CLAIMS

1. An anti-CD47 antibody comprising:

    a. a heavy chain having each of the CDR sequences set forth in SEQ ID NOs: 49-51 (Kabat annotation) or SEQ ID NOs: 52-54 (IMGT annotation) and a light chain having each of the CDR sequences set forth in SEQ ID NOs: 55, 152 and 57 (Kabat annotation) or SEQ ID NOs: 58, 153 and 60 (IMGT annotation); or

    b. a heavy chain having each of the CDR sequences set forth in SEQ ID NOs: 49-51 (Kabat annotation) or SEQ ID NOs: 52-54 (IMGT annotation) and a light chain having each of the CDR sequences set forth in SEQ ID NOs: 55-57 (Kabat annotation) or SEQ ID NOs: 58-60 (IMGT annotation).

2. The antibody of claim 1, comprising:

    a. a VH sequence comprising the sequence set forth in SEQ ID NO:142 and a VL sequence comprising the sequence set forth in SEQ ID NO:159;

    b. a VH sequence comprising the sequence set forth in SEQ ID NO:143 and a VL sequence comprising the sequence set forth in SEQ ID NO:156;

    c. a VH sequence comprising the sequence set forth in SEQ ID NO:143 and a VL sequence comprising the sequence set forth in SEQ ID NO:157;

    d. a VH sequence comprising the sequence set forth in SEQ ID NO:144 and a VL sequence comprising the sequence set forth in SEQ ID NO:158;

    e. a VH sequence comprising the sequence set forth in SEQ ID NO:144 and a VL sequence comprising the sequence set forth in SEQ ID NO:159.

    f. a VH sequence comprising the sequence set forth in SEQ ID NO:141 and a VL sequence comprising the sequence set forth in SEQ ID NO:146;

    g. a VH sequence comprising the sequence set forth in SEQ ID NO:141 and a VL sequence comprising the sequence set forth in SEQ ID NO:147;

h. a VH sequence comprising the sequence set forth in SEQ ID NO:141 and a VL sequence comprising the sequence set forth in SEQ ID NO:148;

i. a VH sequence comprising the sequence set forth in SEQ ID NO:141 and a VL sequence comprising the sequence set forth in SEQ ID NO:149;

j. a VH sequence comprising the sequence set forth in SEQ ID NO:141 and a VL sequence comprising the sequence set forth in SEQ ID NO:150;

k. a VH sequence comprising the sequence set forth in SEQ ID NO:142 and a VL sequence comprising the sequence set forth in SEQ ID NO:146;

l. a VH sequence comprising the sequence set forth in SEQ ID NO:142 and a VL sequence comprising the sequence set forth in SEQ ID NO:147;

m. a VH sequence comprising the sequence set forth in SEQ ID NO:142 and a VL sequence comprising the sequence set forth in SEQ ID NO:148;

n. a VH sequence comprising the sequence set forth in SEQ ID NO:142 and a VL sequence comprising the sequence set forth in SEQ ID NO:149;

o. a VH sequence comprising the sequence set forth in SEQ ID NO:142 and a VL sequence comprising the sequence set forth in SEQ ID NO:150;

p. a VH sequence comprising the sequence set forth in SEQ ID NO:143 and a VL sequence comprising the sequence set forth in SEQ ID NO:146;

q. a VH sequence comprising the sequence set forth in SEQ ID NO:143 and a VL sequence comprising the sequence set forth in SEQ ID NO:147;

r. a VH sequence comprising the sequence set forth in SEQ ID NO:143 and a VL sequence comprising the sequence set forth in SEQ ID NO:148;

s. a VH sequence comprising the sequence set forth in SEQ ID NO:143 and a VL sequence comprising the sequence set forth in SEQ ID NO:149;

t. a VH sequence comprising the sequence set forth in SEQ ID NO:143 and a VL sequence comprising the sequence set forth in SEQ ID NO:150;

u. a VH sequence comprising the sequence set forth in SEQ ID NO:144 and a VL sequence comprising the sequence set forth in SEQ ID NO:146;

v. a VH sequence comprising the sequence set forth in SEQ ID NO:144 and a VL sequence comprising the sequence set forth in SEQ ID NO:147;

w. a VH sequence comprising the sequence set forth in SEQ ID NO:144 and a VL sequence comprising the sequence set forth in SEQ ID NO:148;

x. a VH sequence comprising the sequence set forth in SEQ ID NO:144 and a VL sequence comprising the sequence set forth in SEQ ID NO:149;

y. a VH sequence comprising the sequence set forth in SEQ ID NO:144 and a VL sequence comprising the sequence set forth in SEQ ID NO:150;

z. a VH sequence comprising the sequence set forth in SEQ ID NO:145 and a VL sequence comprising the sequence set forth in SEQ ID NO:146;

aa. a VH sequence comprising the sequence set forth in SEQ ID NO:145 and a VL sequence comprising the sequence set forth in SEQ ID NO:147;

bb. a VH sequence comprising the sequence set forth in SEQ ID NO:145 and a VL sequence comprising the sequence set forth in SEQ ID NO:148;

cc. a VH sequence comprising the sequence set forth in SEQ ID NO:145 and a VL sequence comprising the sequence set forth in SEQ ID NO:149; or

dd. a VH sequence comprising the sequence set forth in SEQ ID NO:145 and a VL sequence comprising the sequence set forth in SEQ ID NO:150.

3. An anti-CD47 antibody comprising a heavy chain having each of the CDR sequences set forth in SEQ ID NOs: 61-63 (Kabat annotation) or SEQ ID NOs: 64-66 (IMGT annotation) and a light chain having each of the CDR sequences set forth in SEQ ID NOs: 67-69 (Kabat annotation) or SEQ ID NOs: 70-72 (IMGT annotation).

4. The antibody of claim 3, comprising:

a. a VH sequence comprising the sequence set forth in SEQ ID NO:168 and a VL sequence comprising the sequence set forth in SEQ ID NO:172;

b. a VH sequence comprising the sequence set forth in SEQ ID NO:168 and a VL sequence comprising the sequence set forth in SEQ ID NO:173;

c. a VH sequence comprising the sequence set forth in SEQ ID NO:168 and a VL sequence comprising the sequence set forth in SEQ ID NO:174;

d. a VH sequence comprising the sequence set forth in SEQ ID NO:168 and a VL sequence comprising the sequence set forth in SEQ ID NO:175;

e. a VH sequence comprising the sequence set forth in SEQ ID NO:169 and a VL sequence comprising the sequence set forth in SEQ ID NO:172;

f. VH sequence comprising the sequence set forth in SEQ ID NO:169 and a VL sequence comprising the sequence set forth in SEQ ID NO:173;

g. a VH sequence comprising the sequence set forth in SEQ ID NO:169 and a VL sequence comprising the sequence set forth in SEQ ID NO:174;

h. a VH sequence comprising the sequence set forth in SEQ ID NO:169 and a VL sequence comprising the sequence set forth in SEQ ID NO:175;

i. a VH sequence comprising the sequence set forth in SEQ ID NO:170 and a VL sequence comprising the sequence set forth in SEQ ID NO:172;

j. a VH sequence comprising the sequence set forth in SEQ ID NO:170 and a VL sequence comprising the sequence set forth in SEQ ID NO:173;

k. a VH sequence comprising the sequence set forth in SEQ ID NO:170 and a VL sequence comprising the sequence set forth in SEQ ID NO:174;

l. a VH sequence comprising the sequence set forth in SEQ ID NO:170 and a VL sequence comprising the sequence set forth in SEQ ID NO:175;

m. a VH sequence comprising the sequence set forth in SEQ ID NO:171 and a VL sequence comprising the sequence set forth in SEQ ID NO:172;

n. a VH sequence comprising the sequence set forth in SEQ ID NO:171 and a VL sequence comprising the sequence set forth in SEQ ID NO:173;

o. a VH sequence comprising the sequence set forth in SEQ ID NO:171 and a VL sequence comprising the sequence set forth in SEQ ID NO:174; or

p. a VH sequence comprising the sequence set forth in SEQ ID NO:171 and a VL sequence comprising the sequence set forth in SEQ ID NO:175.

5. The antibody of any preceding claim, wherein the antibody binds to glycosylated and non-glycosylated CD47, optionally wherein the antibody binds to glycosylated and deglycosylated forms of human CD47, and wherein binding of the antibody to CD47 is not dependent on the glycosylation of CD47, optionally wherein:

a. the glycosylated form of human CD47 comprises one or more N-glycosylated residues at positions N23, N34, N50, N73, N111 and/or N206 in the amino acid sequence of human CD47 (SEQ ID NO:151); and/or

b. the deglycosylated form of human CD47 comprises glycosylated human CD47 that has been treated with a peptide N-glycosidase (PNGase) for removal of N-glycosylations; and/or

c. the antibody binds specifically to glycosylated and non-glycosylated CD47 and disrupts the CD47-SIRPα interaction, preferably the antibody binds specifically to glycosylated and non-glycosylated human CD47 and disrupts the human CD47-SIRPα interaction, respectively.

6. The antibody of any preceding claim, wherein:
(a) the antibody is an antibody fragment, and wherein the antibody fragment is optionally an $F(ab')_2$, an scFv, or an Fab fragment, or
(b) the antibody is a bispecific antibody.

7. The antibody of any preceding claim, having a human IgG4 with optionally the mutation S228P (SEQ ID NO: 162) or with optionally the double mutation S228P-L235E (SEQ ID NO: 164).

8. The antibody of any preceding claim, wherein:

a. the antibody binds to a discontinuous epitope on CD47, preferably human CD47; optionally wherein the discontinuous epitope comprises amino acid residues K59, R63, Y66, T67, H108, T109, T117 and T120 of human CD47 (SEQ ID 151); or the discontinuous epitope comprises amino acid residues K59, K61, S107, H108, T117, T120 and R121 of human CD47 (SEQ ID NO: 151); and/or

b. the antibody binds the CD47 monomer and CD47 dimer, preferably the human CD47 monomer and dimer, respectively.

9. The antibody of any preceding claim, wherein:

a. a ratio of EC50s of binding of the antibody to non-glycosylated versus glycosylated forms of CD47 is less than 4:1, 3:1, 2:1, 1:2, 1:3 or 1:4, preferably in a range from 4:1 to 1:4, more preferably 3:1 to 1:3, most preferably 2:1 to 1:2; and/or

b. a ratio of EC95s of binding of the antibody to non-glycosylated versus glycosylated forms of CD47 is less than 25:1, 20:1 or 10:1, 1:10, 1:20 or 1:25, preferably in a range from 10:1 to 1:10, more preferably 9:1 to 1:9, most preferably 10:1 to 1:10; and/or

c. the antibody binds to each of glycosylated and non-glycosylated CD47 with an equilibrium binding constant of 80 pM or lower, preferably 70 pM or lower, more preferably 60pM or lower; and/or

d. a maximum binding capacity ($Bmax_2$) of the antibody to non-glycosylated CD47 is at least 60% of a maximum binding capacity ($Bmax_1$) of the antibody to glycosylated CD47; and/or

e. the antibody has a Koff value for binding to glycosylated and/or non-glycosylated CD47 of about 1.0×10^{-4} s^{-1} (1/s) or more, such as wherein the antibody has a Koff value for binding to glycosylated and/or non-glycosylated CD47 of from 1.0×10^{-4} s^{-1} to 1.0×10^{-3} s^{-1}, such as wherein the antibody has a Koff value for binding to glycosylated and/or non-glycosylated CD47 of from 2.5×10^{-4} s^{-1} to 8.0×10^{-4} s^{-1}; and/or

f. the antibody has a Koff value for binding to CD47 of from 1.0×10^{-4} s^{-1} to 1.0×10^{-3} s^{-1}.

10. A pharmaceutical composition comprising an antibody set forth in any one of claim 1-9, optionally further comprising a pharmaceutical acceptable excipient.

11. A polynucleotide encoding an antibody set forth in any one of claims 1-9.

12. A cell that produces an antibody set forth in any one of claims 1-9.

13. A process for producing an antibody of any one of claims 1-9, comprising culturing the cell of claim 12 so that the polynucleotide of claim 11 is expressed, and optionally recovering the antibody from the cell culture.

14. Use of the antibody of any one of claims 1-9 or the pharmaceutical composition of claim 10, in the preparation of a medicament for the treatment of a disease in a subject; optionally wherein:

(a) the disease is cancer, optionally wherein the cancer is gastric, lung, ovarian or breast cancer, preferably gastric cancer, and/or
(b) the antibody is to be used as a monotherapy, and/or
(c) the antibody is to be used in combination therapy, preferably a combination with a Her-2 inhibitor or an anti-Her2 antibody or an EGFR inhibitor or an anti-EGFR antibody.

15. The use according to claim 14, wherein the subject is a human or a non-human animal.