

CLAIMS

1. An antibody that binds to glycosylated and non-glycosylated CD47, wherein binding of the antibody to CD47 is not dependent on the glycosylation of CD47.
2. The antibody of claim 1, wherein the antibody is suitable for use as a therapeutic antibody.
3. The antibody of claim 1 or claim 2, wherein the antibody binds glycosylated and deglycosylated forms of human CD47.
4. The antibody of claim 3, wherein 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).
5. The antibody of any preceding claim, wherein 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.
6. The antibody of any preceding claim, wherein (i) 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 (ii) 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.
7. The antibody of any preceding claim, wherein 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.

8. The antibody of any preceding claim, wherein a maximum binding capacity (B_{max2}) of the antibody to non-glycosylated CD47 is at least 60% of a maximum binding capacity (B_{max1}) of the antibody to glycosylated CD47.
9. The antibody of any preceding claim, wherein the antibody has a K_{off} value for binding to glycosylated and/or non-glycosylated CD47 of about $1.0 \times 10^{-4} \text{ s}^{-1}$ (1/s) or more.
10. The antibody of claim 9, wherein the antibody has a K_{off} value for binding to glycosylated and/or non-glycosylated CD47 of from $1.0 \times 10^{-4} \text{ s}^{-1}$ to $1.0 \times 10^{-3} \text{ s}^{-1}$.
11. The antibody of claim 10, wherein the antibody has a K_{off} value for binding to glycosylated and/or non-glycosylated CD47 of from $2.5 \times 10^{-4} \text{ s}^{-1}$ to $8.0 \times 10^{-4} \text{ s}^{-1}$.
12. An antibody that binds to CD47, wherein the antibody has a K_{off} value for binding to CD47 of from $1.0 \times 10^{-4} \text{ s}^{-1}$ to $1.0 \times 10^{-3} \text{ s}^{-1}$.
13. The antibody of any preceding claim, wherein the antibody is a full length chimeric, mouse or humanized antibody.
14. The antibody of any of claims 1 to 12, wherein the antibody is an antibody fragment, and wherein the antibody fragment is optionally an $F(ab')_2$ or an Fab fragment.
15. The antibody of any preceding claim, wherein the antibody is a bispecific antibody.
16. The antibody of any preceding claim, wherein the antibody binds specifically to glycosylated and non-glycosylated CD47 and disrupts the CD47-SIRP α interaction, preferably the antibody binds specifically to glycosylated and non-glycosylated human CD47 and disrupts the human CD47-SIRP α interaction, respectively.
17. 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)
18. The antibody of any preceding claim, wherein the antibody binds to a discontinuous epitope on CD47, preferably human CD47.

19. The antibody of claim 18, 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).
20. The antibody of any preceding claim, wherein the antibody binds the CD47 monomer and CD47 dimer, preferably the human CD47 monomer and dimer, respectively.
21. The antibody of any preceding claim, wherein the antibody is selected from the group of antibodies consisting of (i) a group of antibodies that comprise 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), (ii) a group of antibodies that comprise 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); and (iii) a group of antibodies that comprise 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, 57 (Kabat annotation) or SEQ ID NOs: 58, 153, 60 (IMGT annotation).
22. The antibody of claim 20, wherein said antibody is selected from the group of antibodies consisting of:
- (a) a group of antibodies that comprise a VH having an amino acid sequence set forth in SEQ ID NO: 129 and a VL having an amino acid sequence set forth in SEQ ID NO: 130;
or
- (b) a group of antibodies that comprise a VH having an amino acid sequence set forth in SEQ ID NO: 131 and a VL having an amino acid sequence set forth in SEQ ID NO: 132;
or
- (c) a group of antibodies that comprise a VH having an amino acid sequence set forth in SEQ ID NO: 129 and a VL having an amino acid sequence set forth in SEQ ID NO: 154.

23. The antibody of any of claims 1 to 20, which is a humanized antibody comprising a VH having an amino acid sequence set forth in SEQ ID NO: 141 and a VL that is selected from the group of VLs consisting of amino acid sequences set forth in SEQ ID NOs: 146-150 and/or SEQ ID NOs: 155-159; or wherein the humanized antibody comprises a VH having an amino acid sequence set forth in SEQ ID NO: 142 and a VL that is selected from the group of VLs consisting of amino acid sequences set forth in SEQ ID NOs: 146-150 and/or SEQ ID NOs: 155-159; or wherein the humanized antibody comprises a VH having an amino acid sequence set forth in SEQ ID NO: 143 and a VL that is selected from the group of VLs consisting of amino acid sequences set forth in SEQ ID NOs: 146-150 and/or SEQ ID NOs: 155-159; or wherein the humanized antibody comprises a VH having an amino acid sequence set forth in SEQ ID NO: 144 and a VL that is selected from the group of VLs consisting of amino acid sequences set forth in SEQ ID NOs: 146-150 and/or SEQ ID NOs: 155-159; or wherein the humanized antibody comprises a VH having an amino acid sequence set forth in SEQ ID NO: 145 and a VL that is selected from the group of VLs consisting of amino acid sequences set forth in SEQ ID NOs: 146-150 and/or SEQ ID NOs: 155-159; or wherein the humanized antibody comprises a VH having an amino acid sequence set forth in SEQ ID NO: 168 and a VL that is selected from the group of VLs consisting of amino acid sequences set forth in SEQ ID NOs: 172-175; or wherein the humanized antibody comprises a VH having an amino acid sequence set forth in SEQ ID NO: 169 and a VL that is selected from the group of VLs consisting of amino acid sequences set forth in SEQ ID NOs: 172-175; or wherein the humanized antibody comprises a VH having an amino acid sequence set forth in SEQ ID NO: 170 and a VL that is selected from the group of VLs consisting of amino acid sequences set forth in SEQ ID NOs: 172-175; or wherein the humanized antibody comprises a VH having an amino acid sequence set forth in SEQ ID NO: 171 and a VL that is selected from the group of VLs consisting of amino acid sequences set forth in SEQ ID NOs: 172-175.
24. A polynucleotide encoding an antibody set forth in any preceding claim.
25. A cell that produces an antibody set forth in any one of claims 1 to 23.

26. A pharmaceutical composition comprising an antibody set forth in any one of claims 1-23, optionally further comprising a pharmaceutical acceptable excipient.
27. An antibody of any of claims 1-23 or a pharmaceutical composition of claim 26, for use in the treatment of a disease in a subject.
28. The antibody or composition for use of claim 27, for use in the treatment of cancer.
29. The antibody or composition for use of claim 28, wherein the cancer is gastric, lung, ovarian or breast cancer, preferably gastric cancer.
30. The antibody or composition for use of any of claims 27 to 29, for use as a monotherapy.
31. The antibody or composition for use of any of claims 27 to 29, for use 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.
32. The antibody or composition for use according to claims 27-31, wherein the subject is a human or a non-human animal.