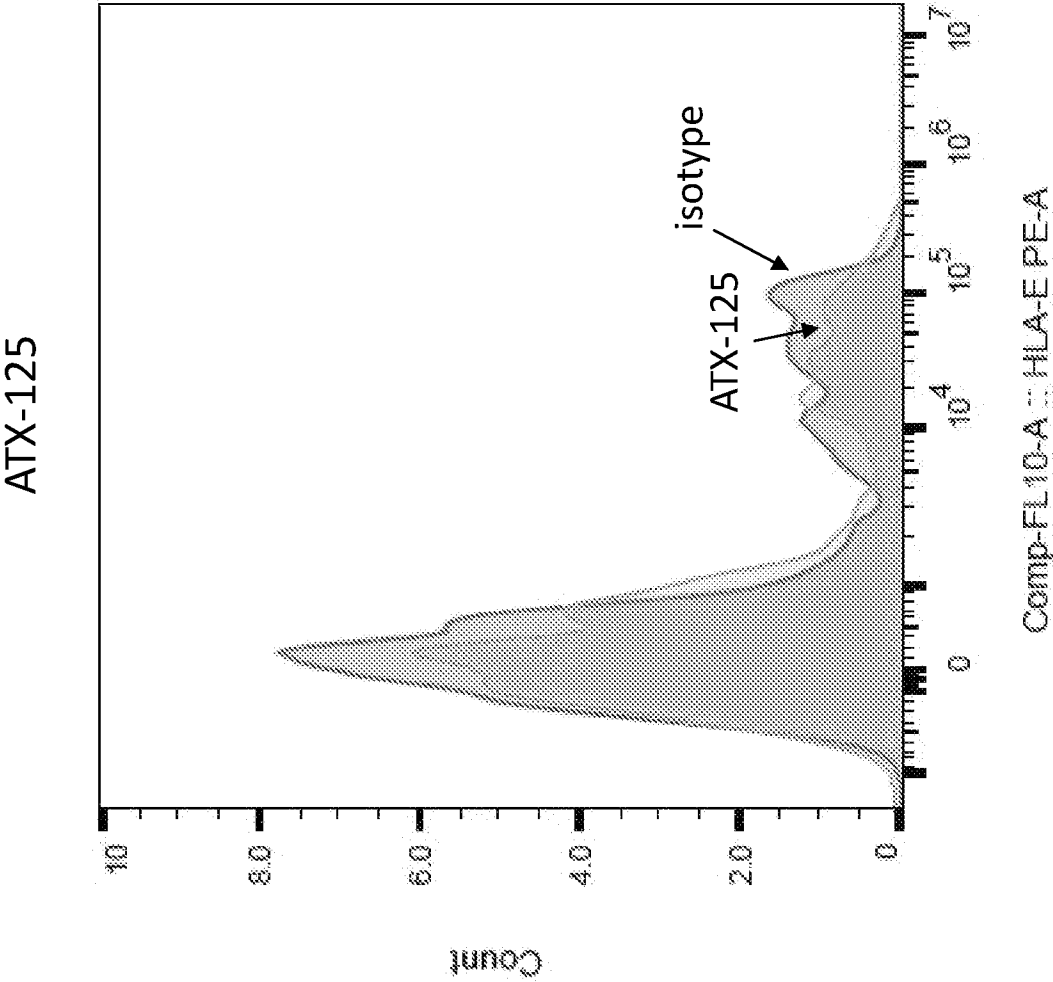


FIG. 32D

ATX-126

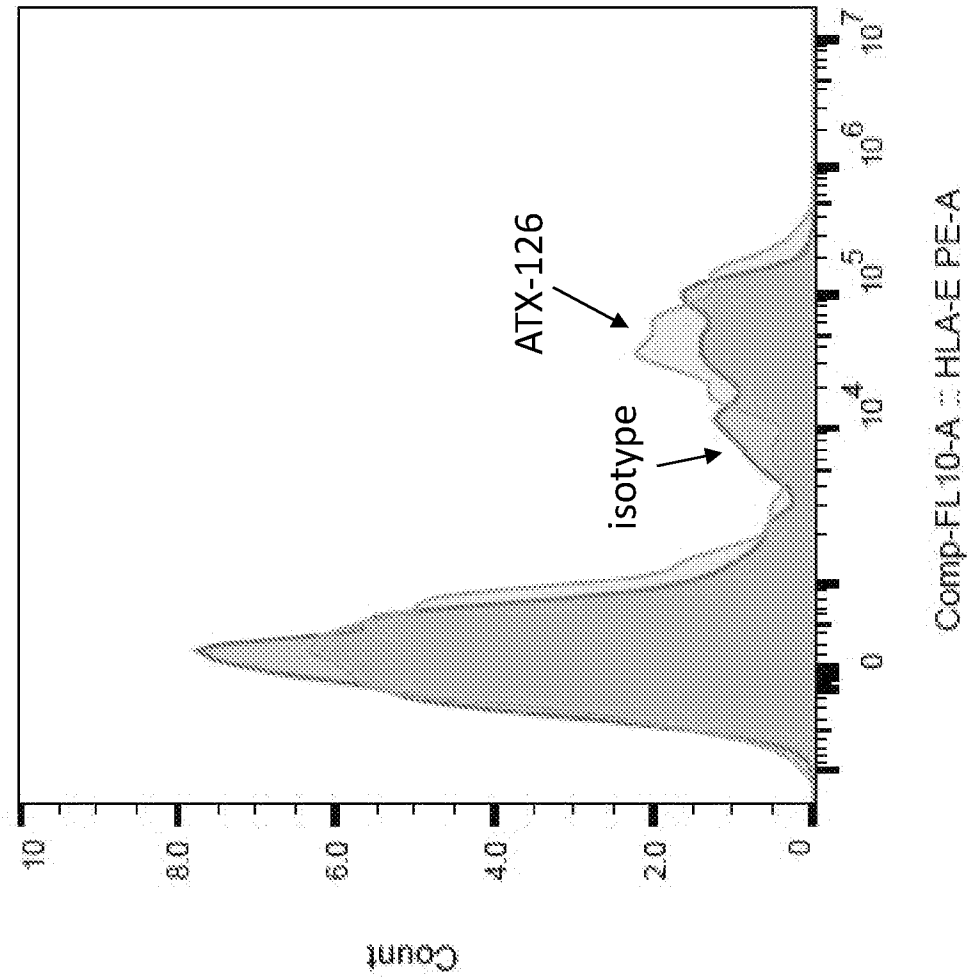


FIG. 32E

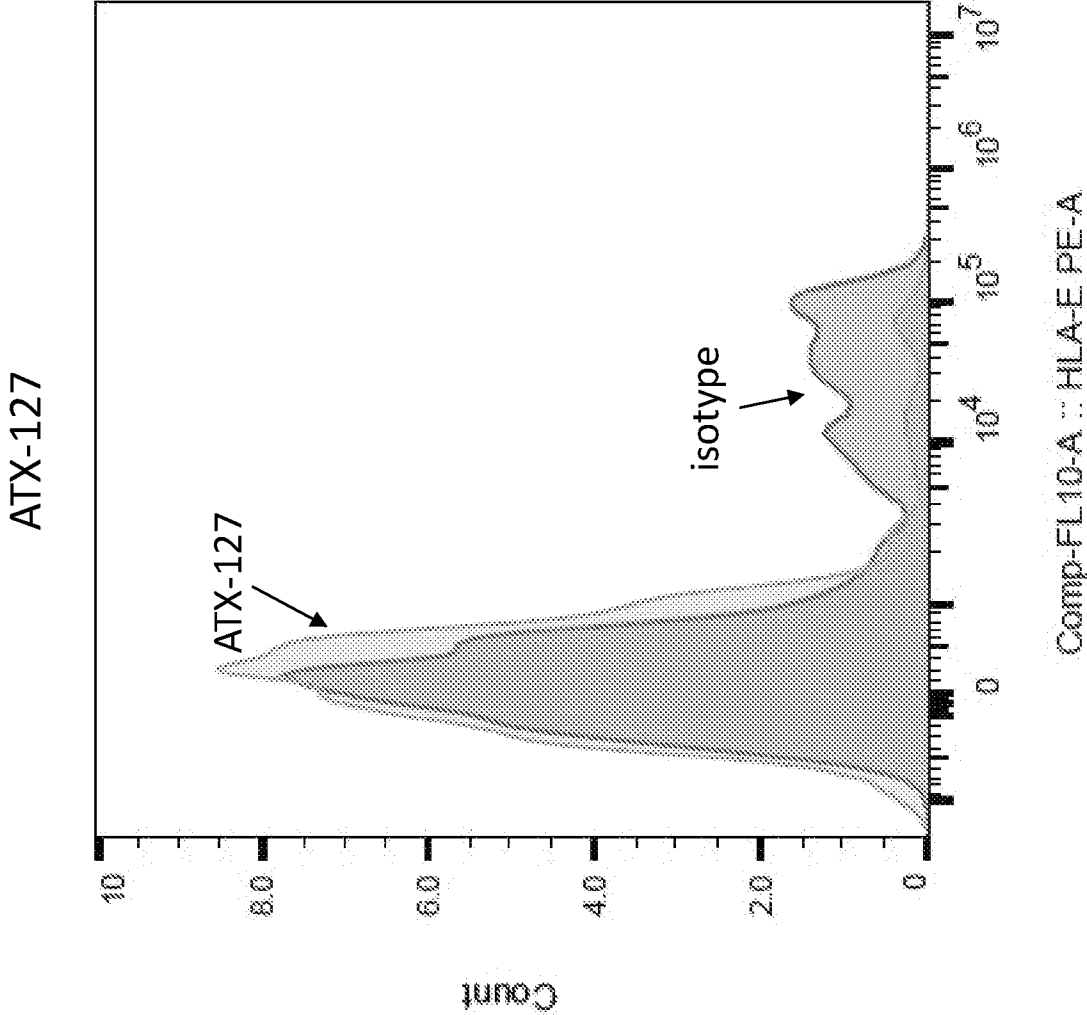


FIG. 32F

ATX-128

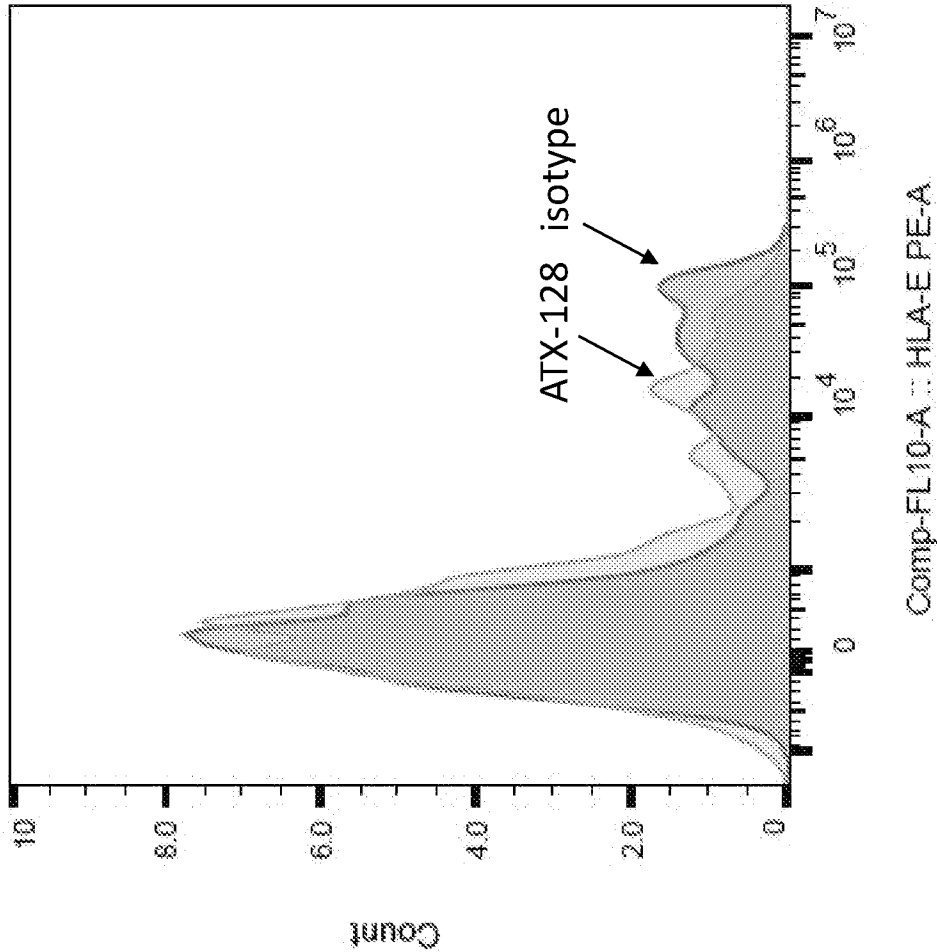


FIG. 32G

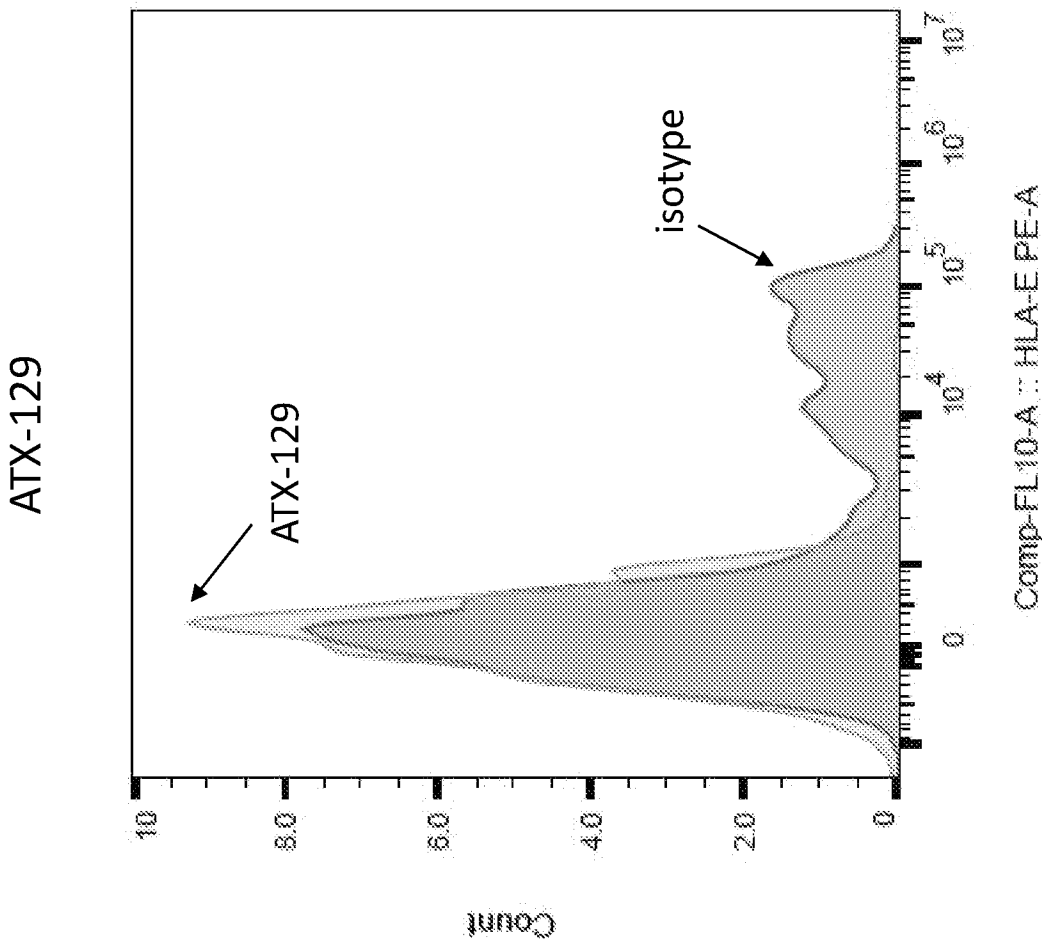


FIG. 32H

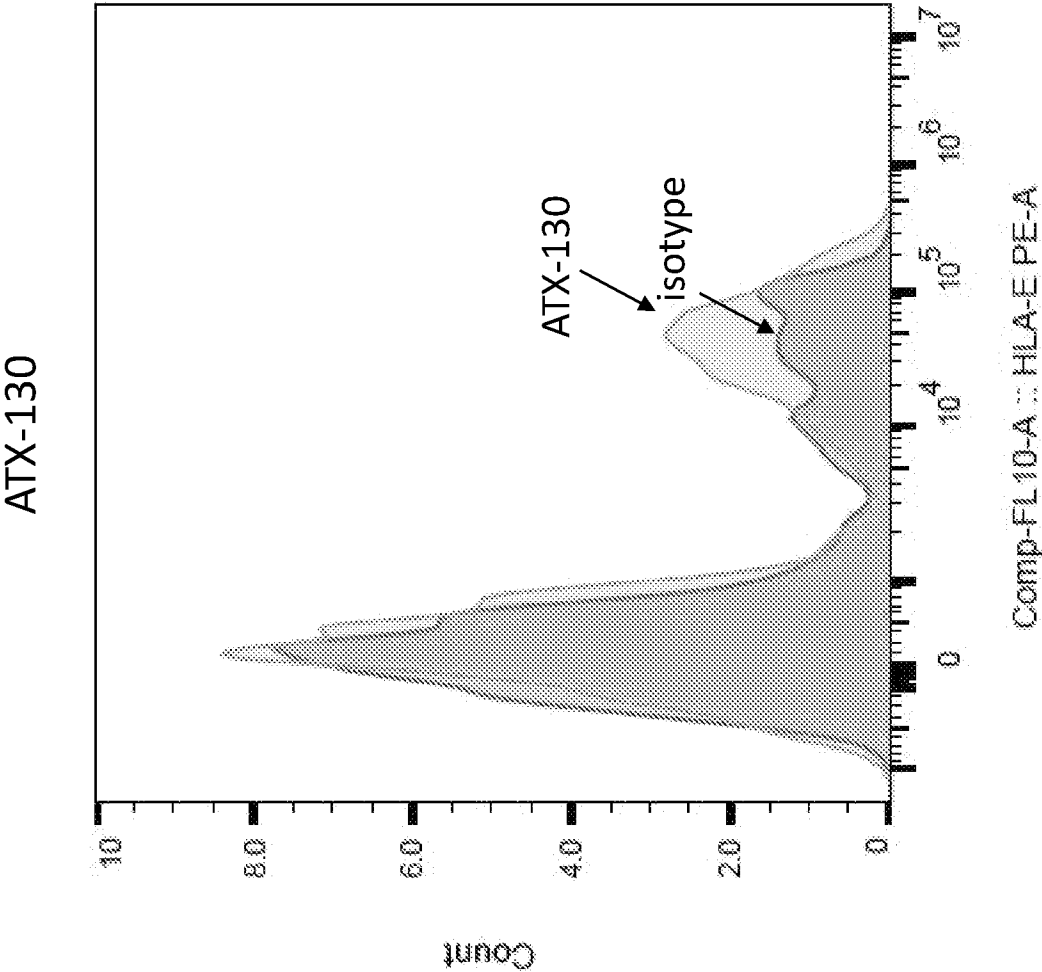


FIG. 32I

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

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
- a. ☒ forming part of the international application as filed:
- ☒ in the form of an Annex C/ST.25 text file.
- ☐ on paper or in the form of an image file.
- b. ☐ furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
- c. ☐ furnished subsequent to the international filing date for the purposes of international search only:
- ☐ in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
- ☐ on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

A search was performed using the following sequences SEQ1-2-3-4-5-6; SEQ7-8-9-10-11-12; SEQ13-14-15-16-17-18; SEQ30-31-32-33-34-35; SEQ87-88-89-90-91-35; SEQ36-37-38-33-34-35; SEQ87-92-93-90-91-35; SEQ36-39-40-33-34-35; SEQ87-92-94-90-91-35; SEQ41-42-43-44-45-46; SEQ95-96-97-98-99-100; SEQ47-48-49-50-51-52; SEQ109-110-114-115-99-52; SEQ53-54-55-50-45-56; SEQ116-117-118-115-99-56; SEQ57-58-59-60-34-61; SEQ101-102-103-104-91-61; SEQ83-84-85-86-34-61; SEQ105-106-107-108-91-61; SEQ47-48-62-63-34-64; SEQ109-110-111-112-113-64.

A. CLASSIFICATION OF SUBJECT MATTER

A61K 39/395 (2006.01) C07K 16/28 (2006.01) A61P 35/00 (2006.01) A61P 19/02 (2006.01)

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)

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

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

DATABASES: MEDLINE, EPODOC, WPIAP, CAPLUS, BIOSIS, EMBASE. KEYWORDS: CD94, KLRD1, KP43, NK cell lectin like receptor subfamily D, NKG2A, anti-CD94, anti-KP43, anti-KLRD1, antibody, immunoglobulin, Antibody dependent cellular cytotoxicity, ADCC, Feltys syndrome, Inclusion body myositis, NK leukemia, large granular lymphocyte Leukemia, LGL leukemia, chronic lymphoproliferative disorders of NK, CLPD NK, NK LGL, rheumatoid arthritis, IBM, IBD, T cell lymphoma, TCL, NK lymphoma, NK cell lymphoma, reduce, decrease, does not bind HLA; as well as synonyms and similar terms. GENOMEQUEST (nucleic acid and protein databases). SEQ1-2-3-4-5-6; SEQ7-8-9-10-11-12; SEQ13-14-15-16-17-18; SEQ30-31-32-33-34-35; SEQ87-88-89-90-91-35; SEQ36-37-38-33-34-35; SEQ87-92-93-90-91-35; SEQ36-39-40-33-34-35; SEQ87-92-94-90-91-35; SEQ41-42-43-44-45-46; SEQ95-96-97-98-99-100; SEQ47-48-49-50-51-52; SEQ109-110-114-115-99-52; SEQ53-54-55-50-45-56; SEQ116-117-118-115-99-56; SEQ57-58-59-60-34-61; SEQ101-102-103-104-91-61; SEQ83-84-85-86-34-61; SEQ105-106-107-108-91-61; SEQ47-48-62-63-34-64; SEQ109-110-111-112-113-64. Applicant and/or Inventor searches of the patent and non-patent literature was performed using DOCDB and DWPI, PubMed, and in internal databases provided by IP Australia.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	Documents are listed in the continuation of Box C	



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	"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
"D" document cited by the applicant in the international application	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"&" document member of the same patent family
"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	

Date of the actual completion of the international search
30 November 2021

Date of mailing of the international search report
30 November 2021

Name and mailing address of the ISA/AU

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Authorised officer

Monica Graham
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(ISO 9001 Quality Certified Service)
Telephone No. +61262833179

INTERNATIONAL SEARCH REPORT		International application No.
C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		PCT/US2021/052668
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2007/042573 A2 (INNATE PHARMA S.A.; UNIVERSITA DI GENOVA; NOVO NORDISK A/S) 19 April 2007 (D1: see abstract, Example 1 and claims)	1-3 and 53-82
Y	Biolegend Purified anti-human CD94 antibody (clone DX22) – technical data sheet (Revision Date: 30/11/2012). Retrieved online (11 Nov 2021): https://www.biolegend.com/en-us/search-results/purified-anti-human-cd94-antibody-649 (D2: see whole document)	4-9 and 53-82
Y	Santa Cruz Anti-CD94 Antibody (HP-3B1): sc-59143 – Datasheet. Retrieved online (11 Nov 2021): https://www.scbt.com/p/cd94-antibody-hp-3b1 (D3: see whole document)	4-9 and 53-82
Y	Santa Cruz Anti-CD94 Antibody (H-3): sc-390776 – Datasheet. Retrieved online (12 Nov 2021): https://www.scbt.com/p/cd94-antibody-h-3 (D4: see whole document)	4-9 and 53-82
Y	Invitrogen CD94 Monoclonal Antibody (HP-3D9), APC – Datasheet Retrieved online 11 Nov 2021): https://www.thermofisher.com/antibody/product/CD94-Antibody-clone-HP-3D9-Monoclonal/17-5094-42 (D5: see whole document)	4-9 and 53-82
Y	WO 2009/092805 A1 (NOVO NORDISK A/S) 30 July 2009 (D6: see abstract and claims)	1-3 and 53-82

INTERNATIONAL SEARCH REPORT		International application No.	
Information on patent family members		PCT/US2021/052668	
This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.			
Patent Document/s Cited in Search Report		Patent Family Member/s	
Publication Number	Publication Date	Publication Number	Publication Date
WO 2007/042573 A2	19 April 2007	WO 2007042573 A2	19 Apr 2007
		AU 2006301163 A1	19 Apr 2007
		AU 2006301163 B2	23 Feb 2012
		CA 2623109 A1	19 Apr 2007
		CN 101300272 A	05 Nov 2008
		CN 101300272 B	18 Sep 2013
		EP 1934260 A2	25 Jun 2008
		EP 1934260 B1	17 May 2017
		EP 2322557 A2	18 May 2011
		EP 2322557 B1	30 Aug 2017
		JP 2009511550 A	19 Mar 2009
		JP 5419067 B2	19 Feb 2014
		US 2008274047 A1	06 Nov 2008
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CN 101952317 B	22 Jul 2015		
EP 2247619 A1	10 Nov 2010		
EP 2628753 A1	21 Aug 2013		
JP 2011510047 A	31 Mar 2011		
JP 5774312 B2	09 Sep 2015		
KR 20100110864 A	13 Oct 2010		
MX 2010007935 A	23 Aug 2010		
RU 2010133892 A	27 Feb 2012		
US 2011052606 A1	03 Mar 2011		
Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.			

INTERNATIONAL SEARCH REPORT Information on patent family members		International application No. PCT/US2021/052668	
This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.			
Patent Document/s Cited in Search Report		Patent Family Member/s	
Publication Number	Publication Date	Publication Number	Publication Date
		US 8796427 B2	05 Aug 2014
		US 2014341896 A1	20 Nov 2014
		US 9422368 B2	23 Aug 2016
		ZA 201004752 B	28 Apr 2011
End of Annex			
Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001. Form PCT/ISA/210 (Family Annex)(July 2019)			