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(71) Applicant: ACTINIUM PHARMACEUTICALS, INC.

[US/US]; 275 Madison Avenue, 7th Floor, New York, New York 10016 (US).

(72) Inventors: ZHAO, Lequn; 201 Industrial Road, San Carlos, California 94070 (US).

KOTANIDES, Helen; 275 Madison Avenue, 7th Floor, New York, New York 10016 (US).

(74) Agent: GEARY, Lisa E.; Dentons Cohen & Grigsby P.C.,

625 Liberty Avenue, Pittsburgh, Pennsylvania 15222 (US).

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(54) Title: HUMANIZED ANTI-CD45 ANTIBODIES

(57) Abstract: Provided are humanized anti-human CD45 antibodies and pharmaceutical compositions including the antibodies.



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HUMANIZED ANTI-CD45 ANTIBODIES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. provisional application serial nos. 63/407,979 filed September 19, 2022, 63/405,237 filed September 9, 2022, and 63/323,257 filed March 24, 2022, each of which is hereby incorporated by reference in its entirety.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing which has been submitted electronically in XML format and is hereby incorporated by reference in its entirety. Said XML copy, created on March 20, 2023, is named ATNM-016PCT_SL_ST26.xml and is 853,669 bytes in size.

FIELD OF THE INVENTION

[0003] The invention relates to the field of antibody-based therapeutics.

BACKGROUND

[0004] The CD45 antigen is a member of the protein tyrosine phosphatase (PTP) family and is a 180-240 kD trans-membrane glycoprotein. It is also known as the leukocyte common antigen (LCA), T200, or Ly-5. CD45 plays a key role in T-cell and B-cells receptor signal transduction. Different isoforms of CD45 exist due to variable splicing of its exons. These isoforms are very specific to the activation and maturation state of the cell as well as cell type. The various isoforms have the same trans-membrane and cytoplasmic segments, but different extra-cellular domains, and are differentially expressed on subpopulations of B- and T-cell lymphocytes. The primary ligands described for CD45 include galectin-1, CD1, CD2, CD3, CD4, TCR, CD22 and Thy-1.

[0005] Monoclonal antibodies (mAbs) restricted in their specificity to one or the other isoforms of CD45 have been identified, as well as mAbs recognizing an epitope common to all CD45 isoforms. The mAbs designated CD45RA recognize the product of exon-A. The mAbs designated CD45RB recognize the product of exon-B. The mAbs designated CD45RO (as exemplified by UCHL1) selectively bind to the 180 kD isoform (without any of the variable exons A, B or C) which is restricted to a subset of cortical thymocytes, activated T cells and memory cells, and is absent on B cells. BC8, also known as apamistamab, is a murine IgG1 monoclonal antibody that recognizes all isoforms of human CD45.

[0006] Cells of hematopoietic origin, except mature erythrocytes and platelets, generally express CD45. High expression of CD45 is seen with most acute lymphoid and myeloid leukemias. Since CD45 is not found on tissues of non-hematopoietic origin, its specific

expression in leukemia has made it a good target for developing therapeutics, including radio-immunotherapeutics. For example, CD45 is expressed at a density of approximately 200,000 to 300,000 sites per cell on circulating leukocytes and malignant B cells.

[0007] What is needed and provided by the various aspects of the present invention are new humanized antibodies against human CD45.

SUMMARY OF THE INVENTION

[0008] One aspect of the invention provides an anti-huCD45 antibody, comprising:

(i) a heavy chain which is mCD45-HC parental, huCD45.HC1, huCD45.HC2, huCD45.HC3, huCD45.HC4, or huCD45.HC4, or any of said heavy chains without the signal sequence, or a heavy chain comprising the heavy chain variable region of any of said heavy chains; and

(ii) a light chain which is mCD45-LC parental, huCD45.LC1, huCD45.LC2, huCD45.LC3, or huCD45.LC4, or any of said light chains without the signal sequence, or a light chain comprising the light chain variable region of any of said light chains,

provided that when the heavy chain is mCD45-HC parental with or without the signal sequence, the light chain is not mCD45-LC parental with or without the signal sequence, or a human CD45-binding fragment of the antibody, such as a Fab fragment or Fab₂ fragment or a corresponding scFv molecule.

[0009] A related aspect of the invention provides an anti-huCD45 antibody or a human CD45-binding antibody fragment, including:

(i) an immunoglobulin heavy chain variable region including SEQ ID NO:2 (from mCD45-HC parental), SEQ ID NO:7 (from huCD45.HC1), SEQ ID NO:12 (from huCD45.HC2), SEQ ID NO:17 (from huCD45.HC3), or SEQ ID NO:22 (from huCD45.HC4); and

(ii) an immunoglobulin light chain variable region including SEQ ID NO:28 (from mCD45-LC parental), SEQ ID NO:33 (from huCD45.LC1), SEQ ID NO:38 (from huCD45.LC2), SEQ ID NO:43 (from huCD45.LC3), or SEQ ID NO:48 (from huCD45.LC4),
provided that when the heavy chain variable region includes SEQ ID NO:2, the light chain variable region is not SEQ ID NO:28.

[0010] In a variation of the preceding aspect of the invention, the anti-huCD45 antibody or human CD45-binding antibody fragment, includes:

(i) an immunoglobulin heavy chain sequence including SEQ ID NO:6 (from mCD45-HC parental), SEQ ID NO:11 (from huCD45.HC1), SEQ ID NO:16 (from huCD45.HC2), SEQ ID NO:21 (from huCD45.HC3), or SEQ ID NO:26 (from huCD45.HC4); and

(ii) an immunoglobulin light chain sequence including SEQ ID NO:32 (from mCD45-LC parental), SEQ ID NO:37 (from huCD45.LC1), SEQ ID NO:42 (from huCD45.LC2), SEQ ID NO:47 (from huCD45.LC3), or SEQ ID NO:52 (from huCD45.LC4).

[0011] Another aspect of the invention provides an anti-huCD45 antibody or a huCD45-binding antibody fragment, including:

(a) a set of immunoglobulin heavy chain complementarity determining regions (CDRs) including heavy chain CDR1, CDR2 and CDR3 amino acid sequences selected from the following sets:

- (i) SEQ ID NO:53, SEQ ID NO:56, and SEQ ID NO:55, respectively,
- (ii) SEQ ID NO:53, SEQ ID NO:57, and SEQ ID NO:55, respectively,
- (iii) SEQ ID NO:53, SEQ ID NO:58, and SEQ ID NO:55, respectively, and
- (iv) SEQ ID NO:53, SEQ ID NO:54, and SEQ ID NO:55, respectively; and

(b) a set of immunoglobulin light chain complementarity determining regions (CDRs) including light chain CDR1, CDR2 and CDR3 amino acid sequences selected from the following sets:

- (i) SEQ ID NO:62, SEQ ID NO:60, and SEQ ID NO:61, respectively,
- (ii) SEQ ID NO:59, SEQ ID NO:63, and SEQ ID NO:61, respectively,
- (iii) SEQ ID NO:59, SEQ ID NO:64, and SEQ ID NO:61, respectively, and
- (iv) SEQ ID NO:59, SEQ ID NO:60, and SEQ ID NO:61,

provided that when the heavy chain CDR set is (a)(iv), the light chain CDR set is not (b)(iv).

[0012] A related aspect of the invention provides an anti-huCD45 antibody or a huCD45-binding antibody fragment, including:

(a) a set of immunoglobulin heavy chain complementarity determining regions (CDRs) including heavy chain CDR1, CDR2 and CDR3 amino acid sequences selected from the following sets:

- (i) SEQ ID NO:53, SEQ ID NO:56, and SEQ ID NO:55, respectively,
- (ii) SEQ ID NO:53, SEQ ID NO:57, and SEQ ID NO:55, respectively, and
- (iii) SEQ ID NO:53, SEQ ID NO:58, and SEQ ID NO:55, respectively; and

(b) a set of immunoglobulin light chain complementarity determining regions (CDRs) including light chain CDR1, CDR2 and CDR3 amino acid sequences selected from the following sets:

- (i) SEQ ID NO:62, SEQ ID NO:60, and SEQ ID NO:61, respectively,
- (ii) SEQ ID NO:59, SEQ ID NO:63, and SEQ ID NO:61, respectively, and

(iii) SEQ ID NO:59, SEQ ID NO:64, and SEQ ID NO:61, respectively.

[0013] Additional features, advantages, and aspects of the invention may be set forth or apparent from consideration of the following detailed description, drawings, and claims. Moreover, it is to be understood that both the foregoing summary of the invention and the following detailed description are exemplary and intended to provide further explanation without limiting the scope of the invention as claimed.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] Various antibody heavy and light chain amino acid sequences are set forth in FIGS. 1-10.

[0015] FIG. 1 shows the amino acid sequence of a heavy chain of mouse anti-huCD45 antibody ("m CD45-HC parental") that binds all isoforms of human CD45 (huCD45) and portions thereof used as the basis for producing humanized anti-huCD45 antibodies.

[0016] FIG. 2 shows the amino acid sequence of a humanized anti-huCD45 antibody heavy chain ("hu CD45.HC1") and portions thereof.

[0017] FIG. 3 shows the amino acid sequence of a humanized anti-huCD45 antibody heavy chain ("hu CD45.HC2") and portions thereof.

[0018] FIG. 4 shows the amino acid sequence of a humanized anti-huCD45 antibody heavy chain ("hu CD45.HC3") and portions thereof.

[0019] FIG. 5 shows the amino acid sequence of a humanized anti-huCD45 antibody heavy chain ("hu CD45.HC4") and portions thereof.

[0020] FIG. 6 shows the amino acid sequence of a light chain of mouse anti-huCD45 antibody ("m CD45-LC parental") and portions thereof used as the basis for producing humanized anti-huCD45 antibodies.

[0021] FIG. 7 shows the amino acid sequence of a humanized anti-huCD45 antibody light chain ("hu CD45.LC1") and portions thereof.

[0022] FIG. 8 shows the amino acid sequence of a humanized anti-huCD45 antibody light chain ("hu CD45.LC2") and portions thereof.

[0023] FIG. 9 shows the amino acid sequence of a humanized anti-huCD45 antibody light chain ("hu CD45.LC3") and portions thereof.

[0024] FIG. 10 shows the amino acid sequence of a humanized anti-huCD45 antibody light chain ("hu CD45.LC4") and portions thereof.

[0025] The complementarity determining region (CDR) amino acid sequences are underlined in the presentation of the variable region sequences in the figures.

DETAILED DESCRIPTION

[0026] One aspect of the invention provides an anti-(human CD45) [“anti-huCD45”] antibody, comprising:

(i) a heavy chain which is mCD45-HC parental, huCD45.HC1, huCD45.HC2, huCD45.HC3, huCD45.HC1, or huCD45.HC4, or any of said heavy chains without the signal sequence, or a heavy chain comprising the heavy chain variable region of any of said heavy chains; and

(ii) a light chain which is mCD45-LC parental, huCD45.LC1, huCD45.LC2, huCD45.LC3, or huCD45.LC4, or any of said light chains without the signal sequence, or a light chain comprising the light chain variable region of any of said light chains, provided that when the heavy chain is mCD45-HC parental with or without the signal sequence, the light chain is not mCD45-LC parental with or without the signal sequence, or a human CD45-binding fragment of the antibody, such as a Fab fragment or Fab₂ fragment or a corresponding scFv molecule.

[0027] The parental murine monoclonal antibody including the parental heavy chain shown in FIG. 1 and the parental light chain shown in FIG. 6, which binds all isoforms of human CD45, was used as the basis for designing humanized anti-huCD45 antibodies. Antibodies consisting of various combinations of the humanized immunoglobulin heavy chains and immunoglobulin light chains were expressed in CHO cells and isolated for analysis and comparison to the parental antibody. Binding experiments were performed using an Octet HTX (Sartorius, Bohemia, New York, USA) at 25°C to determine the K_D's of the antibodies. The antibodies were loaded onto anti-human Fc capture (AHC) sensors. The loaded sensors were dipped into serial dilutions of rhCD45 His tag (900nM start, 1:3 dilution, 3 points; R&D Systems, Minneapolis, MN, USA). Reference sample well (buffer) was used for data analysis. Kinetic constants were calculated using a monovalent (1:1) binding model. Results are shown in Table 1 below.

Table 1

Sample ID	K_D (M)
m CD45 Parental	3.75E-08
hu CD45 HC2+LC1	2.44E-07
hu CD45 HC2+LC3	1.96E-07
hu CD45 HC2+LC4	2.47E-07
hu CD45 HC3+LC1	1.63E-07
hu CD45 HC3+LC3	5.02E-08
hu CD45 HC3+LC4	1.09E-07
hu CD45 HC4+LC1	2.32E-07

hu CD45 HC4+LC3	1.51E-07
hu CD45 HC4+LC4	1.23E-07

hu CD45 HC3+LC3 retained similar binding affinity as the parental antibody while all other humanized samples showed less than 10-fold changes in KD values relative to the parental antibody.

[0028] Another aspect of the invention provides an anti-huCD45 antibody or a human CD45-binding antibody fragment, including:

(i) an immunoglobulin heavy chain variable region including SEQ ID NO:2 (from mCD45-HC parental), SEQ ID NO:7 (from huCD45.HC1), SEQ ID NO:12 (from huCD45.HC2), SEQ ID NO:17 (from huCD45.HC3), or SEQ ID NO:22 (from huCD45.HC4); and

(ii) an immunoglobulin light chain variable region including SEQ ID NO:28 (from mCD45-LC parental), SEQ ID NO:33 (from huCD45.LC1), SEQ ID NO:38 (from huCD45.LC2), SEQ ID NO:43 (from huCD45.LC3), or SEQ ID NO:48 (from huCD45.LC4), provided that when the heavy chain variable region includes SEQ ID NO:2, the light chain variable region is not SEQ ID NO:28.

[0029] In a variation of the preceding aspect of the invention, the anti-huCD45 antibody or human CD45-binding antibody fragment, includes:

(i) an immunoglobulin heavy chain sequence including SEQ ID NO:6 (from mCD45-HC parental), SEQ ID NO:11 (from huCD45.HC1), SEQ ID NO:16 (from huCD45.HC2), SEQ ID NO:21 (from huCD45.HC3), or SEQ ID NO:26 (from huCD45.HC4); and

(ii) an immunoglobulin light chain sequence including SEQ ID NO:32 (from mCD45-LC parental), SEQ ID NO:37 (from huCD45.LC1), SEQ ID NO:42 (from huCD45.LC2), SEQ ID NO:47 (from huCD45.LC3), or SEQ ID NO:52 (from huCD45.LC4).

[0030] A further aspect of the invention provides an anti-huCD45 antibody or a huCD45-binding antibody fragment, including:

(a) a set of immunoglobulin heavy chain complementarity determining regions (CDRs) including heavy chain CDR1, CDR2 and CDR3 amino acid sequences selected from the following sets:

- (i) SEQ ID NO:53, SEQ ID NO:56, and SEQ ID NO:55, respectively,
- (ii) SEQ ID NO:53, SEQ ID NO:57, and SEQ ID NO:55, respectively,
- (iii) SEQ ID NO:53, SEQ ID NO:58, and SEQ ID NO:55, respectively, and
- (iv) SEQ ID NO:53, SEQ ID NO:54, and SEQ ID NO:55, respectively; and

(b) a set of immunoglobulin light chain complementarity determining regions (CDRs) including light chain CDR1, CDR2 and CDR3 amino acid sequences selected from the following sets:

- (i) SEQ ID NO:62, SEQ ID NO:60, and SEQ ID NO:61, respectively,
- (ii) SEQ ID NO:59, SEQ ID NO:63, and SEQ ID NO:61, respectively,
- (iii) SEQ ID NO:59, SEQ ID NO:64, and SEQ ID NO:61, respectively, and
- (iv) SEQ ID NO:59, SEQ ID NO:60, and SEQ ID NO:61,

provided that when the heavy chain CDR set is (a)(iv), the light chain CDR set is not (b)(iv). It should be understood that the antibody or antibody fragment includes a heavy chain variable region that includes the heavy chain CDRs and a light chain variable region that includes the light chain CDRs.

[0031] A related aspect of the invention provides an anti-huCD45 antibody or a huCD45-binding antibody fragment, including:

(a) a set of immunoglobulin heavy chain complementarity determining regions (CDRs) including heavy chain CDR1, CDR2 and CDR3 amino acid sequences selected from the following sets:

- (i) SEQ ID NO:53, SEQ ID NO:56, and SEQ ID NO:55, respectively,
- (ii) SEQ ID NO:53, SEQ ID NO:57, and SEQ ID NO:55, respectively, and
- (iii) SEQ ID NO:53, SEQ ID NO:58, and SEQ ID NO:55, respectively; and

(b) a set of immunoglobulin light chain complementarity determining regions (CDRs) including light chain CDR1, CDR2 and CDR3 amino acid sequences selected from the following sets:

- (i) SEQ ID NO:62, SEQ ID NO:60, and SEQ ID NO:61, respectively,
- (ii) SEQ ID NO:59, SEQ ID NO:63, and SEQ ID NO:61, respectively, and
- (iii) SEQ ID NO:59, SEQ ID NO:64, and SEQ ID NO:61, respectively.

It should again be understood that the antibody or antibody fragment includes a heavy chain variable region that includes the heavy chain CDRs and a light chain variable region that includes the light chain CDRs.

[0032] In a variation of either of the preceding two aspects of the invention or of other aspects of the invention in which CDR sequences are recited, the antibody or antibody fragment or protein further includes with respect to one or more of the recited CDRs, in any and all combinations, additional N-terminal and/or C-terminal amino acid sequence, of 1, 2, 3, 4, 5, 6,

7, 8, 9, or 10 amino acid residues immediately adjacent to the one or more CDRs (on either or both of the N-terminal and C-terminal side of the CDR(s)) as shown in the any of the respective variable region amino acid sequences set forth in FIGS. 1-10.

[0033] Another aspect of the invention provides a protein, such as an anti-CD45 antibody or CD45-binding antibody fragment (such as Fab fragment, Fab₂ fragment, or scFv molecule) or an immunoglobulin light chain, including an antibody light chain variable region including the following light chain CDRs:

a CDR-L1 including the amino acid sequence RASKSVSTSGYSYLH (SEQ ID NO:59), KSSKSVSTSGYSYLH (SEQ ID NO:62), RASKSVSTSGYSYLA (SEQ ID NO:65), RASKSVSTSGYSYLS (SEQ ID NO:66), or RASKSVSTSGYSYLN (SEQ ID NO:67);

a CDR-L2 including the amino acid sequence LASNLES (SEQ ID NO:60), LASNLA (SEQ ID NO:68), LASNLAT (SEQ ID NO:63), LASNLQ (SEQ ID NO:69), LASNLQS (SEQ ID NO:64), LASTRES (SEQ ID NO:70), LASTRAT (SEQ ID NO:71), LASNRAT (SEQ ID NO:72), or LASSQLS (SEQ ID NO:73);

a CDR-L3 including the amino acid sequence QHSRELPFT (SEQ ID NO:61), provided that the combination of a CDR-L1 including the amino acid sequence RASKSVSTSGYSYLH (SEQ ID NO:59) and CDR-L2 including the amino acid sequence LASNLES (SEQ ID NO:60) is excluded.

The next amino acid residues following the CDR-L3 sequence QHSRELPFT (SEQ ID NO:61) in the protein may, for example, be FGQ.

[0034] A further aspect of the invention provides a protein, such as an anti-CD45 antibody or CD45-binding antibody fragment (such as Fab fragment, Fab₂ fragment, or scFv molecule) or an immunoglobulin heavy chain, including an antibody heavy chain variable region including the following light chain CDRs:

a CDR-H1 including the amino acid sequence GFDFSRYWMS (SEQ ID NO:53) or GFDFSRYWMN (SEQ ID NO:85);

a CDR-H2 including the amino acid sequence EINPTSSTINFTPSLKD (SEQ ID NO:54), EINPTSSTINFADSVKG (SEQ ID NO:56), EINPTSSTINYADSVKG (SEQ ID NO:57), EINPTSSTINFVDSVKG (SEQ ID NO:58), YINPTSSTIYYADSVKG (SEQ ID NO:74), AINPTSSTIYYADSVKG (SEQ ID NO:75), NINPTSSTIYYVDSVKG (SEQ ID NO:76), or SINPTSSTIYYADSVKG (SEQ ID NO:77);

a CDR-H3 including the amino acid sequence GNYRYGDAMDY (SEQ ID NO:55),

provided that the combination of a CDR-H1 including the amino acid sequence GFDFSRYWMS (SEQ ID NO:53) and CDR-H2 including the amino acid sequence EINPTSSTINFTPSLKD (SEQ ID NO:54) is excluded.

[0035] Still another aspect of the invention provides a protein, such as an anti-CD45 antibody or CD45-binding antibody fragment (such as Fab fragment, Fab₂ fragment, or scFv molecule), including:

(a) an antibody light chain variable region including the following light chain CDRs:

a CDR-L1 including the amino acid sequence RASKSVSTSGYSYLH (SEQ ID NO:59), KSSKSVSTSGYSYLH (SEQ ID NO:62), RASKSVSTSGYSYLA (SEQ ID NO:65), RASKSVSTSGYSYLS (SEQ ID NO:66), or RASKSVSTSGYSYLN (SEQ ID NO:67);

a CDR-L2 including the amino acid sequence LASNLES (SEQ ID NO:60), LASNLA (SEQ ID NO:68), LASNLAT (SEQ ID NO:63), LASNLQ (SEQ ID NO:69), LASNLQS (SEQ ID NO:64), LASTRES (SEQ ID NO:70), LASTRAT (SEQ ID NO:71), LASNRAT (SEQ ID NO:72), or LASSQLS (SEQ ID NO:73); and

a CDR-L3 including the amino acid sequence QHSRELPFT (SEQ ID NO:61);

and

(b) an antibody heavy chain variable region including the following heavy chain CDRs:

a CDR-H1 including the amino acid sequence GFDFSRYWMS (SEQ ID NO:53) or GFDFSRYWMN (SEQ ID NO:85);

a CDR-H2 including the amino acid sequence EINPTSSTINFTPSLKD (SEQ ID NO:54), EINPTSSTINFADSVKG (SEQ ID NO:56), EINPTSSTINYADSVKG (SEQ ID NO:57), EINPTSSTINFVDSVKG (SEQ ID NO:58), YINPTSSTIYYADSVKG (SEQ ID NO:74), AINPTSSTIYYADSVKG (SEQ ID NO:75), NINPTSSTIYYVDSVKG (SEQ ID NO:76), or SINPTSSTIYYADSVKG (SEQ ID NO:77); and

a CDR-H3 including the amino acid sequence GNYYRYGDAMDY (SEQ ID NO:55),

provided that the combination of CDR-L1 including the amino acid sequence RASKSVSTSGYSYLH (SEQ ID NO:59), CDR-L2 including the amino acid sequence LASNLES (SEQ ID NO:60), CDR-L3 including the amino acid sequence QHSRELPFT (SEQ ID NO:61), CDR-H1 including the amino acid sequence GFDFSRYWMS (SEQ ID NO:53), CDR-H2 including the amino acid sequence EINPTSSTINFTPSLKD (SEQ ID

NO:54), and CDR-H3 including the amino acid sequence GNYRYGDAMDY (SEQ ID NO:55) is excluded.

The next amino acid residues following the CDR-L3 sequence QHSRELPFT (SEQ ID NO:61) in the protein may, for example, be FGQ.

[0036] A further aspect of the invention provides a protein, such as an anti-CD45 antibody or CD45-binding antibody fragment (such as Fab fragment, Fab₂ fragment, or scFv molecule) or an immunoglobulin light chain, including an antibody light chain variable region including the following light chain CDRs:

a CDR-L1 including the amino acid sequence RASKSVSTSGYSYLH (SEQ ID NO:59) or KSSKSVSTSGYSYLH (SEQ ID NO:62);

a CDR-L2 including the amino acid sequence LASNLA (SEQ ID NO:68), LASNLAT (SEQ ID NO:63), LASNLQ (SEQ ID NO:69), or LASNLQS (SEQ ID NO:64); and

a CDR-L3 including the amino acid sequence QHSRELPFT (SEQ ID NO:61).

The next amino acid residues following the CDR-L3 sequence QHSRELPFT (SEQ ID NO:61) in the protein may, for example, be FGQ.

[0037] Another aspect of the invention provides a protein, such as an anti-CD45 antibody or CD45-binding antibody fragment (such as Fab fragment, Fab₂ fragment, or scFv molecule) or an immunoglobulin heavy chain, including an antibody heavy chain variable region including the following heavy chain CDRs:

a CDR-H1 including the amino acid sequence GFDFSRYWMS (SEQ ID NO:53);

a CDR-H2 including the amino acid sequence EINPTSSTINFADSVKG (SEQ ID NO:56), EINPTSSTINYADSVKG (SEQ ID NO:57), or EINPTSSTINFVDSVKG (SEQ ID NO:58); and

a CDR-H3 including the amino acid sequence GNYRYGDAMDY (SEQ ID NO:55).

[0038] A still further aspect of the invention provides a protein, such as an anti-CD45 antibody or CD45-binding antibody fragment (such as Fab fragment, Fab₂ fragment, or scFv molecule), including:

(a) an antibody light chain variable region including the following light chain CDRs:

a CDR-L1 including the amino acid sequence RASKSVSTSGYSYLH (SEQ ID NO:59) or KSSKSVSTSGYSYLH (SEQ ID NO:62);

a CDR-L2 including the amino acid sequence LASNLES (SEQ ID NO:60), LASNLA (SEQ ID NO:68), LASNLAT (SEQ ID NO:63), LASNLQ (SEQ ID NO:69), LASNLQS (SEQ ID NO:64); and

a CDR-L3 including the amino acid sequence QHSRELPFT (SEQ ID NO:61);
and

(b) an antibody heavy chain variable region including the following heavy chain CDRs:

a CDR-H1 including the amino acid sequence GFDFSRYWMS (SEQ ID NO:53);

a CDR-H2 including the amino acid sequence EINPTSSTINFTPSLKD (SEQ ID NO:54), EINPTSSTINFADSVKG (SEQ ID NO:56), EINPTSSTINYADSVKG (SEQ ID NO:57), or EINPTSSTINFVDSVKG (SEQ ID NO:58); and

a CDR-H3 including the amino acid sequence GNYRYGDAMDY (SEQ ID NO:55),

provided that the combination of CDR-L1 including the amino acid sequence RASKSVSTSGYSYLH (SEQ ID NO:59), CDR-L2 including the amino acid sequence LASNLES (SEQ ID NO:60), CDR-L3 including the amino acid sequence QHSRELPFT (SEQ ID NO:61), CDR-H1 including the amino acid sequence GFDFSRYWMS (SEQ ID NO:53), CDR-H2 including the amino acid sequence EINPTSSTINFTPSLKD (SEQ ID NO:54), and CDR-H3 including the amino acid sequence GNYRYGDAMDY (SEQ ID NO:55) is excluded.

The next amino acid residues following the CDR-L3 sequence QHSRELPFT (SEQ ID NO:61) in the protein may, for example, be FGQ. The CDR-H2 may, for example, include the amino acid sequence EINPTSSTINFADSVKG (SEQ ID NO:56), EINPTSSTINYADSVKG (SEQ ID NO:57), or EINPTSSTINFVDSVKG (SEQ ID NO:58).

[0039] One aspect of the invention provides an immunoglobulin heavy chain variable region or a protein, such as an anti-CD45 antibody or CD45 binding antibody fragment such as a Fab, Fab₂ or scFv molecule, including an immunoglobulin heavy chain variable region sequence that includes one or more of the amino acid substitutions disclosed in any of the non-parental immunoglobulin heavy chain variable regions disclosed herein versus the parental immunoglobulin heavy chain variable region disclosed herein, in any combination, but otherwise includes the same amino acid sequence as the parental immunoglobulin heavy chain variable region sequence.

[0040] One aspect of the invention provides an immunoglobulin light chain variable region or a protein, such as an anti-CD45 antibody or CD45 binding antibody fragment such as a Fab, Fab₂ or scFv molecule, including an immunoglobulin light chain variable region that includes one or more of the amino acid substitutions disclosed in any of the non-parental immunoglobulin light chain variable regions disclosed herein versus the parental immunoglobulin light chain variable region disclosed herein, in any combination, but otherwise includes the same amino acid sequence as the parental immunoglobulin light chain variable region sequence.

[0041] One aspect of the invention provides a protein, such as an anti-CD45 antibody or CD45 binding antibody fragment such as a Fab, Fab₂ or scFv molecule, including:

(i) an immunoglobulin heavy chain variable region that includes one or more of the amino acid substitutions disclosed in any of the non-parental immunoglobulin heavy chain variable regions disclosed herein versus the parental immunoglobulin heavy chain variable region disclosed herein, in any combination, but otherwise includes the same amino acid sequence as the parental immunoglobulin heavy chain variable region sequence; and

(ii) an immunoglobulin light chain variable region that includes one or more of the amino acid substitutions disclosed in any of the non-parental immunoglobulin light chain variable regions disclosed herein versus the parental immunoglobulin light chain variable region disclosed herein, in any combination, but otherwise includes the same amino acid sequence as the parental immunoglobulin light chain variable region sequence.

[0042] One aspect of the invention provides a protein, such as an anti-CD45 antibody or CD45 binding antibody fragment such as a Fab, Fab₂ or scFv molecule, including:

(i) the parental immunoglobulin heavy chain variable region disclosed herein, or an immunoglobulin heavy chain variable region that includes one or more of the amino acid substitutions disclosed in any of the non-parental immunoglobulin heavy chain variable regions disclosed herein versus the parental immunoglobulin heavy chain variable region disclosed herein, in any combination, but otherwise includes the same amino acid sequence as the parental immunoglobulin heavy chain variable region sequence; and

(ii) the parental immunoglobulin light chain variable region disclosed herein, or an immunoglobulin light chain variable region that includes one or more of the amino acid substitutions disclosed in any of the non-parental immunoglobulin light chain variable regions disclosed herein versus the parental immunoglobulin light chain variable region disclosed herein, in any combination, but otherwise includes the same amino acid sequence as the parental immunoglobulin heavy chain variable region sequence.

provided that the protein does not include both the parental immunoglobulin heavy chain variable region disclosed herein and the parental immunoglobulin light chain variable region disclosed herein.

[0043] In one variation of this aspect, the protein does not include the parental immunoglobulin heavy chain variable region disclosed herein and does not include the parental immunoglobulin light chain variable region disclosed herein.

[0044] One aspect of the invention provides an immunoglobulin heavy chain variable region or a protein, such as an anti-CD45 antibody or CD45 binding antibody fragment such as a Fab, Fab₂ or scFv molecule, including an immunoglobulin heavy chain variable region sequence that includes the amino acid sequence:

EVKLLESGGGLVQPGGSLKLSCAASGFDFSRYWMX₁WVRQAPGKGLEWX₂X₃X₄INP
TSSTIX₅X₆X₇X₈SLKX₉X₁₀X₁₁X₁₂ISRDNX₁₃KNX₁₄LYLQMSX₁₅X₁₆RX₁₇EDTAX₁₈YYCA
RGNYRYRGDAMDYWGQGTX₁₉VTVSS (SEQ ID NO:78),

wherein

X₁ is S or N,

X₂ is I or V,

X₃ is G, S or A,

X₄ is E, Y, A, N, or S,

X₅ is N or Y,

X₆ is F or Y,

X₇ is T, A, or V,

X₈ is P or D,

X₉ is D or G,

X₁₀ is K or R,

X₁₁ is V or F,

X₁₂ is F or T,

X₁₃ is A or S,

X₁₄ is T or S,

X₁₅ is K or S,

X₁₆ is V or L,

X₁₇ is S or A

X₁₈ is L or V, and

X₁₉ is S or M,

provided that the amino acid sequence does not include the sequence

EVKLLESGGGLVQPGGSLKLSCAASGFDFSRYWMSWVRQAPGKGLEWIGEINPTSST
INFTPSLKDKVFISRDNAKNTLYLQMSKVRSEDALYYCARGNYYRYGDAMDYWG
 QGTSVTVSS (SEQ ID NO:2).

The heavy chain variable region amino acid sequence of this aspect may be referred to herein as “the Modified Heavy Chain Variable Region Sequence” or the “M.H.C.V.R. Sequence”.

[0045] One aspect of the invention provides an immunoglobulin light chain variable region or a protein, such as an anti-CD45 antibody or CD45 binding antibody fragment such as a Fab, Fab₂ or scFv molecule, including an immunoglobulin light chain variable region sequence that includes the amino acid sequence:

DIX_{L1}X_{L2}TQSPX_{L3}X_{L4}LX_{L5}X_{L6}SX_{L7}GX_{L8}RX_{L9}TX_{L10}X_{L11}CX_{L12}X_{L13}SKSVSTSGYSYLX_{L14}
 WYQQKPGQX_{L15}PX_{L16}LLIYLASX_{L17}X_{L18}X_{L19}X_{L20}GX_{L21}PX_{L22}RFSGSGSGTDFTLX_{L23}IX_{L24}X_{L25}X_{L26}X_{L27}X_{L28}EDX_{L29}AX_{L30}YYCQHSRELPTFGX_{L31}GTKLEIK (SEQ ID NO:79),
 wherein

X_{L1} is D or E,

X_{L2} is A or V or Q,

X_{L3} is L or M,

X_{L4} is A or D or S,

X_{L5} is S or T,

X_{L6} is A or S,

X_{L7} is V or L or A,

X_{L8} is L or P or V,

X_{L9} is Q or E or D,

X_{L10} is A or V,

X_{L11} is I or L,

X_{L12} is S or N or T,

X_{L13} is A or S,

X_{L14} is H, A, S, or N,

X_{L15} is P or A,

X_{L16} is K or R,

X_{L17} is N or T or S,

X_{L18} is L or R,

X_{L19} is E or A or Q,

X_{L20} is S or T,

XL21 is V or I,
 XL22 is A or D or S,
 XL23 is N or T,
 XL24 is H or S,
 XL25 is P or S,
 XL26 is V or L,
 XL27 is E or Q,
 XL28 is E or A or P,
 XL29 is A or V or F,
 XL30 is T or V,
 XL31 is S or Q, and
 XL32 is R or K

provided that the amino acid sequence does not include the sequence

DIALTQSPASLAVSLGQRATISCRASKSVSTSGYSYLHWYQQKPGQPPKLLIYLASNL
 ESGVPARFSGSGSGTDFTLNIHPVEEEDAATYYCQHSRELPTFGSGTKLEIK (SEQ ID
 NO:28).

The light chain variable region amino acid sequence of this aspect may be referred to herein as “the Modified Light Chain Variable Region Sequence” or the “M.L.C.V.R. Sequence”.

[0046] One aspect of the invention provides a protein, such as an anti-CD45 antibody or CD45 binding antibody fragment such as a Fab, Fab₂ or scFv molecule, including:

(i) a heavy chain variable region including the M.H.C.V.R. Sequence or the parental heavy chain variable region amino sequence disclosed herein; and

(ii) a light chain variable region including the M.L.C.V.R. Sequence or the parental light chain variable region amino sequence disclosed herein,

provided that the protein does not include both the parental heavy chain variable region amino sequence disclosed herein and the parental light chain variable region amino sequence disclosed herein.

[0047] One aspect of the invention provides a protein, such as an anti-CD45 antibody or CD45 binding antibody fragment such as a Fab, Fab₂ or scFv molecule, including:

(i) a heavy chain variable region including the M.H.C.V.R. Sequence; and

(ii) a light chain variable region including the M.L.C.V.R. Sequence.

[0048] One aspect of the invention provides a protein, such as a CD45 binding scFv molecule or a protein including at least one scFv segment, that includes a consecutive (amino to carboxy terminal order) amino acid sequence that includes amino acids 1-120 (the amino

acids through and including the sequence VTVS or corresponding amino acid positions) or amino acids 1-121 of a heavy chain variable region as disclosed herein, followed by a linker amino acid sequence, followed by the amino acid sequence of a light chain variable region disclosed herein, provided that the protein does not include both amino acids 1-120 of the parental heavy chain variable region sequence disclosed herein and the parental light chain variable region sequence disclosed herein. In one variation, the protein does not include either of amino acids 1-120 of the parental heavy chain variable region sequence disclosed herein and the parental light chain variable region sequence disclosed herein.

[0049] The linker amino acid sequence may, for example, include any of the amino acid sequences:

KISGGGSGGGSGGGSGGGSGGGSS (SEQ ID NO:80);

SPNSASHSGSAPQTSSAPGSQ (SEQ ID NO:81);

(G3S)_n where, for example, n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, such as (G3S)₄, i.e.,

GGGSGGGSGGGSGGG (SEQ ID NO:82); or

(G4S)_n, i.e., (GGGGS [SEQ ID NO:83])_n where, for example, n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, such as (G4S)₅, i.e., GGGSGGGSGGGSGGGSGGGSGGGGS, (SEQ ID NO:84).

[0050] The heavy chain variable region and light chain variable regions disclosed herein each include three (3) complementarity determining regions (CDRs). The CDRs are surrounded by immunoglobulin framework regions (FRs) in the following manner: FR1 is the amino acid sequence preceding (N-terminal to) CDR1, FR2 is the amino acid sequence between CDR1 and CDR2, FR3 is the amino acid sequence between CDR2 and CDR3, and FR4 is the amino acid sequence following (C-terminal to) CDR3 to the end of the variable region sequence.

[0051] As used herein, the term “antibody fragment” includes without limitation proteolytic fragments of antibodies, such as Fab or Fab₂ (F(ab')₂) fragments, recombinant antibody fragments with covalently associated or non-covalently associated chains, scFv molecules, and rIgG fragments (“rIgG” refers to reduced IgG (~75,000 daltons)) also known as half-IgG.

[0052] The proteins, such as antibodies and antibody fragments, may, for example, be linked directly or indirectly, via a chemically conjugated chelator, to a radionuclide, for example, to target cytotoxic radiation to CD45-expressing cells in mammalian subject such as a human patient, or to non-cytotoxically image CD45-expression in a mammalian subject such as a human patient. For example, the antibody may be directly labeled with ¹³¹I according to the methods disclosed in U.S. Patent No. 10,420,851 or the antibody may be chemically

conjugated to a chelator, such as p-SCN-DOTA and labeled with a radionuclide ^{225}Ac , according to the procedures described in U.S. Patent No. 9,603,954.

[0053] The radionuclide may, for example, be selected from ^{131}I , ^{125}I , ^{123}I , ^{32}P , ^{213}Po , ^{134}Ce , ^{43}Sc , ^{44}Sc , ^{47}Sc , ^{55}Co , ^{60}Cu , ^{61}Cu , ^{62}Cu , ^{64}Cu , ^{67}Cu , ^{66}Ga , ^{67}Ga , ^{68}Ga , ^{82}Rb , ^{86}Y , ^{87}Y , ^{90}Y , ^{89}Zr , ^{97}Ru , ^{105}Rh , ^{109}Pd , ^{111}In , $^{117\text{m}}\text{Sn}$, ^{149}Pm , ^{149}Tb , ^{161}Tb , ^{153}Sm , ^{177}Lu , ^{186}Re , ^{188}Re , ^{199}Au , ^{201}Tl , ^{137}Cs , ^{223}Ra , ^{203}Pb , ^{212}Pb , ^{211}At , ^{212}Bi , ^{213}Bi , ^{225}Ac , and ^{227}Th .

[0054] The chelator group in the various aspects of the invention may, for example, include: 1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid (DO3A) or a derivative thereof; 1,4,7-triazacyclononane-1,4-diacetic acid (NODA) or a derivative thereof; 1,4,7-triazacyclononane-1,4,7-triacetic acid (NOTA) or a derivative thereof; 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) or a derivative thereof; 1,4,7-triazacyclononane, 1-glutaric acid-4,7-diacetic acid (NODAGA) or a derivative thereof; 1,4,7,10-tetraazacyclodecane, 1-glutaric acid-4,7,10-triacetic acid (DOTAGA) or a derivative thereof; 1,4,8,11-tetraazacyclotetradecane-1,4,8,11-tetraacetic acid (TETA) or a derivative thereof; 1,4,8,11-tetraazabicyclo[6.6.2]hexadecane-4,11-diacetic acid (CB-TE2A) or a derivative thereof; diethylene triamine pentaacetic acid (DTPA), its diester, or a derivative thereof; 2-cyclohexyl diethylene triamine pentaacetic acid (CHX-A"-DTPA) or a derivative thereof; deferoxamine (DFO) or a derivative thereof; 1,2-[[6-carboxypyridin-2-yl]methylamino]ethane (H_2dedpa) or a derivative thereof; DADA or a derivative thereof; 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetra(methylene phosphonic acid) (DOTP) or a derivative thereof; 4-amino-6-[[16-[(6-carboxypyridin-2-yl)methyl]-1,4,10,13-tetraoxa-7,16-diazacyclooctadec-7-yl]methyl]pyridine-2-carboxylic acid (MACROPA- NH_2) or a derivative thereof; MACROPA or a derivative thereof; 1,4,7,10-tetrakis(carbamoylmethyl)-1,4,7,10-tetraazacyclododecane (TCMC) or a derivative thereof; {4-[2-(bis-carboxymethylamino)-ethyl]-7-carboxymethyl-[1,4,7]triazonan-1-yl}-acetic acid (NETA) or a derivative thereof; Diamsar or a derivative thereof; 1,4,7-triazacyclononane-1,4,7-tris[methyl(2-carboxyethyl)phosphinic acid (TRAP, PRP9, TRAP-Pr) or a derivative thereof; N,N' -bis(6-carboxy-2-pyridylmethyl)ethylenediamine- N,N' -diacetic acid (H_4octapa) or a derivative thereof; N,N' -[1-benzyl-1,2,3-triazole-4-yl]methyl- N,N' -[6-(carboxy)pyridin-2-yl]-1,2-diaminoethane (H_2azapa) or a derivative thereof; N,N'' -[[6-(carboxy)pyridin-2-yl]methyl]diethylenetriamine- N,N',N'' -triacetic acid (H_5decapa) or a derivative thereof; N,N' -bis(2-hydroxy-5-sulfobenzyl)ethylenediamine- N,N' -diacetic acid (SHBED) or a derivative thereof; N,N' -bis(2-hydroxybenzyl)ethylenediamine- N,N' -diacetic acid (HBED) or a derivative thereof; 3,6,9,15-tetraazabicyclo[9.3.1]pentadeca-1(15),11,13-triene-3,6,9,-triacetic

acid (PCTA) or a derivative thereof; desferrioxamine B (DFO) or a derivative thereof; N,N'-(methylenephosphonate)-N,N'-[6-(methoxycarbonyl)pyridin-2-yl]methyl-1,2-diaminoethane (H6phospa) or a derivative thereof; 1,4,7,10,13,16-hexaazacyclohexadecane-N,N',N'',N''',N''',N''''-hexaacetic acid (HEHA) or a derivative thereof; 1,4,7,10,13-pentaazacyclopentadecane-N,N',N'',N''',N''''-pentaacetic acid (PEPA) or a derivative thereof; or 3,4,3-LI(1,2-HOPO) or a derivative thereof.

[0055] The proteins, such as antibodies and antibody fragments, may, for example, be linked to one or more cytotoxic drugs to target and deplete CD45-expressing cells in a mammalian subject such as a human patient. Thus, one aspect of the invention provides an antibody-drug-conjugate (ADC) that includes an antibody or antigen-binding antibody fragment according to the invention as a component. The ADC may, for example, be a conjugate with a cytotoxin containing a benzodiazepine moiety, for example, a pyrrolbenzodiazepine (PBD) or an indolinbenzodiazepine (IGN) moiety, as disclosed in U.S. Pub. No. 20220175951.

[0056] The words “comprising” and forms of the word “comprising” as well as the word “including” and forms of the word “including,” as used in this description and in the claims, do not limit the inclusion of elements beyond what is referred to. Additionally, although throughout the present disclosure various aspects or elements thereof are described in terms of “including” or “comprising,” corresponding aspects or elements thereof described in terms of “consisting essentially of” or “consisting of” are similarly disclosed. For example, while certain aspects of the invention have been described in terms of a protein “including” or “comprising” one or more particular amino acid sequences, corresponding aspects instead reciting a protein “consisting essentially of” or “consisting of” the one or more particular amino acid sequences are also within the scope of said aspects and disclosed by this disclosure.

[0057] In addition, compositions including a radiolabeled antibody may include one or more pharmaceutically acceptable carriers or pharmaceutically acceptable excipients. Such carriers are well known to those skilled in the art. For example, injectable drug delivery systems include solutions, suspensions, gels, microspheres and polymeric injectables, and can include excipients such as solubility-altering agents (e.g., ethanol, propylene glycol and sucrose) and polymers (e.g., polycaprylactones and PLGA's). An exemplary formulation may be as substantially described in U.S. Patent 10,420,851 or International Pub. No. WO 2017/155937, incorporated by reference herein. For example, according to certain aspects, the formulation may include 0.5% to 5.0% (w/v) of an excipient selected from the group consisting of ascorbic acid, polyvinylpyrrolidone (PVP), human serum albumin (HSA), a water-soluble salt of HSA,

and mixtures thereof. Certain formulations may include 0.5-5% ascorbic acid; 0.5-4% polyvinylpyrrolidone (PVP); and the monoclonal antibody in 50 mM PBS buffer, pH 7.

[0058] The humanized and various anti-huCD45 antibodies disclosed herein may, for example, be labeled with a radionuclide, such as ^{131}I , ^{177}Lu , ^{211}At , ^{227}Th or ^{225}Ac , or conjugated to a cytotoxic drug, for use as a conditioning agent in preparation of a bone marrow transplant (BMT) or of a hematopoietic stem cell transplant (HSCT), for example, for the treatment of a hematological cancer, or in preparation of administration of a genetically engineered cell therapy such as a CAR-T therapy for the treatment of a cancer, or for use as a direct treatment of a hematological cancer, such as a myeloid or lymphoid hematological cancer, such as a leukemia, for example acute myeloid leukemia (AML), or a lymphoma, for example non-Hodgkin lymphoma (NHL), or for use as an immunological resetting agent in the treatment of an autoimmune disease such as multiple sclerosis. The hematological cancer or disorder treated may, for example, be a leukemia (such as acute myeloid leukemia (AML), acute promyelocytic leukemia, acute lymphoblastic leukemia (ALL), acute mixed lineage leukemia, chronic myeloid leukemia (CML), chronic lymphocytic leukemia (CLL), hairy cell leukemia, or large granular lymphocytic leukemia), myelodysplastic syndrome (MDS), a myeloproliferative disorder (such as polycythemia vera, essential thrombocytosis, primary myelofibrosis or chronic myeloid leukemia), multiple myeloma, MGUS and similar disorders, a lymphoma (such as Hodgkin's lymphoma (HL), non-Hodgkin lymphoma (NHL), primary mediastinal large B-cell lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, transformed follicular lymphoma, splenic marginal zone lymphoma, lymphocytic lymphoma, or T-cell lymphoma), or another B-cell malignancy. In one aspect, the radiolabeled or drug-conjugated anti-huCD45 antibody is administered as a maintenance therapy to a subject who previously received a BMT or HSCT in treatment of a hematological cancer such as AML or another described herein, for example, to treat or to prevent a relapse or recurrence of the cancer. In each case described here, the subject may be a mammal such as a human patient.

[0059] Example 1: Production of a radiolabeled chelator-conjugated anti-huCD45 antibody

[0060] *Conjugation to a chelator:* A vial of lyophilized p-SCN-Bn-DOTA is reconstituted with metal-free water to a concentration of 10 mg/ml. To the actinium reaction vial, 0.02 ml of ascorbic acid solution (150 mg/ml) and 0.05 ml of reconstituted p-SCN-Bn-DOTA are added and the pH adjusted to between 5 and 5.5 with 2M tetramethylammonium acetate (TMAA). The mixture is then heated at $55 \pm 4^\circ\text{C}$ for 30 minutes.

[0061] To determine the labeling efficiency of the ^{225}Ac -p-SCN-Bn-DOTA, an aliquot of the reaction mixture is removed and applied to a 1 ml column of Sephadex C25 cation exchange resin. The product is eluted in 2-4 ml fractions with a 0.9% saline solution. The fraction of ^{225}Ac activity that elutes is ^{225}Ac -p-SCN-Bn-DOTA and the fraction that is retained on the column is un-chelated, unreactive ^{225}Ac . Typically, the labeling efficiency is greater than 95%.

[0062] To the reaction mixture, 0.22 ml of previously prepared anti-CD45 mAb in DTPA (1 mg) and 0.02 ml of ascorbic acid are added. The DTPA is added to bind any trace amounts of metals that may compete with the labeling of the antibody. The ascorbic acid is added as a radio-protectant. The pH is adjusted with carbonate buffer to pH 8.5-9. The mixture is heated at $37 \pm 3^\circ\text{C}$ for 30 minutes.

[0063] The final product may be purified by size exclusion chromatography using 10DG resin and eluted with 2 ml of 1% HSA.

[0064] Radiolabeling: The antibody may be conjugated to a linker, such as any of the linkers described in the above indicated patent applications. An exemplary linker includes at least dodecane tetraacetic acid (DOTA), wherein a goal of the conjugation reaction is to achieve a DOTA-antibody ratio of 3:1 to 5:1. Chelation with the radionuclide, such as ^{177}Lu , ^{90}Y , or ^{225}Ac may then be performed and efficiency and purity of the resulting radiolabeled antibody, such as an anti-CD45 antibody, may be determined by HPLC and iTLC.

[0065] An exemplary labeling reaction for ^{225}Ac is as follows: A reaction including 15 μL 0.15M NH_4OAc buffer, pH=6.5 and 2 μL (10 μg) DOTA-anti-CD45 (5 mg/ml) may be mixed in an Eppendorf reaction tube, and 4 μL ^{225}Ac (10 μCi) in 0.05 M HCl subsequently added. The contents of the tube may be mixed with a pipette tip and the reaction mixture incubated at 37°C for 90 min with shaking at 100 rpm. At the end of the incubation period, 3 μL of a 1mM DTPA solution may be added to the reaction mixture and incubated at room temperature for 20 min to bind the unreacted ^{225}Ac into the ^{225}Ac -DTPA complex. Instant thin layer chromatography with 10cm silica gel strip and 10mM EDTA/normal saline mobile phase may be used to determine the radiochemical purity of ^{225}Ac -DOTA-anti-CD45 through separating ^{225}Ac -labeled anti-CD45 (^{225}Ac -DOTA-anti-CD45) from free ^{225}Ac (^{225}Ac -DTPA). In this system, the radiolabeled antibody stays at the point of application and ^{225}Ac -DTPA moves with the solvent front. The strips may be cut in halves and counted in the gamma counter equipped with the multichannel analyzer using channels 72-110 for ^{225}Ac to exclude its daughters.

[0066] *Purification*: An exemplary radiolabeled targeting agent, such as ^{225}Ac -DOTA-antibody, may be purified either on PD10 columns pre-blocked with 1% HSA or on Vivaspin centrifugal concentrators with a 50 kDa MW cut-off with 2 x 1.5 mL washes, 3 min per spin. HPLC analyses of the ^{225}Ac -DOTA-antibody after purification may be conducted using a Waters HPLC system equipped with flow-through Waters UV and Bioscan Radiation detectors, using a TSK3000SW XL column eluted with PBS at pH=7.4 and a flow rate of 1ml/min.

[0067] Example 2: Radio-iodination of anti-huCD45 antibody and purification in the presence of Ascorbic acid

[0068] Anti-CD45 antibodies may be radio-iodinated according to the following method.

[0069] One mg of an anti-CD45 antibody is labeled with 20 to 30 mCi of ^{131}I —Na (30 mCi) in the presence of chloramine-T (23 micrograms) in PBS buffer (pH 7.2). The reaction is quenched with the addition of aqueous sodium thiosulfate (69 micrograms) and diluted with cold NaI (1 mg). Immediately following, a concentrated ascorbic acid solution made in 50 mM PBS (pH 7) is added to achieve 2.5% (w/v) ascorbic acid strength in the quenched reaction mixture. Labeling reactions up to 3,000 mCi per batch may, for example, be successfully performed using this method.

[0070] The radiolabeled antibody, such as radiolabeled immunoglobulin, can be purified by gel filtration on a sterile, pre-packed commercially available Sephadex G25 column (GE HiPrep 26/10 column, bed volume 53 mL) using PBS (50 mM, pH 7) mobile phase supplemented with 2.5% (w/v) ascorbic acid to stabilize the radiolabeled product. Up to 1,000 mCi reaction volume can be purified on a single column. The product can be collected in a 5 to 35 mL elution volume from the column.

[0071] Radio-iodinated reaction batches of <200 mCi may be purified in a similar fashion on a smaller desalting column (GE PD10 column, bed volume 8.6 mL).

[0072] Example 3: Radio-iodination of anti-CD45 immunoglobulin and purification in the presence of Ascorbic acid and HSA

[0073] The radio-iodination and purification may be performed essentially as described in Example 2, except that 2% or 4% (w/v) HSA is also added along with 2.5% (w/v) ascorbic acid to the quenched reaction as well as in the elution buffer during the purification process.

[0074] While various specific embodiments have been illustrated and described herein, it will be appreciated that various changes can be made without departing from the spirit and scope of the invention(s). Moreover, features described in connection with one aspect of the

invention may be used in conjunction with other aspects of the invention, even if not explicitly exemplified in combination within.

WHAT IS CLAIMED IS:

1. An anti-huCD45 antibody or a huCD45-binding antibody fragment, comprising:
 - (i) an immunoglobulin heavy chain variable region comprising SEQ ID NO:17, SEQ ID NO:7, SEQ ID NO:12, SEQ ID NO:22, or SEQ ID NO:2,; and
 - (ii) an immunoglobulin light chain variable region comprising SEQ ID NO:43, SEQ ID NO:48, SEQ ID NO:33, SEQ ID NO:38, or SEQ ID NO:28,provided that when the heavy chain variable region comprises SEQ ID NO:2, , the light chain variable region is not SEQ ID NO:28.
2. The anti-huCD45 antibody or huCD45-binding antibody fragment of claim 1, comprising:
 - (i) an immunoglobulin heavy chain sequence comprising SEQ ID NO:21, SEQ ID NO:26, SEQ ID NO:11, SEQ ID NO:16, or SEQ ID NO:6; and
 - (ii) an immunoglobulin light chain sequence comprising SEQ ID NO:47, SEQ ID NO:52, SEQ ID NO:37, SEQ ID NO:42, or SEQ ID NO:32.
3. An anti-huCD45 antibody or huCD45-binding antibody fragment, comprising:
 - (a) a set of immunoglobulin heavy chain complementarity determining regions (CDRs) comprising heavy chain CDR1, CDR2 and CDR3 amino acid sequences selected from the following sets:
 - (i) SEQ ID NO:53, SEQ ID NO:58, and SEQ ID NO:55, respectively,
 - (ii) SEQ ID NO:53, SEQ ID NO:56, and SEQ ID NO:55, respectively, and
 - (iii) SEQ ID NO:53, SEQ ID NO:57, and SEQ ID NO:55, respectively; and
 - (b) a set of immunoglobulin light chain complementarity determining regions (CDRs) comprising light chain CDR1, CDR2 and CDR3 amino acid sequences selected from the following sets:
 - (i) SEQ ID NO:59, SEQ ID NO:63, and SEQ ID NO:61, respectively, and
 - (ii) SEQ ID NO:59, SEQ ID NO:64, and SEQ ID NO:61, respectively, and
 - (iii) SEQ ID NO:62, SEQ ID NO:60, and SEQ ID NO:61, respectively.
4. A pharmaceutical composition comprising the antibody or antibody fragment of any one of the preceding claims and at least one pharmaceutically acceptable excipient.
5. A radiopharmaceutical composition comprising:

the antibody or antibody fragment of any one of claims 1-3;
a radionuclide linked to the antibody or antibody fragment, and
at least one pharmaceutically acceptable excipient.

6. The radiopharmaceutical composition of claim 5, wherein the radionuclide is an alpha particle emitter or a beta particle emitter.

7. The radiopharmaceutical composition of claim 5, wherein the radionuclide comprises ¹³¹I.

8. The radiopharmaceutical composition of claim 5, wherein the radionuclide comprises ²²⁵Ac, ¹⁷⁷Lu or ⁹⁰Y.

9. A composition comprising the antibody or antibody fragment of any one of claims 1-3, chemically conjugated to a chelator.

10. The composition of claim 9, wherein the chelator comprises DOTA or a DOTA derivative.

11. The composition of claim 9 or 10, further comprising a radionuclide chelated by the chelator.

12. A protein, such as an anti-CD45 antibody or CD45-binding antibody fragment (such as Fab fragment, Fab₂ fragment, or scFv molecule) or an immunoglobulin light chain, comprising an antibody light chain variable region comprising the following light chain CDRs:

a CDR-L1 comprising the amino acid sequence RASKSVSTSGYSYLH (SEQ ID NO:59), KSSKSVSTSGYSYLH (SEQ ID NO:62), RASKSVSTSGYSYLA (SEQ ID NO:65), RASKSVSTSGYSYLS (SEQ ID NO:66), or RASKSVSTSGYSYLN (SEQ ID NO:67);

a CDR-L2 comprising the amino acid sequence LASNLES (SEQ ID NO:60), LASNLA (SEQ ID NO:68), LASNLAT (SEQ ID NO:63), LASNLQ (SEQ ID NO:69), LASNLQS (SEQ ID NO:64), LASTRES (SEQ ID NO:70), LASTRAT (SEQ ID NO:71), LASNRAT (SEQ ID NO:72), or LASSQLS (SEQ ID NO:73);

a CDR-L3 comprising the amino acid sequence QHSRELPFT (SEQ ID NO:61),

provided that the combination of a CDR-L1 comprising the amino acid sequence RASKSVSTSGYSYLH (SEQ ID NO:59) and CDR-L2 comprising the amino acid sequence LASNLES (SEQ ID NO:60) is excluded.

13. The protein of claim 12, wherein next amino acid residues following the CDR-L3 sequence QHSRELPFT (SEQ ID NO:61) in the protein are FGQ.

14. A protein, such as an anti-CD45 antibody or CD45-binding antibody fragment (such as Fab fragment, Fab₂ fragment, or scFv molecule) or an immunoglobulin heavy chain, comprising an antibody heavy chain variable region comprising the following light chain CDRs:

a CDR-H1 comprising the amino acid sequence GFDFSRYWMS (SEQ ID NO:53) or GFDFSRYWMN (SEQ ID NO:85);

a CDR-H2 comprising the amino acid sequence EINPTSSTINFTPSLKD (SEQ ID NO:54), EINPTSSTINFADSVKG (SEQ ID NO:56), EINPTSSTINYADSVKG (SEQ ID NO:57), EINPTSSTINFVDSVKG (SEQ ID NO:58), YINPTSSTIYYADSVKG (SEQ ID NO:74), AINPTSSTIYYADSVKG (SEQ ID NO:75), NINPTSSTIYYVDSVKG (SEQ ID NO:76), or SINPTSSTIYYADSVKG (SEQ ID NO:77);

a CDR-H3 comprising the amino acid sequence GNYYRYGDAMDY (SEQ ID NO:55), provided that the combination of a CDR-H1 comprising the amino acid sequence GFDFSRYWMS (SEQ ID NO:53) and CDR-H2 comprising the amino acid sequence EINPTSSTINFTPSLKD (SEQ ID NO:54) is excluded.

15. A protein, such as an anti-CD45 antibody or CD45-binding antibody fragment (such as Fab fragment, Fab₂ fragment or scFv molecule), comprising:

(a) an antibody light chain variable region comprising the following light chain CDRs:

a CDR-L1 comprising the amino acid sequence RASKSVSTSGYSYLH (SEQ ID NO:59), KSSKSVSTSGYSYLH (SEQ ID NO:62), RASKSVSTSGYSYLA (SEQ ID NO:65), RASKSVSTSGYSYLS (SEQ ID NO:66), or RASKSVSTSGYSYLN (SEQ ID NO:67);

a CDR-L2 comprising the amino acid sequence LASNLES (SEQ ID NO:60), LASNLA (SEQ ID NO:68), LASNLAT (SEQ ID NO:63), LASNLQ (SEQ ID NO:69), LASNLQS (SEQ ID NO:64)

LASTRES (SEQ ID NO:70), LASTRAT (SEQ ID NO:71), LASNRAT (SEQ ID NO:72), or LASSQLS (SEQ ID NO:73); and

a CDR-L3 comprising the amino acid sequence QHSRELPFT (SEQ ID NO:61); and

(b) an antibody heavy chain variable region comprising the following heavy chain CDRs:

a CDR-H1 comprising the amino acid sequence GFDFSRYWMS (SEQ ID NO:53) or GFDFSRYWMN (SEQ ID NO:85);

a CDR-H2 comprising the amino acid sequence EINPTSSTINFTPSLKD (SEQ ID NO:54), EINPTSSTINFADSVKG (SEQ ID NO:56), EINPTSSTINYADSVKG (SEQ ID NO:57), EINPTSSTINFVDSVKG (SEQ ID NO:58), YINPTSSTIYYADSVKG (SEQ ID NO:74), AINPTSSTIYYADSVKG (SEQ ID NO:75), NINPTSSTIYYVDSVKG (SEQ ID NO:76), or SINPTSSTIYYADSVKG (SEQ ID NO:77); and

a CDR-H3 comprising the amino acid sequence GNYYRYGDAMDY (SEQ ID NO:55), provided that the combination of CDR-L1 comprising the amino acid sequence RASKSVSTSGYSYLH (SEQ ID NO:59), CDR-L2 comprising the amino acid sequence LASNLES (SEQ ID NO:60), CDR-L3 comprising the amino acid sequence QHSRELPFT (SEQ ID NO:61), CDR-H1 comprising the amino acid sequence GFDFSRYWMS (SEQ ID NO:53), CDR-H2 comprising the amino acid sequence EINPTSSTINFTPSLKD (SEQ ID NO:54), and CDR-H3 comprising the amino acid sequence GNYYRYGDAMDY (SEQ ID NO:55) is excluded.

16. The protein of claim 15, wherein next amino acid residues following the CDR-L3 sequence QHSRELPFT (SEQ ID NO:61) in the protein are FGQ.

17. A protein, such as an anti-CD45 antibody or CD45-binding antibody fragment (such as Fab fragment, Fab₂ fragment, or scFv molecule) or an immunoglobulin light chain, comprising an antibody light chain variable region comprising the following light chain CDRs:

a CDR-L1 comprising the amino acid sequence RASKSVSTSGYSYLH (SEQ ID NO:59) or KSSKSVSTSGYSYLH (SEQ ID NO:62);

a CDR-L2 comprising the amino acid sequence LASNLA (SEQ ID NO:68), LASNLAT (SEQ ID NO:63), LASNLQ (SEQ ID NO:69), or LASNLQS (SEQ ID NO:64);

a CDR-L3 comprising the amino acid sequence QHSRELPFT (SEQ ID NO:61).

18. The protein of claim 17, wherein the next amino acid residues following the CDR-L3 sequence QHSRELPFT (SEQ ID NO:61) in the protein are FGQ.

19. A protein, such as an anti-CD45 antibody or CD45-binding antibody fragment (such as Fab fragment, Fab₂ fragment, or scFv molecule) or an immunoglobulin heavy chain, comprising an antibody heavy chain variable region comprising the following heavy chain CDRs:

a CDR-H1 comprising the amino acid sequence GFDFSRYWMS (SEQ ID NO:53);

a CDR-H2 comprising the amino acid sequence EINPTSSTINFADSVKG (SEQ ID NO:56), EINPTSSTINYADSVKG (SEQ ID NO:57), or EINPTSSTINFVDSVKG (SEQ ID NO:58); and

a CDR-H3 comprising the amino acid sequence GNYRYGDAMDY (SEQ ID NO:55).

20. A protein, such as an anti-CD45 antibody or CD45-binding antibody fragment (such as Fab fragment, Fab₂ fragment, or scFv molecule), comprising:

(a) an antibody light chain variable region comprising the following light chain CDRs:

a CDR-L1 comprising the amino acid sequence RASKSVSTSGYSYLH (SEQ ID NO:59) or KSSKSVSTSGYSYLH (SEQ ID NO:62);

a CDR-L2 comprising the amino acid sequence LASNLES (SEQ ID NO:60), LASNLA (SEQ ID NO:68), LASNLAT (SEQ ID NO:63), LASNLQ (SEQ ID NO:69), LASNLQS (SEQ ID NO:64); and

a CDR-L3 comprising the amino acid sequence QHSRELPFT (SEQ ID NO:61); and

(b) an antibody heavy chain variable region comprising the following heavy chain CDRs:

a CDR-H1 comprising the amino acid sequence GFDFSRYWMS (SEQ ID NO:53);

a CDR-H2 comprising the amino acid sequence EINPTSSTINFTPSLKD (SEQ ID NO:54), EINPTSSTINFADSVKG (SEQ ID NO:56), EINPTSSTINYADSVKG (SEQ ID NO:57), or EINPTSSTINFVDSVKG (SEQ ID NO:58); and

a CDR-H3 comprising the amino acid sequence GNYRYGDAMDY (SEQ ID NO:55), provided that the combination of CDR-L1 comprising the amino acid sequence RASKSVSTSGYSYLH (SEQ ID NO:59), CDR-L2 comprising the amino acid sequence LASNLES (SEQ ID NO:60), CDR-L3 comprising the amino acid sequence QHSRELPFT (SEQ ID NO:61), CDR-H1 comprising the amino acid sequence GFDFSRYWMS (SEQ ID NO:53), CDR-H2 comprising the amino acid sequence EINPTSSTINFTPSLKD (SEQ ID

NO:54), and CDR-H3 comprising the amino acid sequence GNYRYGDAMDY (SEQ ID NO:55) is excluded.

21. The protein of claim 20, wherein the next amino acid residues following the CDR-L3 sequence QHSRELPFT (SEQ ID NO:61) in the protein are FGQ.

22. The protein of claim 20 or 21, wherein the CDR-H2 comprises the amino acid sequence EINPTSSTINFADSVKG (SEQ ID NO:56), EINPTSSTINYADSVKG (SEQ ID NO:57), or EINPTSSTINFVDSVKG (SEQ ID NO:58).

23. An immunoglobulin heavy chain variable region or a protein, such as an anti-CD45 antibody or CD45 binding antibody fragment such as a Fab, Fab₂ or scFv molecule, comprising an immunoglobulin heavy chain variable region sequence that comprises one or more of the amino acid substitutions disclosed in any of the non-parental immunoglobulin heavy chain variable regions disclosed herein versus the parental immunoglobulin heavy chain variable region disclosed herein, in any combination, but otherwise comprises the same amino acid sequence as the parental immunoglobulin heavy chain variable region sequence.

24. An immunoglobulin light chain variable region or a protein, such as an anti-CD45 antibody or CD45 binding antibody fragment such as a Fab, Fab₂ or scFv molecule, comprising an immunoglobulin light chain variable region that comprises one or more of the amino acid substitutions disclosed in any of the non-parental immunoglobulin light chain variable regions disclosed herein versus the parental immunoglobulin light chain variable region disclosed herein, in any combination, but otherwise comprises the same amino acid sequence as the parental immunoglobulin light chain variable region sequence.

25. A protein, such as an anti-CD45 antibody or CD45 binding antibody fragment such as a Fab, Fab₂ or scFv molecule, comprising:

(i) an immunoglobulin heavy chain variable region that comprises one or more of the amino acid substitutions disclosed in any of the non-parental immunoglobulin heavy chain variable regions disclosed herein versus the parental immunoglobulin heavy chain variable region disclosed herein, in any combination, but otherwise comprises the same amino acid sequence as the parental immunoglobulin heavy chain variable region sequence; and

(ii) an immunoglobulin light chain variable region that comprises one or more of the amino acid substitutions disclosed in any of the non-parental immunoglobulin light chain variable regions disclosed herein versus the parental immunoglobulin light chain variable region disclosed herein, in any combination, but otherwise comprises the same amino acid sequence as the parental immunoglobulin light chain variable region sequence.

26. A protein, such as an anti-CD45 antibody or CD45 binding antibody fragment such as a Fab, Fab₂ or scFv molecule, comprising:

- (i) the parental immunoglobulin heavy chain variable region disclosed herein, or
an immunoglobulin heavy chain variable region that comprises one or more of the amino acid substitutions disclosed in any of the non-parental immunoglobulin heavy chain variable regions disclosed herein versus the parental immunoglobulin heavy chain variable region disclosed herein, in any combination, but otherwise comprises the same amino acid sequence as the parental immunoglobulin heavy chain variable region sequence; and
 - (ii) the parental immunoglobulin light chain variable region disclosed herein, or
an immunoglobulin light chain variable region that comprises one or more of the amino acid substitutions disclosed in any of the non-parental immunoglobulin light chain variable regions disclosed herein versus the parental immunoglobulin light chain variable region disclosed herein, in any combination, but otherwise comprises the same amino acid sequence as the parental immunoglobulin heavy chain variable region sequence
- provided that the protein does not comprise both the parental immunoglobulin heavy chain variable region disclosed herein and the parental immunoglobulin light chain variable region disclosed herein.

27. An immunoglobulin heavy chain variable region or a protein, such as an anti-CD45 antibody or CD45 binding antibody fragment such as a Fab, Fab₂ or scFv molecule, comprising an immunoglobulin heavy chain variable region sequence that comprises the amino acid sequence:

EVKLLESGGGLVQPGGSLKLSCAASGFDFSRYWMX₁WVRQAPGKGLEWX₂X₃X₄INP
TSSTIX₅X₆X₇X₈SLKX₉X₁₀X₁₁X₁₂ISRDNX₁₃KNX₁₄LYLQMSX₁₅X₁₆RX₁₇EDTAX₁₈YYCA
RGNYRYGDAMDYWGQGTGX₁₉VTVSS (SEQ ID NO:78)

wherein

X₁ is S or N,

X₂ is I or V,

X₃ is G, S or A,

X₄ is E, Y, A, N, or S,

X₅ is N or Y,

X₆ is F or Y,

X₇ is T, A, or V,

X₈ is P or D,

X₉ is D or G,

X₁₀ is K or R,

X₁₁ is V or F,

X₁₂ is F or T,

X₁₃ is A or S,

X₁₄ is T or S,

X₁₅ is K or S,

X₁₆ is V or L,

X₁₇ is S or A

X₁₈ is L or V, and

X₁₉ is S or M,

provided that the amino acid sequence does not comprise the sequence

EVKLLESGGGLVQPGGSLKLSCAASGFDFSRYWMSWVRQAPGKGLEWIGEINPTSST
INFTPSLKDKVFISRDNAKNTLYLQMSKVRSEDTALYYCARGNYYRYGDAMDYWG
QGTSVTTVSS (SEQ ID NO:2).

28. An immunoglobulin light chain variable region or a protein, such as an anti-CD45 antibody or CD45 binding antibody fragment such as a Fab, Fab₂ or scFv molecule, comprising an immunoglobulin light chain variable region sequence that comprises the amino acid sequence:

DIX_{L1}X_{L2}TQSPX_{L3}X_{L4}LX_{L5}X_{L6}SX_{L7}GX_{L8}RX_{L9}TX_{L10}X_{L11}CX_{L12}X_{L13}SKSVSTSGYSYLX_{L14}
WYQQKPGQX_{L15}PX_{L16}LLIYLASX_{L17}X_{L18}X_{L19}X_{L20}GX_{L21}PX_{L22}RFSGSGSGTDFTLX_{L23}IX_{L24}X_{L25}X_{L26}X_{L27}X_{L28}EDX_{L29}AX_{L30}YYCQHSRELPFTFGX_{L31}GTKLEIK (SEQ ID NO:79)

wherein

X_{L1} is D or E,

X_{L2} is A or V or Q,

X_{L3} is L or M,

X_{L4} is A or D or S,

X_{L5} is S or T,
X_{L6} is A or S,
X_{L7} is V or L or A,
X_{L8} is L or P or V,
X_{L9} is Q or E or D,
X_{L10} is A or V,
X_{L11} is I or L,
X_{L12} is S or N or T,
X_{L13} is A or S,
X_{L14} is H, A, S, or N,
X_{L15} is P or A,
X_{L16} is K or R,
X_{L17} is N or T or S,
X_{L18} is L or R,
X_{L19} is E or A or Q,
X_{L20} is S or T,
X_{L21} is V or I,
X_{L22} is A or D or S,
X_{L23} is N or T,
X_{L24} is H or S,
X_{L25} is P or S,
X_{L26} is V or L,
X_{L27} is E or Q,
X_{L28} is E or A or P,
X_{L29} is A or V or F,
X_{L30} is T or V,
X_{L31} is S or Q, and
X_{L32} is R or K

provided that the amino acid sequence does not comprise the sequence

DIALTQSPASLAVSLGQRATISCRASKSVSTSGYSYLHWYQQKPGQPPKLLIYLASNL
ESGVPARFSGSGSGTDFTLNHPVEEEDAATYYCQHSRELPFTFGSGTKLEIK (SEQ ID
NO:28).

29. A protein, such as an anti-CD45 antibody or CD45 binding antibody fragment such as a Fab, Fab₂ or scFv molecule, comprising:

- (i) a heavy chain variable region comprising the M.H.C.V.R. Sequence or the parental heavy chain variable region amino sequence disclosed herein; and
 - (ii) a light chain variable region comprising the M.L.C.V.R. Sequence or the parental light chain variable region amino sequence disclosed herein,
- provided that the protein does not comprise both the parental heavy chain variable region amino sequence disclosed herein and the parental light chain variable region amino sequence disclosed herein.

30. The protein of claim 29, comprising:

- (i) a heavy chain variable region comprising the M.H.C.V.R. Sequence; and
- (ii) a light chain variable region comprising the M.L.C.V.R. Sequence.

31. A protein, such as a CD45 binding scFv molecule or a protein including at least one scFv segment, that includes a consecutive (amino to carboxy terminal order) amino acid sequence that includes amino acids 1-120 (the amino acids through and including the sequence VTVS or corresponding amino acid positions) or amino acids 1-121 of a heavy chain variable region as disclosed herein, followed by a linker amino acid sequence, followed by the amino acid sequence of a light chain variable region disclosed herein, provided that the protein does not include both amino acids 1-120 of the parental heavy chain variable region sequence disclosed herein and the parental light chain variable region sequence disclosed herein.

32. The protein of claim 31, wherein the protein includes amino acids 1-120 (the amino acids through and including the sequence VTVS or corresponding amino acid positions) of a heavy chain variable region as disclosed herein and not amino acids 1-121 of the heavy chain variable region as disclosed herein.

33. The protein of claim 31 or 32, wherein the protein does not include either of amino acids 1-120 of the parental heavy chain variable region sequence disclosed herein and the parental light chain variable region sequence disclosed herein.

34. The protein of any one of claims 31-33, wherein the linker amino acid sequence includes:

KISGGGSGGGSGGGSGGGSGGGSGGGSS (SEQ ID NO:80);

SPNSASHSGSAPQTSSAPGSQ (SEQ ID NO:81);

(G3S)_n wherein n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10; or

(G4S)_n wherein n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10.

35. A pharmaceutical composition comprising a protein according to any one of claims 12-34.

36. The pharmaceutical composition of claim 35, further comprising at least one pharmaceutically acceptable excipient.

37. The pharmaceutical composition of claim 35 or 36, wherein at least a fraction of the protein in the composition is radiolabeled or conjugated with a cytotoxic drug.

38. The pharmaceutical composition of any one of claims 35-37, for the treatment of a hematological cancer or solid tumor cancer in a mammalian subject.

39. The composition of any one of claims 4-8 and 35-38, for use as a conditioning agent in preparation of a bone marrow transplant (BMT), a hematopoietic stem cell transplant (HSCT), or administration of a genetically modified cell therapy, such as CAR-T cell therapy, in a mammalian subject.

40. The pharmaceutical composition of claim 38 or 39, wherein the mammalian subject is a human patient.

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mAb chain ID: m CD45-HC parental

(hHeavy-m CD45-HC parental; Human IgG1 (G1m17))

Signal peptide: MDPKGSLSWRILLFLSLAFELSYG (SEQ ID NO:1)Heavy chain variable region:

EVKLL ESGGGLVQPGGSLKLSCAASGFDFSRYWMSWVRQAPGKGLEWIGEINPTSSTIN
 FTPSLKDKVFISRDNAKNTLYLQMSKVRSEDTALYYCARGNYYRYGDAMDYWGQGTST
 VTVSS (SEQ ID NO:2)

CDR_{H1}: GFDFSRYWMS (SEQ ID NO:53), CDR_{H2}: EINPTSSTINFTPSLKD (SEQ ID NO:54),
CDR_{H3}: GNYRYGDAMDY (SEQ ID NO:55)

1st Residue: A Heavy chain constant region with 1st Residue: SEQ ID NO:4Heavy chain constant region:

STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG
 LYSLSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
 NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
 EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDK
 SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:3)

Full length heavy chain including signal peptide:

MDPKGSLSWRILLFLSLAFELSYGEVKLL ESGGGLVQPGGSLKLSCAASGFDFSRYWMS
 WVRQAPGKGLEWIGEINPTSSTINFTPSLKDKVFISRDNAKNTLYLQMSKVRSEDTALYY
 CARGNYYRYGDAMDYWGQGTSTVTSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKD
 YFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNVNHKPSN
 TKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
 EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVS
 NKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN
 GQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLS
 LSPG (SEQ ID NO:5)

Full length heavy chain without signal peptide: (SEQ ID NO:6)**FIG. 1**

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mAb chain ID: hu CD45.HC1

(hHeavy-hu CD45.HC1; Human IgG1 (G1m17))

Signal peptide: MDPKGSLSWRILLFLSLAFELSYG (SEQ ID NO:1)Heavy chain variable region:

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRYWMSWVRQAPGKGLEWVSEINPTSSTIN
FADSVKGRFFISRDNAKNSLYLQMNSLRAEDTAVYYCARGNYRYGDAMDYWGQGT
 MVTVSS (SEQ ID NO:7)

CDR_{H1}: GFDFSRYWMS (SEQ ID NO:53), CDR_{H2}: EINPTSSTINFADSVKG (SEQ ID NO:56), CDR_{H3}: GNYRYGDAMDY (SEQ ID NO:55)

1st Residue: A Heavy chain constant region with 1st Residue: SEQ ID NO:9Heavy chain constant region:

STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG
 LYSLSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
 NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
 EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
 SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:8)

Full length heavy chain including signal peptide:

MDPKGSLSWRILLFLSLAFELSYGEVQLVESGGGLVQPGGSLRLSCAASGFDFSRYWMS
WVRQAPGKGLEWVSEINPTSSTINFADSVKGRFFISRDNAKNSLYLQMNSLRAEDTAVY
 YCARGNYRYGDAMDYWGQGTMTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVK
 DYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNVNHKPS
 NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
 HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV
 SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES
 NGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
 SLSPG (SEQ ID NO:10)

Full length heavy chain without signal peptide: SEQ ID NO:11**FIG. 2**

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mAb chain ID: hu CD45.HC2

(hHeavy-hu CD45.HC2; Human IgG1 (G1m17))

Signal peptide: MDPKGSLSWRILLFLSLAFELSYG (SEQ ID NO:1)Heavy chain variable region:EVQLLESGGGLVQPGGSLRLSCAASGFD¹FSRYWMSWVRQAPGKGLEWVSEINPTSSTIN
YADSVKGRFTISRDN²SKNTLYLQMNSLRAEDTAVYYCARGNYYRYGDAMDYWGQGT
MVTVSS (SEQ ID NO:12)CDR_{H1}: GFD¹FSRYWMS (SEQ ID NO:53), CDR_{H2}: EINPTSSTINYADSVKGRFTISRDN²SKNTLYLQMNSLRAEDTAVYYCARGNYYRYGDAMDY (SEQ ID NO:57), CDR_{H3}: GNYRYRYGDAMDY (SEQ ID NO:55)1st Residue: A Heavy chain constant region with 1st Residue: (SEQ ID NO:14)Heavy chain constant region:STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVT³SWNSGALTSGVHTFPAVLQSSG
LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGP
SVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:13)Full length heavy chain including signal peptide:MDPKGSLSWRILLFLSLAFELSYGEVQLLESGGGLVQPGGSLRLSCAASGFD¹FSRYWMS
WVRQAPGKGLEWVSEINPTSSTINYADSVKGRFTISRDN²SKNTLYLQMNSLRAEDTAVY
YCARGNYYRYGDAMDYWGQGTMTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVK
DYFPEPVT³SWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPS
NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDV
SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV
SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES
NGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS
LSLSPG (SEQ ID NO:15)Full length heavy chain without signal peptide: SEQ ID NO:16**FIG. 3**

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mAb chain ID: hu CD45.HC3

(hHeavy-hu CD45.HC3; Human IgG1 (G1m17))

Signal peptide: MDPKGSLSWRILLFLSLAFELSYG (SEQ ID NO:1)Heavy chain variable region:

EVQLVESGGGLVQPGGSLRLSCAASGFDFSRYWMSWVRQAPGKGLEWVAEINPTSSTI
NFVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARGNYRYGDAMDYWGQG
 TMVTVSS (SEQ ID NO:17)

CDR_{H1}: GFDFSRYWMS (SEQ ID NO:53), CDR_{H2}: EINPTSSTINFVDSVKG (SEQ ID NO:58), CDR_{H3}: GNYRYGDAMDY (SEQ ID NO:55)

1st Residue: A Heavy chain constant region with 1st Residue: SEQ ID NO:19

Heavy chain constant region:

STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG
 LYSLSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
 NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
 EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
 SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:18)

Full length heavy chain including signal peptide:

MDPKGSLSWRILLFLSLAFELSYGEVQLVESGGGLVQPGGSLRLSCAASGFDFSRYWMS
WVRQAPGKGLEWVAEINPTSSTINFVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVY
 YCARGNYRYGDAMDYWGQGTMTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVK
 DYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNVNHKPS
 NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
 HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV
 SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES
 NGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS
 LSLSPG (SEQ ID NO:20)

Full length heavy chain without signal peptide: SEQ ID NO:21

FIG. 4

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mAb chain ID: hu CD45.HC4

(hHeavy-hu CD45.HC4; Human IgG1 (G1m17))

Signal peptide: MDPKGSLSWRILLFLSLAFELSYG (SEQ ID NO:1)Heavy chain variable region:

EVQLVESGGGLVKPGGSLRLSCAASGFDFSRYWMSWVRQAPGKGLEWVSEINPTSSTIN
YADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARGNYYRYGDAMDYWGQGT
 MVTVSS (SEQ ID NO:22)

CDR_{H1}: GFDFSRYWMS (SEQ ID NO:53), CDR_{H2}: EINPTSSTINYADSVKG (SEQ ID
 NO:57), CDR_{H3}: GNYYRYGDAMDY (SEQ ID NO:55)

1st Residue: A Heavy chain constant region with 1st Residue: SEQ ID NO:24Heavy chain constant region:

STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG
 LYSLSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGP
 SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY
 NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR
 EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
 SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG (SEQ ID NO:23)

Full length heavy chain including signal peptide:

MDPKGSLSWRILLFLSLAFELSYGEVQLVESGGGLVKPGGSLRLSCAASGFDFSRYWMS
WVRQAPGKGLEWVSEINPTSSTINYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVY
 YCARGNYYRYGDAMDYWGQGTMTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVK
 DYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSVVTVPSSSLGTQTYICNVNHKPS
 NTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
 HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV
 SNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWES
 NGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS
 LSLSPG (SEQ ID NO:25)

Full length heavy chain without signal peptide: SEQ ID NO:26**FIG. 5**

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mAb chain ID: m CD45-LC parental

(hKappa-m CD45-LC parental; Human Kappa)

Signal peptide:

METDTLLLWVLLLWVPGSTG (SEQ ID NO:27)

Light chain variable region:

DIALTQSPASLAVSLGQRATISCRASKSVSTSGYSYLHWYQQKPGQPPKLLIYLASNLES
GVPARFSGSGSGTDFTLNIHPVEEEDAATYYCQHSRELPFTFGSGTKLEIK
(SEQ ID NO:28)

CDR_{L1}: RASKSVSTSGYSYLH (SEQ ID NO:59)CDR_{L2}: LASNLES (SEQ ID NO:60)CDR_{L3}: QHSRELPFT (SEQ ID NO:61)1st Residue: R Light chain constant region with 1st Residue: SEQ ID NO:30Light chain constant region:

TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD
SKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:29)

Full length light chain including signal peptide:

METDTLLLWVLLLWVPGSTGDIALTQSPASLAVSLGQRATISCRASKSVSTSGYSYLHW
YQQKPGQPPKLLIYLASNLESGVPARFSGSGSGTDFTLNIHPVEEEDAATYYCQHSRELP
FTFGSGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ
SGNSQESVTEQDSKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
(SEQ ID NO:31)

Full length light chain without signal peptide: SEQ ID NO:32**FIG. 6**

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mAb chain ID: hu CD45.LC1

(hKappa-hu CD45.LC1; Human Kappa)

Signal peptide:

METDTLLLWVLLLWVPGSTG (SEQ ID NO:27)

Light chain variable region:

DIVMTQSPDSLAVSLGERATINCKSSKSVSTSGYSYLHWYQQKPGQPPKLLIYLASNLES
GVPDRFSGSGSGTDFTLTISLQAEDVAVYYCQHSRELPFTFGQGTKLEIK
(SEQ ID NO:33)

CDR_{L1}: KSSKSVSTSGYSYLH (SEQ ID NO:62)CDR_{L2}: LASNLES (SEQ ID NO:60)CDR_{L3}: QHSRELPFT (SEQ ID NO:61)1st Residue: R Light chain constant region with 1st Residue: SEQ ID NO:35Light chain constant region:

TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD
SKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:34)

Full length light chain including signal peptide:

METDTLLLWVLLLWVPGSTGDIVMTQSPDSLAVSLGERATINCKSSKSVSTSGYSYLHW
YQQKPGQPPKLLIYLASNLESGVPDRFSGSGSGTDFTLTISLQAEDVAVYYCQHSRELP
FTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNAL
QSGNSQESVTEQDSKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGE
C (SEQ ID NO:36)

Full length light chain without signal peptide: SEQ ID NO:37**FIG. 7**

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mAb chain ID: hu CD45.LC2

(hKappa-hu CD45.LC2; Human Kappa)

Signal peptide:

METDTLLLWVLLLWVPGSTG (SEQ ID NO:27)

Light chain variable region:EIVMTQSPATLSLSPGERATLSCRASKSVSTSGYSYLHWYQQKPGQAPRLLIYLASNLAT
GIPARFSGSGSGTDFTLTISLQPEDFAVYYCQHSRELPFTFGQGTKLEIK (SEQ ID NO:38)CDR_{L1}: RASKSVSTSGYSYLH (SEQ ID NO:59)CDR_{L2}: LASNLAT (SEQ ID NO:63)CDR_{L3}: QHSRELPFT (SEQ ID NO:61)1st Residue: R Light chain constant region with 1st Residue: SEQ ID NO:40Light chain constant region:TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD
SKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:39)Full length light chain including signal peptide:METDTLLLWVLLLWVPGSTGEIVMTQSPATLSLSPGERATLSCRASKSVSTSGYSYLHW
YQQKPGQAPRLLIYLASNLATGIPARFSGSGSGTDFTLTISLQPEDFAVYYCQHSRELPF
TFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ
SGNSQESVTEQDSKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
(SEQ ID NO:41)Full length light chain without signal peptide: SEQ ID NO:42**FIG. 8**

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mAb chain ID: hu CD45.LC3

(hKappa-hu CD45.LC3; Human Kappa)

Signal peptide:

METDTLLLWVLLLWVPGSTG (SEQ ID NO:27)

Light chain variable region:EIVLTQSPATLSLSPGERATLSCRASKSVSTSGYSYLHWYQQKPGQAPRLLIYLASNLAT
GIPARFSGSGSGTDFTLTSSLEPEDFAVYYCQHSRELPFTFGQGTKLEIK (SEQ ID
NO:43)CDR_{L1}: RASKSVSTSGYSYLH (SEQ ID NO:59)CDR_{L2}: LASNLAT (SEQ ID NO:63)CDR_{L3}: QHSRELPFT (SEQ ID NO:61)1st Residue: R Light chain constant region with 1st Residue: SEQ ID NO:45Light chain constant region:TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD
SKDSTYLSSTLTLSKADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:44)Full length light chain including signal peptide:METDTLLLWVLLLWVPGSTGEIVLTQSPATLSLSPGERATLSCRASKSVSTSGYSYLHW
YQQKPGQAPRLLIYLASNLATGIPARFSGSGSGTDFTLTSSLEPEDFAVYYCQHSRELPF
TFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ
SGNSQESVTEQDSKDSTYLSSTLTLSKADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC
(SEQ ID NO:46)Full length light chain without signal peptide: SEQ ID NO:47**FIG. 9**

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mAb chain ID: hu CD45.LC4

(hKappa-hu CD45.LC4; Human Kappa)

Signal peptide:

METDTLLLWVLLLWVPGSTG (SEQ ID NO:27)

Light chain variable region:DIQMTQSPSSLSASVGDRVTITCRASKSVSTSGYSYLHWYQQKPGKAPKLLIYLASNLS
GVPSRFGSGSGTDFTLTISLQPEDFATYYCQHSRELPFTFGQGTKLEIK (SEQ ID
NO:48)CDR_{L1}: RASKSVSTSGYSYLH (SEQ ID NO:59)CDR_{L2}: LASNLQS (SEQ ID NO:64)CDR_{L3}: QHSRELPFT (SEQ ID NO:61)1st Residue: R Light chain constant region with 1st Residue: SEQ ID NO:50Light chain constant region:TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQD
SKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:49)Full length light chain including signal peptide:METDTLLLWVLLLWVPGSTGDIQMTQSPSSLSASVGDRVTITCRASKSVSTSGYSYLHW
YQQKPGKAPKLLIYLASNLSGVPSRFGSGSGTDFTLTISLQPEDFATYYCQHSRELPF
TFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQ
SGNSQESVTEQDSKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
(SEQ ID NO:51)Full length light chain without signal peptide: SEQ ID NO:52**FIG. 10**