

CLAIMS

1. An antibody or an antigen-binding fragment thereof that specifically binds to CD47, wherein the antibody comprises:
- 5 an HCDR1 comprising or consisting of a sequence set forth in SEQ ID NO: 5;
- an HCDR2 comprising or consisting of a sequence set forth in SEQ ID NO: 6;
- an HCDR3 comprising or consisting of a sequence set forth in SEQ ID NO: 7;
- 10 an LCDR1 comprising or consisting of an amino acid sequence set forth in SEQ ID NO: 8;
- an LCDR2 comprising or consisting of an amino acid sequence set forth in SEQ ID NO: 9; and
- 15 an LCDR3 comprising or consisting of a sequence set forth in SEQ ID NO: 10;
- and the antibody comprises a heavy chain variable region comprising or consisting of:
- an amino acid sequence set forth in SEQ ID NO: 12, or
- 20 a sequence having at least 88% sequence identity to the sequence set forth in SEQ ID NO: 12; and
- a light chain variable region comprising or consisting of:
- an amino acid sequence set forth in SEQ ID NO: 14, or
- a sequence having at least 88% sequence identity to the sequence set forth in SEQ ID NO: 14.
- 25 forth in SEQ ID NO: 14.
2. The antibody or the antigen-binding fragment thereof according to claim 1, wherein the antibody further comprises a combination of FRs in a heavy chain variable region and FRs in a light chain variable region selected from the group consisting of the
- 30 following:

the FRs in the heavy chain variable region include FR-H1, FR-H2, FR-H3 and FR-H4, wherein the FR-H1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 31; the FR-H2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 32; the FR-H3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 33; and the FR-H4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 34; and

the FRs in the light chain variable region include FR-L1, FR-L2, FR-L3 and FR-L4, wherein the FR-L1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 35; the FR-L2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 36; the FR-L3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 37; and the FR-L4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 38.

3. The antibody or the antigen-binding fragment thereof according to claim 1 or 2, wherein the antibody comprises:

a heavy chain variable region comprising or consisting of
an amino acid sequence set forth in SEQ ID NO: 12; and
a light chain variable region comprising or consisting of
an amino acid sequence set forth in SEQ ID NO: 14.

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4. The antibody or the antigen-binding fragment thereof according to any one of claims 1–3, wherein the antibody further comprises a heavy chain constant region and a light chain constant region, and the constant regions are derived from species other than murine.

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5. The antibody or the antigen-binding fragment thereof according to any one of claims 1–3, wherein the constant regions are derived from a human antibody.

6. The antibody or the antigen-binding fragment thereof according to any one of claims 1–3, wherein the constant regions are derived from a human IgG or IgM.

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7. The antibody or the antigen-binding fragment thereof according to any one of claims 1–3, wherein the constant regions are derived from IgG1 or IgG4.
- 5 8. The antibody or the antigen-binding fragment thereof according to any one of claims 1–3, wherein the heavy chain constant region is represented by SEQ ID NO: 58 or SEQ ID NO: 56; the light chain constant region is represented by SEQ ID NO: 57.
9. The antibody or the antigen-binding fragment thereof according to any one of
10 claims 1–8, wherein the antibody comprises a combination of a heavy chain and a light chain selected from the group consisting of the following:
- (1) a heavy chain set forth in SEQ ID NO: 59 and a light chain set forth in SEQ ID NO: 60; and
 - (2) a heavy chain set forth in SEQ ID NO: 65 and a light chain set forth in
15 SEQ ID NO: 66.
10. The antibody or the antigen-binding fragment thereof according to any one of claims 1–9, wherein the antibody further comprises an amino acid mutation introduced at position 234 and/or 235 according to the EU numbering system.
- 20 11. The antibody or the antigen-binding fragment thereof according to any one of claims 1–10, wherein the antibody comprises mutation L234A and/or L235A according to the EU numbering system.
- 25 12. The antibody or the antigen-binding fragment thereof according to any one of claims 1–11, wherein the antigen-binding fragment is selected from Fab, Fab', F(ab')₂, Fv, Fab/c, complementarity determining region (CDR) fragment, single chain antibody, and bivalent antibody.

13. The antibody or the antigen-binding fragment thereof according to any one of claims 1–11, wherein the antigen-binding fragment is scFv.
14. The antibody or the antigen-binding fragment thereof according to any one of
5 claims 1–13, wherein the antibody is a humanized antibody, a chimeric antibody or a multispecific antibody.
15. The antibody or the antigen-binding fragment thereof according to any one of claims 1–13, wherein the antibody is a bispecific antibody.
- 10 16. The antibody or the antigen-binding fragment thereof according to any one of claims 1–15, wherein the antibody binds to human CD47 protein with a KD less than 10^{-5} M, e.g., less than 10^{-6} M, 10^{-7} M, 10^{-8} M, 10^{-9} M or 10^{-10} M or less.
- 15 17. The antibody or the antigen-binding fragment thereof according to any one of claims 1–15, wherein the antibody binds to human CD47 protein with an EC50 less than 100 nM, e.g., less than 10 nM, 1 nM, 0.9 nM, 0.8 nM, 0.7 nM, 0.6 nM, 0.5 nM, 0.4 nM, 0.3 nM, 0.2 nM, or 0.1 nM or less.
- 20 18. An isolated polynucleotide encoding the antibody or the antigen-binding fragment thereof according to any one of claims 1-17.
19. The isolated polynucleotide according to claim 18, wherein
the polynucleotide molecule comprises or consists of a nucleotide sequence set
25 forth in SEQ ID NO: 11; and
a nucleotide sequence set forth in SEQ ID NO: 13.
20. A vector, comprising the polynucleotide molecule according to claim 18 or 19.

21. A host cell, comprising the polynucleotide molecule according to claim 18 or 19 or the vector according to claim 20.
22. A method for preparing the antibody or the antigen-binding fragment thereof according to any one of claims 1–17, comprising: culturing the host cell according to claim 21 in a suitable condition, and isolating the antibody or the antigen-binding fragment thereof from the cell cultures.
23. An antibody conjugate, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1–17 and a conjugated moiety coupled thereto, wherein the conjugated moiety is a purification tag, a cytotoxic agent or a detectable label.
24. The antibody conjugate according to claim 23, wherein the conjugated moiety is a radioisotope, a luminescent substance, a His tag, a colored substance, an enzyme or polyethylene glycol.
25. A multispecific antibody, preferably a bispecific antibody, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1–17, and an antibody or an antigen-binding fragment against another antigen and/or another antigenic epitope.
26. A fusion protein, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1–17.
27. A kit, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1–17, or the antibody conjugate according to claim 23 or 24, the multispecific antibody according to claim 25 or the fusion protein according to claim 26.

28. The kit according to claim 27, further comprising a second antibody that specifically identifies the antibody or the antigen-binding fragment thereof.
29. The kit according to claim 28, wherein the second antibody further comprises a detectable label, such as a radioisotope, a luminescent substance, a colored substance, an enzyme or polyethylene glycol.
30. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1–17, the antibody conjugate according to claim 23 or 24, the multispecific antibody according to claim 25 or the fusion protein according to claim 26 in detecting the presence or level of human CD47 in a sample, or in preparing a kit for detecting the presence or level of human CD47 in a sample.
31. A pharmaceutical composition, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1–17, the antibody conjugate according to claim 23 or 24, the multispecific antibody according to claim 25 or the fusion protein according to claim 26, and optionally, a pharmaceutically acceptable carrier and/or excipient.
32. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1–17, the antibody conjugate according to claim 23 or 24, the multispecific antibody according to claim 25 or the fusion protein according to claim 26 in preparing:
a medicament for blocking cellular response mediated by the binding of human SIRP α to CD47, or
a medicament for treating a tumor expressing CD47.
33. Use according to claim 32, wherein the tumor is cancer.

34. Use according to claim 33, wherein the tumor is a hematological malignancy or a solid tumor.
35. Use according to claim 34, wherein the tumor is lymphoma, colon cancer or breast cancer.
36. Use according to claim 35, wherein the tumor is non-Hodgkin lymphoma.
37. Use according to claim 35, wherein the tumor is B cell lymphoma cells.
38. The use according to claim 32, wherein the medicament is in a form suitable for injection, preferably in a form suitable for administration by subcutaneous injection, intradermal injection, intravenous injection, intramuscular injection or intralesional injection.
39. An *in vitro* method, comprising administering a cell comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1–17, the antibody conjugate according to claim 23 or 24, the multispecific antibody according to claim 25 or the fusion protein according to claim 26, wherein the method is selected from:
- a method for blocking the binding of CD47 to human SIRP α ,
 - a method for blocking the activity of human CD47 or down-regulating the level of human CD47, and
 - a method for blocking cellular response mediated by the binding of human SIRP α to CD47.