

can be removed (e.g., cleaved) by one or more molecules (e.g., proteases) that are present in a cancer cell environment. Removal of the masking agent restores the ability of the anti-CD47 antibodies or the antigen-binding fragments thereof to bind CD47, thus enabling specific targeting of the anti-CD47 antibodies or the antigen-binding fragments thereof to the CD47 protein in the context of cancer cells.

[006] In one example, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds human CD47, wherein the antibody or antigen-binding fragment comprising a light chain variable region and a heavy chain variable region, wherein the heavy chain variable region comprises HCDR1 selected from SEQ ID NOs: 16, 19, 21, and 23; HCDR2 selected from SEQ ID NOs: 17, 20, 22, and 24; and HCDR3 of SEQ ID NO: 18; wherein the light chain variable region comprises LCDR1 selected from SEQ ID NOs: 31 and 34; LCDR2 selected from SEQ ID NOs: 32 and 35; and LCDR3 selected from SEQ ID NOs: 33 and 36; wherein the heavy chain variable region comprises an amino acid sequence with at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to an amino acid sequence selected from SEQ ID NOs: 2, 3, 4, 5, 6, 7 and 8; and wherein the light chain variable region comprises an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to an amino acid sequence selected from SEQ ID NOs: 10, 11, 12, 13, 14 and 15.

[006a] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds human CD47, the antibody or antigen-binding fragment comprising a light chain variable region and a heavy chain variable region, wherein the heavy chain variable region comprises HCDR1 selected from SEQ ID NOs: 16, 19, 21, and 23; HCDR2 selected from SEQ ID NOs: 17, 20, 22, and 24; and HCDR3 of SEQ ID NO: 18; wherein the light chain variable region comprises LCDR1 selected from SEQ ID NOs: 31 and 34; LCDR2 selected from SEQ ID NOs: 32 and 35; and LCDR3 selected from SEQ ID NOs: 33 and 36; wherein the heavy chain variable region comprises an amino acid sequence with at least 97% identity to an amino acid sequence selected from SEQ ID NOs: 3, 4, 5, 6, 7 and 8; and wherein the light chain variable region comprises an amino acid sequence with at least 85% identity to an amino acid sequence selected from SEQ ID NOs: 11, 12, 13, 14 and 15.

[007] In one example, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds human CD47, the antibody or antigen-binding fragment comprising a light chain variable region and a heavy chain variable region, wherein the heavy chain variable region comprises HCDR1 selected from SEQ ID NOs: 16, 19, 21, and 23; HCDR2 selected from SEQ ID NOs: 17, 20, 22, and 24; and HCDR3 of SEQ ID NO: 18; wherein the light chain variable region comprises LCDR1 selected from SEQ ID NOs: 31 and 34; LCDR2 selected from SEQ ID NOs: 32 and 35; and LCDR3 selected from SEQ ID NOs: 33 and 36; wherein the heavy chain variable region comprises:

- a) a human IGHV3-23/HJ4 framework set forth in SEQ ID NO: 88, wherein framework positions H44, H49, H82, H89, H91, and H94 are donor residues, according to Kabat numbering; or
- b) a human IGHV3-48/HJ4 framework set forth in SEQ ID NO: 89, wherein framework position H49 is a donor residue, according to Kabat numbering; or
- c) a human IGHV3-66/HJ4 framework set forth in SEQ ID NO: 90, wherein framework position H29, H49, and H82 is a donor residue, according to Kabat numbering; or
- d) a human IGHV3-74/HJ4 framework set forth in SEQ ID NO: 91, wherein framework position H49 is a donor residue, according to Kabat numbering; and

wherein the light chain variable region comprises:

- a) a human IGKV6-21/KJ2 framework set forth in SEQ ID NO: 92, wherein framework positions L4, L21, L69, and L85 are donor residues, according to Kabat numbering; or
- b) a human IGKV1-27/KJ2 framework set forth in SEQ ID NO: 93, wherein framework positions L21, L49, and L69 are donor residues, according to Kabat numbering.

[008] In some examples, the heavy chain variable region comprises HCDR1, HCDR2, and HCDR3 selected from: SEQ ID NOs: 16, 17, and 18; SEQ ID NOs: 19, 20, and 18; SEQ ID NOs: 21, 22, and 18; SEQ ID NOs: 16, 20, and 18; and SEQ ID NOs: 23, 24, and 18. In some examples, the light chain variable region comprises LCDR1, LCDR2, and LCDR3 selected from SEQ ID NOs: 31, 32, and 33; SEQ ID NOs: 31, 32, and 36; and SEQ ID NOs: 34, 35, and 33. In some examples, the antibody or antigen-binding fragment thereof comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 selected from SEQ ID NOs: 16, 17, 18, 31, 32, and 33; SEQ ID NOs: 16, 17, 18, 34, 35, and 33; SEQ ID NOs: 19, 20, 18, 31, 32, and 33; SEQ ID NOs: 19, 20, 18, 34, 35, and 33; SEQ ID NOs: 21, 22, 18, 31, 32, and 33; SEQ ID NOs: 21, 22, 18, 34, 35, and 33; SEQ ID NOs: 16, 20, 18, 31, 32, and 33; SEQ ID NOs: 16, 20, 18, 34, 35, and 33; SEQ ID NOs: 23, 24, 18, 31, 32, and 33; SEQ ID NOs: 23, 24, 18, 34, 35, and 33; SEQ ID NOs: 16, 17, 18, 31, 32, and 36; SEQ ID NOs: 19, 20, 18, 31, 32, and 36; SEQ ID NOs: 21, 22, 18, 31, 32, and 36; 16, 20, 18, 31, 32, and 36; and SEQ ID NOs: 23, 24, 18, 31, 32, and 36.

[009] In one example, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds human CD47, the antibody or antigen-binding fragment comprising a light chain variable region and a heavy chain variable region, wherein the heavy chain variable region comprises HCDR1 selected from SEQ ID NOs: 25, 28, and 29; HCDR2 selected from SEQ ID NOs: 26 and 30; and HCDR3 of SEQ ID NO: 27; and wherein the light chain variable region comprises LCDR1 selected from SEQ ID NOs: 37 and 40; LCDR2 of SEQ ID NO: 38; and LCDR3 selected from SEQ ID NOs: 39 and 41; wherein the heavy chain variable region comprises an amino acid sequence with at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to an amino acid sequence selected from SEQ ID NOs: 2, 3, 4, 5, 6, 7 and 8; and wherein the light chain variable region comprises an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to an amino acid sequence selected from SEQ ID NOs: 10, 11, 12, 13, 14 and 15.

[010] In one example, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds human CD47, the antibody or antigen-binding fragment comprising a light chain variable region and a heavy chain variable region, wherein the heavy chain variable

[012] In some examples, the heavy chain variable region comprises an amino acid sequence selected from SEQ ID NOs: 2, 3, 4, 5, 6, 7 and 8. In some examples, the light chain variable region comprises an amino acid sequence selected from SEQ ID NOs: 10, 11, 12, 13, 14 and 15. In some examples, the heavy chain variable region and light chain variable region comprise SEQ ID NOs: 2 and 10; SEQ ID NOs: 3 and 11; SEQ ID NOs: 3 and 12; SEQ ID NOs: 3 and 13; SEQ ID NOs: 3 and 14; SEQ ID NOs: 4 and 11; SEQ ID NOs: 4 and 12; SEQ ID NOs: 4 and 13; SEQ ID NOs: 4 and 14; SEQ ID NOs: 5 and 11; SEQ ID NOs: 5 and 12; SEQ ID NOs: 5 and 13; SEQ ID NOs: 5 and 14; SEQ ID NOs: 6 and 11; SEQ ID NOs: 6 and 12; SEQ ID NOs: 6 and 13; SEQ ID NOs: 6 and 14; SEQ ID NOs: 7 and 11; SEQ ID NOs: 7 and 12; SEQ ID NOs: 7 and 13; SEQ ID NOs: 7 and 14; SEQ ID NOs: 8 and 11; SEQ ID NOs: 8 and 12; SEQ ID NOs: 8 and 13; SEQ ID NOs: 8 and 14; SEQ ID NOs: 3 and 15.

[013] In one example, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds human CD47, the antibody or antigen-binding fragment comprising a light chain variable region and a heavy chain variable region, wherein the heavy chain variable region comprises HCDR1 of SEQ ID NO: 16, HCDR2 of SEQ ID NO: 17, and HCDR3 of SEQ ID NO: 18; and wherein the light chain variable region comprises LCDR1 of SEQ ID NO: 31, LCDR2 of SEQ ID NO: 32, and LCDR3 of SEQ ID NO: 33; and wherein the heavy chain variable region comprises an amino acid sequence with at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 3 and the light chain variable region comprises an amino acid sequence with at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 13; and wherein the antibody has reduced hemagglutination of red blood cells compared to Ab47. In some examples, the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 3 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 13.

[013a] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds human CD47, the antibody or antigen-binding fragment comprising a light chain variable region and a heavy chain variable region, wherein the heavy chain variable region comprises HCDR1 of SEQ ID NO: 16, HCDR2 of SEQ ID NO: 17, and HCDR3 of SEQ ID NO: 18; and wherein the light chain variable region comprises LCDR1 of SEQ ID NO: 31, LCDR2 of SEQ ID NO: 32, and LCDR3 of SEQ ID NO: 33; and wherein the heavy chain variable region comprises an amino acid sequence with at least 95% identity to SEQ ID NO: 3 and the light chain variable region comprises an amino acid sequence with at least 85% identity to SEQ ID NO: 13; and wherein the antibody has reduced hemagglutination of red blood cells compared to Ab47 comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 2 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 10.

[014] In some examples of the humanized antibody or antigen-binding fragment thereof provided herein, the heavy chain variable region comprises:

- a) a human IGHV3-23/HJ4 framework set forth in SEQ ID NO: 88, wherein framework positions H44, H49, H82, H89, H91, and H94 are donor residues, according to Kabat numbering; or
- b) a human IGHV3-48/HJ4 framework set forth in SEQ ID NO: 89, wherein framework position H49 is a donor residue, according to Kabat numbering; or
- c) a human IGHV3-66/HJ4 framework set forth in SEQ ID NO: 90, wherein framework position H29, H49, and H82 is a donor residue, according to Kabat numbering; or

- d) a human IGHV3-74/HJ4 framework set forth in SEQ ID NO: 91, wherein framework position H49 is a donor residue, according to Kabat numbering.

In some such examples, H29 is F, H44 is R or G, H49 is A, H82 is M or I, H89 is I or V, H91 is F or Y, and H94 is R, according to Kabat numbering.

[015] In some examples of the humanized antibody or antigen-binding fragment thereof provided herein, the light chain variable region comprises:

- a) a human IGKV6-21/KJ2 framework set forth in SEQ ID NO: 92, wherein framework positions L4, L21, L69, and L85 are donor residues, according to Kabat numbering; or
- b) a human IGKV1-27/KJ2 framework set forth in SEQ ID NO: 93, wherein framework positions L21, L49, and L69 are donor residues, according to Kabat numbering.

In some such examples, L4 is M, L21 is L, L49 is K, L69 is T or S, and L85 is V or T, according to Kabat numbering.

[016] In some examples, the antibody or antigen-binding fragment thereof is of an IgG1 isotype. In some examples, the antibody or antigen-binding fragment thereof has enhanced antibody dependent cellular cytotoxicity (ADCC) compared to its parental antibody. In some examples, the antibody or antigen-binding fragment thereof has enhanced antibody dependent cellular phagocytosis (ADCP) compared to its parental antibody. In some examples, the antibody or antigen-binding fragment thereof has enhanced complement-dependent cytotoxicity (CDC) compared to its parental antibody. In some examples, the antibody or antigen-binding fragment thereof is a Fab, a Fab', a F(ab')₂, a Fv fragment, a diabody, a single-chain antibody, an scFv fragment or an scFv-Fc. In some examples, the antibody or antigen-binding fragment thereof induces apoptosis of CD47-expressing cells *in vitro* and/or *in vivo*. In some examples, the antibody or antigen-binding fragment thereof has reduced core fucosylation compared to its parental antibody. In some examples, the antibody or antigen-binding fragment thereof is afucosylated. In some examples, the antibody or antigen-binding fragment thereof blocks an interaction between CD47 and SIRP α . In some examples, the antibody or antigen-binding fragment thereof has reduced hemagglutination of red blood cells compared to Ab47.

[017] In one aspect, the present disclosure refers to a nucleic acid sequence encoding the antibody or antigen-binding fragment thereof provided herein. In one example, the present disclosure refers to an expression vector comprising the nucleic acid sequence. In one aspect, the present disclosure refers to an expression vector comprising the nucleic acid provided herein. In one example, the present disclosure refers to a host cell comprising the nucleic acid or the expression vector. In one aspect, the present disclosure refers to a host cell comprising the nucleic acid provided herein. In one aspect, the present disclosure refers to a host cell that expresses the antibody or antigen-binding fragment thereof provided herein. In one aspect, the present disclosure refers to a method of producing an antibody or antigen-binding fragment thereof

comprising culturing the host cell provided herein. In some examples, the method further comprises isolating the antibody or antigen-binding fragment thereof.

[018] In some examples, methods of treating a CD47-expressing cancer in a subject are provided, comprising administering to the subject a therapeutically effective amount of an anti-CD47 antibody or antigen-binding fragment thereof provided herein. In one example, the present disclosure refers to use of the anti-CD47 antibody or antigen-binding fragment provided herein in the manufacture of a medicament for treating a CD47-expressing cancer in a subject.

[019] In some examples, methods of treating a CD47-expressing cancer in a subject are provided, comprising:

- a) identifying a subject as having a CD47-expressing cancer; and
- b) administering to the subject a therapeutically effective amount of an anti-CD47 antibody or antigen-binding fragment thereof provided herein.

In one example, the present disclosure refers to use of the anti-CD47 antibody or antigen-binding fragment thereof provided herein in the manufacture of a medicament for treating a CD47-expressing cancer in a subject, wherein the use comprises identifying the subject as having a CD47-expressing cancer.

In some such examples, step a) or the use comprises:

- i) isolating cancer tissue; and
- ii) detecting CD47 in the isolated cancer tissue.

[020] In some examples, methods for treating a CD47-expressing cancer in a subject are provided, comprising:

- a) identifying a subject as having elevated levels of macrophage infiltration in cancer tissue relative to non-cancer tissue; and
- b) administering to the subject a therapeutically effective amount of an anti-CD47 antibody or antigen-binding fragment thereof provided herein.

In one example, the present disclosure refers to use of the anti-CD47 antibody or antigen-binding fragment thereof provided herein in the manufacture of a medicament for treating a CD47-expressing cancer in a subject, wherein the use comprises identifying the subject as having elevated levels of macrophage infiltration in cancer tissue relative to non-cancer tissue.

In some such examples, step a) or the use comprises:

- i) isolating cancer tissue and surrounding non-cancer tissue from the subject;
- ii) detecting macrophages in the isolated cancer tissue and in non-cancer tissue; and
- iii) comparing the amount of staining in the cancer tissue relative to the non-cancer tissue. In some examples, the macrophage staining is performed with an anti-CD163 antibody.

[021] In some examples, methods of treating cancer comprise identifying a subject as having a CD47-expressing cancer and elevated levels of macrophage infiltration in cancer tissue relative to non-cancer tissue.

[022] In some examples, a method of inducing apoptosis of a CD47-expressing cell is provided, comprising contacting the cell with an antibody or antigen-binding fragment thereof provided herein. In some examples, the cell is *in vitro*. In some examples, the cell is *in vivo*. In one example, the present disclosure refers to an *in vitro* method of inducing apoptosis of a CD47-expressing cell comprising contacting the cell with an antibody or antigen-binding fragment thereof provided herein. In one example, the present disclosure refers to use of an antibody or antigen-binding fragment thereof provided herein in the manufacture of a medicament for inducing apoptosis of a CD47-expressing cell *in vivo*.

[023] In one example, the present disclosure refers to a masked antibody comprising an antibody or antigen-binding fragment thereof that specifically binds to the human CD47 protein and at least one masking domain, wherein at least one masking domain comprises an amino acid sequence selected from SEQ ID NOs: 44-55, 75-86, 94, and 95. In one example, the present disclosure refers to a masked antibody

comprises a heavy chain linked to a first masking domain and having the amino acid sequence of SEQ ID NO: 42 and a light chain linked to a second masking domain and having the amino acid sequence of SEQ ID NO: 43.

[028] In one example, the present disclosure refers to a nucleic acid sequence encoding a masked antibody provided herein. In one example, the present disclosure refers to an expression vector comprising the nucleic acid. In one example, the present disclosure refers to a host cell comprising the nucleic acid or the expression vector. In one example, the present disclosure refers to a host cell that expresses the masked antibody provided herein. In one example, the present disclosure refers to a method of producing the masked antibody provided herein comprises culturing the host cell. In some examples, the method further comprises isolating the masked antibody.

[029] In some examples, methods of treating a CD47-expressing cancer in a subject are provided, comprising administering to the subject a therapeutically effective amount of a masked antibody provided herein. In one example, the present disclosure refers to use of the masked antibody provided herein in the manufacture of a medicament for treating a CD47-expressing cancer in a subject.

[030] In some examples, methods for treating a CD47-expressing cancer in a subject are provided, comprising:

a) identifying a subject as having elevated levels of MMP in the cancer relative to surrounding non-cancer tissue; and

b) administering to the subject a therapeutically effective amount of a masked antibody provided herein, wherein each masking domain of the masked antibody comprises a protease-cleavable linker and wherein the protease-cleavable linker comprises a matrix metalloprotease (MMP) cleavage site. In one example, the present disclosure refers to use of the masked antibody provided herein in the manufacture of a medicament for treating a CD47-expressing cancer in a subject, wherein the use comprises identifying the subject as having elevated levels of MMP in the cancer relative to surrounding non-cancer tissue, wherein each masking domain of the masked antibody comprises a protease-cleavable linker and wherein the protease-cleavable linker comprises a matrix metalloprotease (MMP) cleavage site. In some examples, the MMP cleavage site is selected from an MMP2 cleavage site, an MMP7 cleavage site, an MMP9 cleavage site and an MMP13 cleavage site. In some examples, the MMP is selected from MMP2, MMP7, MMP9, and MMP13. In some examples, step a) or the use comprises:

i) isolating cancer tissue and non-cancer tissue from the subject;
ii) detecting MMPs in the isolated cancer tissue and the non-cancer tissue; and
iii) comparing the amount of staining in the cancer tissue relative to the non-cancer tissue.

[031] In some examples, methods for treating a CD47-expressing cancer in a subject are provided, comprising:

a) identifying a subject as having a CD47-expressing cancer; and

b) administering to the subject a therapeutically effective amount of a masked antibody provided herein.

In one example, the present disclosure refers to use of a masked antibody provided herein in the manufacture of a medicament for treating a CD47-expressing cancer in a subject, wherein the use comprises identifying the subject as having a CD47-expressing cancer.

In some examples, step a) or the use comprises:

i) isolating cancer tissue; and

ii) detecting CD47 in the isolated cancer tissue.

[032] In some examples, methods for treating a CD47-expressing cancer in a subject are provided, comprising:

- a) identifying a subject as having elevated levels of macrophage infiltration in cancer tissue relative to non-cancer tissue; and
- b) administering to the subject a therapeutically effective amount of a masked antibody provided herein.

In one example, the present disclosure refers to use of the masked antibody provided herein in the manufacture of a medicament for treating a CD47-expressing cancer in a subject, wherein the use comprises identifying the subject as having elevated levels of macrophage infiltration in cancer tissue relative to non-cancer tissue.

In some examples, step a) or the use comprises:

- i) isolating cancer tissue and surrounding non-cancer tissue from the subject;
- ii) detecting macrophages in the isolated cancer tissue and in non-cancer tissue; and
- iii) comparing the amount of staining in the cancer tissue relative to the non-cancer tissue. In some examples, the macrophage staining is performed with an anti-CD163 antibody.

[033] In some examples, methods for treating a CD47-expressing cancer in a subject are provided, comprising identifying a subject as having (a) elevated levels of MMP in the cancer relative to surrounding non-cancer tissue, and (b) a CD47-expressing cancer. In some examples, methods for treating a CD47-expressing cancer in a subject are provided, comprising identifying a subject as having (a) elevated levels of MMP in the cancer relative to surrounding non-cancer tissue, and (b) elevated levels of macrophage infiltration in cancer tissue relative to non-cancer tissue. In some examples, methods for treating a CD47-expressing cancer in a subject are provided, comprising identifying a subject as having (a) a CD47-expressing cancer, and (b) elevated levels of macrophage infiltration in cancer tissue relative to non-cancer tissue. In some examples, methods for treating a CD47-expressing cancer in a subject are provided, comprising identifying a subject as having (a) elevated levels of MMP in the cancer relative to surrounding non-cancer tissue, (b) a CD47-expressing cancer, and (c) elevated levels of macrophage infiltration in cancer tissue relative to non-cancer tissue.

[034] In some examples, the masked antibody comprises at least one masking domain comprising a protease-cleavable linker, and wherein the protease-cleavable linker is cleaved in the tumor microenvironment. In some examples, following cleavage of the protease-cleavable linker in the tumor microenvironment, the masking domain is released from the anti-CD47 antibody or antigen-binding fragment thereof. In some examples, the protease-cleavable linker comprises the amino acid sequence IPVSLRSG (SEQ ID NO: 73) or GPLGVR (SEQ ID NO: 57). In some examples, the protease-cleavable linker comprises a MMP cleavage site. In some examples, the MMP cleavage site is selected from an MMP2 cleavage site, an MMP7 cleavage site, an MMP9 cleavage site and an MMP13 cleavage site. In some examples, following release of the anti-CD47 antibody or antigen-binding fragment thereof, the anti-CD47 antibody or antigen-binding fragment thereof has a stub amino acid remnant of the protease-

CLAIMS

What is claimed:

1. A humanized antibody or antigen-binding fragment thereof that specifically binds human CD47, the antibody or antigen-binding fragment comprising a light chain variable region and a heavy chain variable region, wherein the heavy chain variable region comprises HCDR1 selected from SEQ ID NOs: 16, 19, 21, and 23; HCDR2 selected from SEQ ID NOs: 17, 20, 22, and 24; and HCDR3 of SEQ ID NO: 18; wherein the light chain variable region comprises LCDR1 selected from SEQ ID NOs: 31 and 34; LCDR2 selected from SEQ ID NOs: 32 and 35; and LCDR3 selected from SEQ ID NOs: 33 and 36; wherein the heavy chain variable region comprises an amino acid sequence with at least 97% identity to an amino acid sequence selected from SEQ ID NOs: 3, 4, 5, 6, 7 and 8; and wherein the light chain variable region comprises an amino acid sequence with at least 85% identity to an amino acid sequence selected from SEQ ID NOs: 11, 12, 13, 14 and 15.

2. The humanized antibody or antigen-binding fragment thereof of claim 1, wherein the heavy chain variable region comprises HCDR1, HCDR2, and HCDR3 selected from: SEQ ID NOs: 16, 17, and 18; SEQ ID NOs: 19, 20, and 18; SEQ ID NOs: 21, 22, and 18; SEQ ID NOs: 16, 20, and 18; and SEQ ID NOs: 23, 24, and 18.

3. The humanized antibody or antigen-binding fragment thereof of claim 1, wherein the light chain variable region comprises LCDR1, LCDR2, and LCDR3 selected from SEQ ID NOs: 31, 32, and 33; SEQ ID NOs: 31, 32, and 36; and SEQ ID NOs: 34, 35, and 33.

4. The humanized antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment thereof comprises HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 selected from SEQ ID NOs: 16, 17, 18, 31, 32, and 33; SEQ ID NOs: 16, 17, 18, 34, 35, and 33; SEQ ID NOs: 19, 20, 18, 31, 32, and 33; SEQ ID NOs: 19, 20, 18, 34, 35, and 33; SEQ ID NOs: 21, 22, 18, 31, 32, and 33; SEQ ID NOs: 21, 22, 18, 34, 35, and 33; SEQ ID NOs: 16, 20, 18, 31, 32, and 33; SEQ ID NOs: 16, 20, 18, 34, 35, and 33; SEQ ID NOs: 23, 24, 18, 31, 32, and 33; SEQ ID NOs: 23, 24, 18, 34, 35, and 33; SEQ ID NOs: 16, 17, 18, 31, 32, and 36; SEQ ID NOs: 19, 20, 18, 31, 32, and 36; SEQ ID NOs: 21, 22, 18, 31, 32, and 36; 16, 20, 18, 31, 32, and 36; and SEQ ID NOs: 23, 24, 18, 31, 32, and 36.

5. The humanized antibody or antigen-binding fragment thereof of claim 1, wherein the heavy chain variable region comprises an amino acid sequence selected from SEQ ID NOs: 3, 4, 5, 6, 7 and 8.

6. The humanized antibody or antigen-binding fragment thereof of claim 1, wherein the light chain variable region comprises an amino acid sequence selected from SEQ ID NOs: 11, 12, 13, 14 and 15.

7. The humanized antibody or antigen-binding fragment thereof of claim 1, wherein the heavy chain variable region and light chain variable region comprise SEQ ID NOs: 3 and 11; SEQ ID NOs: 3 and 12; SEQ ID NOs: 3 and 13; SEQ ID NOs: 3 and 14; SEQ ID NOs: 4 and 11; SEQ ID NOs: 4 and 12; SEQ ID NOs: 4 and 13; SEQ ID NOs: 4 and 14; SEQ ID NOs: 5 and 11; SEQ ID NOs: 5 and 12; SEQ ID NOs: 5 and 13; SEQ ID NOs: 5 and 14; SEQ ID NOs: 6 and 11; SEQ ID NOs: 6 and 12; SEQ ID NOs: 6 and 13; SEQ ID NOs: 6 and 14; SEQ ID NOs: 7 and 11; SEQ ID NOs: 7 and 12; SEQ ID NOs: 7 and 13; SEQ ID NOs: 7 and 14; SEQ ID NOs: 8 and 11; SEQ ID NOs: 8 and 12; SEQ ID NOs: 8 and 13; SEQ ID NOs: 8 and 14; or SEQ ID NOs: 3 and 15.

8. A humanized antibody or antigen-binding fragment thereof that specifically binds human CD47, the antibody or antigen-binding fragment comprising a light chain variable region and a heavy chain variable region, wherein the heavy chain variable region comprises HCDR1 of SEQ ID NO: 16, HCDR2 of SEQ ID NO: 17, and HCDR3 of SEQ ID NO: 18; and wherein the light chain variable region comprises LCDR1 of SEQ ID NO: 31, LCDR2 of SEQ ID NO: 32, and LCDR3 of SEQ ID NO: 33; and wherein the heavy chain variable region comprises an amino acid sequence with at least 95% identity to SEQ ID NO: 3 and the light chain variable region comprises an amino acid sequence with at least 85% identity to SEQ ID NO: 13; and wherein the antibody has reduced hemagglutination of red blood cells compared to Ab47 comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 2 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 10.

9. The humanized antibody or antigen-binding fragment thereof of claim 8, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 3 and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 13.

10. A nucleic acid sequence encoding the antibody or antigen-binding fragment thereof of claim 1.

11. An expression vector comprising the nucleic acid of claim 10.

12. A host cell comprising the nucleic acid of claim 10.

13. A host cell that expresses the antibody or antigen-binding fragment thereof of claim 1.

14. A method of producing an antibody or antigen-binding fragment thereof comprising culturing the host cell of claim 12.

15. A method of producing an antibody or antigen-binding fragment thereof comprising culturing the host cell of claim 13.

16. A nucleic acid sequence encoding the antibody or antigen-binding fragment thereof of claim 4.

17. An expression vector comprising the nucleic acid of claim 16.
18. A host cell comprising the nucleic acid of claim 16.
19. A host cell that expresses the antibody or antigen-binding fragment thereof of claim 4.
20. A method of producing an antibody or antigen-binding fragment thereof comprising culturing the host cell of claim 18.
21. A method of producing an antibody or antigen-binding fragment thereof comprising culturing the host cell of claim 19.
22. A nucleic acid sequence encoding the antibody or antigen-binding fragment thereof of claim 8.
23. An expression vector comprising the nucleic acid of claim 22.
24. A host cell comprising the nucleic acid of claim 22.
25. A host cell that expresses the antibody or antigen-binding fragment thereof of claim 8.
26. A method of producing an antibody or antigen-binding fragment thereof comprising culturing the host cell of claim 24.
27. A method of producing an antibody or antigen-binding fragment thereof comprising culturing the host cell of claim 25.
28. A nucleic acid sequence encoding the antibody or antigen-binding fragment thereof of claim 9.
29. An expression vector comprising the nucleic acid of claim 28.
30. A host cell comprising the nucleic acid of claim 29.
31. A host cell that expresses the antibody or antigen-binding fragment thereof of claim 9.
32. A method of producing an antibody or antigen-binding fragment thereof comprising culturing the host cell of claim 30.
33. A method of producing an antibody or antigen-binding fragment thereof comprising culturing the host cell of claim 31.