

CLAIMS

What is claimed is:

1. An anti-CD47 antibody comprising at least one antibody-antigen binding site, wherein said antibody comprises any one of the following:

(1) a V_H comprising the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 65, 161 and 257, respectively, and a V_L comprising the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 76, 172 and 268, respectively;

(2) a V_H comprising the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 51, 147 and 243, respectively, and a V_L comprising the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 52, 148 and 244, respectively;

(3) a V_H comprising the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 53, 149 and 245, respectively, and a V_L comprising the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 54, 150 and 246, respectively;

(4) a V_H comprising the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 55, 151 and 247, respectively, and a V_L comprising the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 56, 152 and 248, respectively;

(5) a V_H comprising the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 57, 153 and 249, respectively, and a V_L comprising the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 58, 154 and 250, respectively;

(6) a V_H comprising the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 59, 155 and 251, respectively, and a V_L comprising the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 60, 156 and 252, respectively;

(7) a V_H comprising the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 62, 158 and 254, respectively, and a V_L comprising the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 76, 172 and 268, respectively;

(8) a V_H comprising the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs:63, 159 and 255, respectively, and a V_L comprising the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 77, 173 and 269, respectively;

(9) a V_H comprising the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs:64, 160 and 256, respectively, and a V_L comprising the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 78, 174 and 270, respectively;

(10) a V_H comprising the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs:65, 161 and 257, respectively, and a V_L comprising the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 79, 175 and 271, respectively;

(11) a V_H comprising the heavy chain CDR1, CDR2 and CDR3 sequences having the amino acid sequences of SEQ ID NOs: 49, 145 and 241, respectively, and a V_L comprising the light chain CDR1, CDR2 and CDR3 having the amino acid sequences of SEQ ID NOs: 50, 146 and 242, respectively.

2. The antibody of claim 1, wherein said antibody comprises a variable heavy chain selected from SEQ ID NOs: 349, 351, 353, 355, 357, 359, 361-373, 380-383, 388-392 and a variable light chain selected from SEQ ID NOs: 350, 352, 354, 356, 358, 360, 374-379, 384-387 and 393-396.

3. The antibody of claim 1 or 2, wherein said antibody comprises:

(1) a V_H comprising the sequence having the amino acid sequence of SEQ ID NO: 365, and a V_L comprising the amino acid sequence of SEQ ID NO: 376;

(2) a V_H comprising the sequence having the amino acid sequence of SEQ ID NO: 351, and a V_L comprising the amino acid sequence of SEQ ID NO: 352;

(3) a V_H comprising the sequence having the amino acid sequence of SEQ ID NO: 353, and a V_L comprising the amino acid sequence of SEQ ID NO: 354;

(4) a V_H comprising the sequence having the amino acid sequence of SEQ ID NO: 355, and a V_L comprising the amino acid sequence of SEQ ID NO: 356;

(5) a V_H comprising the sequence having the amino acid sequence of SEQ ID NO: 357, and a V_L comprising the amino acid sequence of SEQ ID NO: 358;

(6) a V_H comprising the sequence having the amino acid sequence of SEQ ID NO: 359, and a V_L comprising the amino acid sequence of SEQ ID NO: 360;

- (7) a VH comprising the sequence having the amino acid sequence of SEQ ID NO: 362, and a VL comprising the amino acid sequence of SEQ ID NO: 376;
- (8) a VH comprising the sequence having the amino acid sequence of SEQ ID NO: 363, and a VL comprising the amino acid sequence of SEQ ID NO: 377;
- (9) a VH comprising the sequence having the amino acid sequence of SEQ ID NO: 364, and a VL comprising the amino acid sequence of SEQ ID NO: 378;
- (10) a VH comprising the sequence having the amino acid sequence of SEQ ID NO: 365, and a VL comprising the amino acid sequence of SEQ ID NO: 379;
- (11) a VH comprising the sequence having the amino acid sequence of SEQ ID NO: 349, and a VL comprising the amino acid sequence of SEQ ID NO: 350.

4. The antibody of any one of the preceding claims, wherein said antibody comprises a constant region modified at amino acid Asn297, Leu235 and/or Leu234, and/or, wherein said antibody comprises a constant region with an amino acid modification of N297A, and/or, wherein said constant region has an amino acid modification of Leu235Glu (L235E) or Leu235Ala (L235A), and/or an amino acid modification of Leu234Ala (L234A).

5. The antibody of any one of the preceding claims, wherein said antibody comprises a human IgG₃ constant region that is modified at amino acid Arg435, and/or, wherein said human IgG₃ constant region has an amino acid modification of Arg435His (R435H).

6. The antibody of any one of the preceding claims, wherein said antibody comprises a human IgG₄ constant region that is modified within the hinge region to prevent or reduce strand exchange, and/or, wherein said antibody comprises a human IgG₄ constant region with an amino acid modification of Ser228Pro (S228P); and/or, wherein said human IgG₄ constant region is further modified at amino acid 235; and/or, wherein said human IgG₄ constant region has an amino acid modification of Leu235Glu (S228P/L235E).

7. The antibody of any one of the preceding claims, wherein said antibody comprises a human IgG constant region modified to enhance FcRn binding, wherein said human

IgG constant region has one or more amino acid modifications of Met252Tyr, Ser254Thr, Thr256Glu, Met428Leu or Asn434Ser (M252Y, S254T, T256E M428L, or N434S).

8. The antibody of any one of the preceding claims,

wherein said antibody comprises a human IgG constant region modified to alter antibody-dependent cellular cytotoxicity (ADCC) and/or complement-dependent cytotoxicity (CDC), and/or,

wherein said antibody comprises a human IgG constant region modified to induce heterodimerization, wherein said antibody has an amino acid modification of T366W or T366S and/or an amino acid modification of L368A, or Y407V, S354C, or Y349C.

9. The antibody of any one of the preceding claims, wherein said antibody is a humanized antibody or a human antibody having a variable heavy chain region (V_H) and/or variable light (V_L) chain region that at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more identical to a sequence selected from the group consisting of: SEQ ID NOs: 361-373, 375-379, 381-383, 385-387, 389-392, 394-396, 399-404.

10. The antibody of claim 9, wherein said antibody is a humanized or human antibody having a variable heavy chain region (V_H) and/or variable light (V_L) chain region selected from the group consisting of: SEQ ID NOs: 361-373, 375-379, 381-383, 385-387, 389-392, 394-396, 399-404.

11. An isolated nucleic acid encoding the antibody of any one of the preceding claims.

12. The isolated nucleic acid of claim 11, wherein the nucleic acid comprises a sequence selected from the group consisting of: SEQ ID NOs: 337-348 and 413-421 or a sequence that is at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more identical to a sequence selected from the group consisting of: SEQ ID NOs: 337-348 and 413-421.

13. A vector comprising the nucleic acid of claim 11 or 12.

14. A cell comprising the nucleic acid of any one of claims 11-12 or the vector of claim 13, wherein said cell expresses the antibody of any one of claims 1-10.

15. A pharmaceutical composition comprising the antibody of any one of claims 1-10 and a pharmaceutically acceptable excipient.

16. Use of an effective amount of the antibody of any one of claims 1-10, or the pharmaceutical composition of claim 15 in the manufacture of a medicament for treating a cancer or other neoplastic condition.

17. The use of claim 16, wherein said cancer or other neoplastic condition is selected from the group consisting of acute lymphocytic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), and multiple myeloma (MM), breast cancer, ovarian cancer, head and neck cancer, bladder cancer, melanoma, colorectal cancer, pancreatic cancer, lung cancer, leiomyoma, leiomyosarcoma, glioma, glioblastoma, breast tumors, ovarian tumors, lung tumors, pancreatic tumors, prostate tumors, melanoma tumors, colorectal tumors, lung tumors, head and neck tumors, bladder tumors, esophageal tumors, liver tumors, and kidney tumors, Myeloproliferative disorder/neoplasm (MPDS), myelodysplasia syndrome, Hodgkin's lymphoma, both indolent and aggressive non-Hodgkin's lymphoma(NHL), Burkitt's lymphoma, follicular lymphoma (small cell and large cell), multiple myeloma (MM), giant cell myeloma, heavy-chain myeloma, light chain or Bence-Jones myeloma.

18. The use of claim 16 or 17, wherein said cancer or other neoplastic condition is selected from the group consisting of non-Hodgkin's lymphoma (NHL), acute myeloid leukemia (AML), small cell lung cancer (SCLC), esophageal tumors, and Myelodysplastic syndromes (MDS).