

CLAIMS

What is claimed is:

1. An antibody, or antigen-binding fragment thereof, that binds to human CD47, comprising a variable heavy chain (VH) and a variable light chain (VL), wherein:
 - a) the VH comprises
 - a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 48,
 - a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 65,
 - a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 82; and
 - b) the VL comprises
 - a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 99,
 - a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 116, and
 - a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 133.
2. The antibody, or antigen-binding fragment thereof, of claim 1, wherein the VH comprises the amino acid sequence of SEQ ID NO: 27, and/or the VL comprises the amino acid sequence of SEQ ID NO: 28.
3. The antibody, or antigen-binding fragment thereof, of claim 1 or claim 2, wherein the antibody comprises a first polypeptide comprising a light chain comprising the VL, wherein the first polypeptide comprises the amino acid sequence of SEQ ID NO: 140.
4. The antibody of any one of claims 1-3, wherein the antibody comprises a human IgG4 Fc region.
5. The antibody of any one of claims 1-4, wherein the antibody comprises a second polypeptide comprising a heavy chain comprising, from N terminus to C terminus, the VH and a human IgG4 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 141.
6. The antibody of any one of claims 1-5, wherein the antibody comprises a first polypeptide comprising a light chain comprising the VL, wherein the first polypeptide comprises the amino acid sequence of SEQ ID NO: 140; and a second polypeptide comprising a heavy chain comprising, from N terminus to C terminus, the VH and a human

IgG4 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 141.

7. The antibody of any one of claims 1-3, wherein the antibody comprises a human IgG1 Fc region.

8. The antibody of any one of claims 1-3 and 7, wherein the antibody comprises a second polypeptide comprising a heavy chain comprising, from N terminus to C terminus, the VH and a human IgG1 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 145.

9. The antibody of any one of claims 1-3, 7, and 8, wherein the antibody comprises a first polypeptide comprising a light chain comprising the VL, wherein the first polypeptide comprises the amino acid sequence of SEQ ID NO: 140; and a second polypeptide comprising a heavy chain comprising, from N terminus to C terminus, the VH and a human IgG1 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 145.

10. The antibody of any one of claims 1-3 and 7, wherein the antibody comprises a second polypeptide comprising a heavy chain comprising, from N terminus to C terminus, the VH and a human IgG1 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 147.

11. The antibody of any one of claims 1-3, 7, and 10, wherein the antibody comprises a first polypeptide comprising a light chain comprising the VL, wherein the first polypeptide comprises the amino acid sequence of SEQ ID NO: 140; and a second polypeptide comprising a heavy chain comprising, from N terminus to C terminus, the VH and a human IgG1 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 147.

12. A masked antibody, comprising:

(a) a masking peptide comprising, from N terminus to C terminus, a masking moiety (MM) and a linkage moiety (LM), and

(b) a target binding moiety (TBM) comprising an antibody heavy chain variable region (VH) and an antibody light chain variable region (VL), wherein the TBM binds to human CD47;

wherein the masking peptide is linked to the N terminus of the VH or the VL; and wherein:

1) the VH comprises:

- a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 48,
- a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 65,
- a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 82; and

2) the VL comprises

- a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 99,
- a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 116, and
- a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 133.

13. The masked antibody of claim 12, wherein the MM comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 197-200.

14. The masked antibody of claim 12 or claim 13, wherein the MM comprises an amino acid sequence of SEQ ID NO: 137.

15. The masked antibody of any one of claims 12-14, wherein the LM comprises a cleavable moiety (CM) comprising at least one cleavage site, and wherein the activatable antibody has a higher binding affinity to human CD47 *in vitro* upon cleavage of the CM than before the cleavage of the CM.

16. The masked antibody of claim 15, wherein the cleavage site is a protease cleavage site for a protease selected from the group consisting of urokinase-type plasminogen activator (uPA), matrix metalloproteinase-1 (MMP-1), MMP-2, MMP-3, MMP-8, MMP-9, MMP-14, Tobacco Etch Virus (TEV) protease, plasmin, Thrombin, Factor X, PSA, PSMA, Cathepsin D, Cathepsin K, Cathepsin S, ADAM10, ADAM12, ADAMTS, Caspase-1, Caspase-2, Caspase-3, Caspase-4, Caspase-5, Caspase-6, Caspase-7, Caspase-8, Caspase-9, Caspase-10, Caspase-11, Caspase-12, Caspase-13, Caspase-14, and TACE.

17. The masked antibody of claim 15 or claim 16, wherein the CM comprises an MMP-9 cleavage site that is cleavable by MMP-9.
18. The masked antibody of any one of claims 15-17, wherein the CM comprises the amino acid sequence of SEQ ID NO: 138.
19. The masked antibody of any one of claims 12-18, wherein the masking peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 139 and 152-166.
20. The masked antibody of any one of claims 12-19, wherein the masking peptide comprises the amino acid sequence of SEQ ID NO: 139.
21. The masked antibody of any one of claims 12-20, wherein the VH comprises the amino acid sequence of SEQ ID NO: 27, and/or the VL comprises the amino acid sequence of SEQ ID NO: 28.
22. The masked antibody of any one of claims 12-21, wherein the antibody comprises a first polypeptide comprising a light chain comprising the VL, wherein the first polypeptide comprises the amino acid sequence of SEQ ID NO: 140.
23. The masked antibody of any one of claims 12-22, wherein the antibody comprises a human IgG4 Fc region.
24. The masked antibody of any one of claims 12-23, wherein the antibody comprises a second polypeptide comprising a heavy chain comprising, from N terminus to C terminus, the VH and a human IgG4 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 141.
25. The masked antibody of any one of claims 12-24, wherein the antibody comprises a first polypeptide comprising a light chain comprising the VL, wherein the first polypeptide comprises the amino acid sequence of SEQ ID NO: 140; and a second polypeptide comprising a heavy chain comprising, from N terminus to C terminus, the VH and a human

IgG4 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 141.

26. The masked antibody of any one of claims 12-22, wherein the antibody comprises a human IgG1 Fc region.

27. The masked antibody of any one of claims 12-22 and 26, wherein the antibody comprises a second polypeptide comprising a heavy chain comprising, from N terminus to C terminus, the VH and a human IgG1 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 145.

28. The masked antibody any one of claims 12-22, 26, and 27, wherein the antibody comprises a first polypeptide comprising a light chain comprising the VL, wherein the first polypeptide comprises the amino acid sequence of SEQ ID NO: 140; and a second polypeptide comprising a heavy chain comprising, from N terminus to C terminus, the VH and a human IgG1 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 145.

29. The masked antibody of any one of claims 12-22 and 26, wherein the antibody comprises a second polypeptide comprising a heavy chain comprising, from N terminus to C terminus, the VH and a human IgG1 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 147.

30. The masked antibody of any one of claims 12-22, 16, and 29, wherein the antibody comprises a first polypeptide comprising a light chain comprising the VL, wherein the first polypeptide comprises the amino acid sequence of SEQ ID NO: 140; and a second polypeptide comprising a heavy chain comprising, from N terminus to C terminus, the VH and a human IgG1 Fc domain, wherein the second polypeptide comprises the amino acid sequence of SEQ ID NO: 147.

31. An isolated polynucleotide encoding one or more polypeptide chains of the masked antibody of any one of claims 12-30 or the antibody, or antigen-binding fragment thereof, of any one of claims 1-11.

32. A vector comprising the polynucleotide of claim 31.
33. A host cell comprising the vector of claim 32.
34. A method of making a masked antibody, or an antibody, or antigen-binding fragment thereof, comprising culturing the host cell of claim 33 under conditions suitable for producing the masked antibody, or the antibody or antigen-binding fragment thereof.
35. The method of claim 34, further comprising recovering the masked antibody, or the antibody or antigen-binding fragment thereof, produced by the cell.
36. A pharmaceutical composition comprising the masked antibody of any one of claims 12-30, or the antibody or antigen-binding fragment thereof of any one of claims 1-12, and a pharmaceutically acceptable carrier.
37. Use of the pharmaceutical composition of claim 36, in the manufacture of a medicament for treating a CD47-positive disease or condition in a subject in need thereof.
38. The use of claim 37, wherein the disease or condition is cancer.
39. The use of claim 37 or claim 38, wherein one or more additional therapeutic agents is to be administered to the subject.
40. The use of claim 39, wherein the one or more therapeutic agents comprise viral gene therapy, an immune checkpoint inhibitor, a target therapy, a radiation therapy, a chemotherapy, or any combination thereof.