

CLAIMS

1. An antibody or an antigen-binding fragment thereof, comprising a VH that comprises four VH framework regions (VH FR1-4) and three VH complementarity determining regions (VH CDR1-3) in the following N-terminal to C-terminal order: VH FR1-VH CDR1-VH FR2-VH CDR2-VH FR3-VH CDR3-VH FR4, wherein VH FR1, VH FR2, VH FR3 and VH FR4 comprise the amino acid sequence of $X_{H1}QX_{H3}QLVQSGAEVKKX_{H5}GX_{H6}SVKVSCKAS$ (SEQ ID NO: 5),
WVRQAPGX_{H12}X_{H13}LEWMG (SEQ ID NO: 6),
YAQKX_{H16}QX_{H17}RVTX_{H18}TX_{H19}DX_{H21}SX_{H22}STAYMELX_{H25}SLRX_{H31}X_{H27}DTAX_{H28}YYC (SEQ ID NO: 7), and
WGX_{H29}GTX_{H30}VTVSS (SEQ ID NO: 4) respectively,
wherein X_{H1} is M or no amino acid, X_{H3} is M, X_{H5} is P or T, X_{H6} is A, S, or T, X_{H12} is K, X_{H13} is G, R, or A, X_{H16} is F or L, X_{H17} is G, D, or E, X_{H18} is M or I, X_{H19} is R, T, E or A, X_{H21} is T, R, M, E, or K, X_{H22} is I, A T, or M, X_{H25} is S or R, X_{H31} is S or A, X_{H27} is D or E, and X_{H28} is V or M, X_{H29} is Q or R, and X_{H30} is L, M or T.
2. The antibody or antigen-binding fragment of claim 1, wherein X_{H1} is M or no amino acid, X_{H3} is M, X_{H5} is P, X_{H6} is S, X_{H12} is K, X_{H13} is G, X_{H16} is F, X_{H17} is G, X_{H18} is I, X_{H19} is R, X_{H21} is R, X_{H22} is T, X_{H25} is R, X_{H31} is A, X_{H27} is E, and X_{H28} is V, X_{H29} is Q, and X_{H30} is L.
3. The antibody or antigen-binding fragment of claim 1, wherein X_{H1} is M or no amino acid, X_{H3} is M, X_{H5} is P, X_{H6} is S, X_{H12} is K, X_{H13} is G, X_{H16} is F, X_{H17} is G, X_{H18} is I, X_{H19} is R, X_{H21} is R, X_{H22} is T, X_{H25} is R, X_{H31} is A, X_{H27} is E, and X_{H28} is V, X_{H29} is Q, and X_{H30} is T.
4. The antibody or antigen-binding fragment of claim 1, wherein X_{H1} is M or no amino acid, X_{H3} is M, X_{H5} is P, X_{H6} is S, X_{H12} is K, X_{H13} is G, X_{H16} is F, X_{H17} is G, X_{H18} is I, X_{H19} is R, X_{H21} is R, X_{H22} is T, X_{H25} is R, X_{H31} is S, X_{H27} is E, and X_{H28} is V, X_{H29} is Q, and X_{H30} is L.

5. The antibody or antigen-binding fragment of claim 1, wherein X_{H1} is M or no amino acid, X_{H3} is M, X_{H5} is P, X_{H6} is S, X_{H12} is K, X_{H13} is G, X_{H16} is F, X_{H17} is G, X_{H18} is I, X_{H19} is R, X_{H21} is R, X_{H22} is T, X_{H25} is R, X_{H31} is S, X_{H27} is E, and X_{H28} is V, X_{H29} is Q, and X_{H30} is T.

6. The antibody or antigen-binding fragment of any of claims 1-5, further comprising a light chain variable region (VL) that comprises four VL framework regions (VL FR1-4) and three VL complementarity determining regions (VL CDR1-3) in the following N-terminal to C-terminal order: VL FR1-VL CDR1-VL FR2-VL CDR2-VL FR3-VL CDR3-VL FR4, wherein VL FR1, VL FR2, VL FR3 and VL FR4 comprise the amino acid sequence of NIQMTQSPS X_{L1} X_{L2} SASVGDRVITTC (SEQ ID NO: 8);
W X_{L3} QQKPGK X_{L4} PKHLIY (SEQ ID NO: 9);
GVPSRFSGSGSGTEFTLTISLQPEDFATYYC (SEQ ID NO: 10); and
FGGGTKVEIK (SEQ ID NO: 11), respectively,
wherein X_{L1} is A or S, X_{L2} is M or L, X_{L3} is F or Y, and X_{L4} is V or A.

7. The antibody or antigen-binding fragment of claim 6, wherein X_{L1} is S, X_{L2} is L, X_{L3} is F, and X_{L4} is V.

8. The antibody or antigen-binding fragment of claim 6, wherein X_{L1} is S, X_{L2} is L, X_{L3} is Y, and X_{L4} is A.

9. The antibody or antigen-binding fragment of claim 6, wherein X_{L1} is S, X_{L2} is M, X_{L3} is F, and X_{L4} is V.

10. The antibody or antigen-binding fragment of any of claims 1-9, which specifically binds to CD47 and comprises a VH that comprises four VH framework regions (VH FR1-4) and three VH complementarity determining regions (VH CDR1-3) in the following N-terminal to C-terminal order: VH FR1-VH CDR1-VH FR2-VH CDR2-VH FR3-VH CDR3-VH FR4, wherein at least one of the following is satisfied: (1) VH CDR1 comprises the amino acid sequence of GFNIKDYLYH (SEQ ID NO: 59); (2) VH CDR2 comprises the amino acid sequence of

WIDPDQGDTE (SEQ ID NO: 60); and (3) VH CDR3 comprises the amino acid sequence of NAAYGSSSYPM DY (SEQ ID NO: 61).

11. The antibody or antigen-binding fragment of any of claims 1-10, which specifically binds to CD47 and comprises a VL that comprises four VL framework regions (VL FR1-4) and three VL complementarity determining regions (VL CDR1-3) in the following N-terminal to C-terminal order: VL FR1-VL CDR1-VL FR2-VL CDR2-VL FR3-VL CDR3-VL FR4, wherein: (A) at least one of the following is satisfied: (1) VL CDR1 comprises the amino acid sequence of X_{C1} ASQDIHRYLS (SEQ ID NO: 62), wherein X_{C1} is K or R; (2) VL CDR2 comprises the amino acid sequence of RANRLVS (SEQ ID NO: 63); and (3) VL CDR3 comprises the amino acid sequence of LQYDEFPYT (SEQ ID NO: 64); or (B) at least one of the following is satisfied: (1) VL CDR1 comprises the amino acid sequence of X_{C1} ASQDIHRYLS (SEQ ID NO: 62), wherein X_{C1} is K or R; (2) VL CDR2 comprises the amino acid sequence of $RX_{C2}X_{C3}$ RFVD (SEQ ID NO: 65), wherein X_{C2} is any amino acid with a polar or charged side chain, and X_{C3} is V, I, E, or S; and (3) VL CDR3 comprises the amino acid sequence of LQYDEFPYT (SEQ ID NO: 64).

12. The antibody or antigen-binding fragment of claim 11, wherein X_{C2} is Y, E, or H.

13. The antibody or antigen-binding fragment of any of claims 1-12, which comprises a heavy chain constant region that is a human constant region.

14. The antibody or antigen-binding fragment of any of claims 1-13, which comprises a light chain constant region selected from the group consisting of a human kappa constant region and a human lambda constant region.

15. A pharmaceutical composition comprising a therapeutically effective amount of the antibody or antigen-binding fragment of any of claims 1-14, and a pharmaceutically acceptable carrier.

16. Use of an antibody or antigen-binding fragment as defined in any of Claims 1-14 or a pharmaceutical composition as defined in claim 15 in the manufacture of a medicament for treating cancer in a subject in need thereof.

17. A polynucleotide comprising a nucleotide sequence encoding the antibody or antigen-binding fragment of any of claims 1-15.

18. A vector comprising the polynucleotide of claim 17.

19. An isolated cell comprising the polynucleotide of claim 17.

20. A method of making an antibody or antigen-binding fragment thereof, comprising (a) culturing an isolated cell comprising the polynucleotide of claim 17; and (b) isolating the antibody or antigen-binding fragment thereof.