

CLAIMS

1. An isolated anti-CD47 antibody or antigen-binding fragment thereof, comprising
HCDR1, HCDR2 and HCDR3 of a VH and
LCDR1, LCDR2 and LCDR3 of a VL, wherein the VH and VL are selected from:
(1) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 1, and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 2;
(2) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 3, and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 4;
(3) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 5, and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 8, 9 or 10;
(4) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 6, and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 9 or 10; or
(5) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 7, and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 8, 9 or 10.
2. An isolated anti-CD47 antibody or antigen-binding fragment thereof, comprising heavy chain complementary determining region 1 (HCDR1), HCDR2 and HCDR3, and light chain complementary determining region 1 (LCDR1), LCDR2 and LCDR3, wherein
(1) the HCDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 11, the HCDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 12, and the HCDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 17; and
the LCDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 14, the LCDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 18, and the LCDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 16; or
(2) the HCDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 11, the HCDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 12, and the HCDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 13; and

the LCDR1 comprises the amino acid sequence as set forth in SEQ ID NO: 14, the LCDR2 comprises the amino acid sequence as set forth in SEQ ID NO: 15, and the LCDR3 comprises the amino acid sequence as set forth in SEQ ID NO: 16.

3. An isolated anti-CD47 antibody or antigen-binding fragment thereof, comprising heavy chain complementary determining region 1 (HCDR1), HCDR2 and HCDR3, and light chain complementary determining region 1 (LCDR1), LCDR2 and LCDR3, wherein

(1) the HCDR1 consists of the amino acid sequence as set forth in SEQ ID NO: 11, the HCDR2 consists of the amino acid sequence as set forth in SEQ ID NO: 12, and the HCDR3 consists of the amino acid sequence as set forth in SEQ ID NO: 17; and

the LCDR1 consists of the amino acid sequence as set forth in SEQ ID NO: 14, the LCDR2 consists of the amino acid sequence as set forth in SEQ ID NO: 18, and the LCDR3 consists of the amino acid sequence as set forth in SEQ ID NO: 16; or

(2) the HCDR1 consists of the amino acid sequence as set forth in SEQ ID NO: 11, the HCDR2 consists of the amino acid sequence as set forth in SEQ ID NO: 12, and the HCDR3 consists of the amino acid sequence as set forth in SEQ ID NO: 13; and

the LCDR1 consists of the amino acid sequence as set forth in SEQ ID NO: 14, the LCDR2 consists of the amino acid sequence as set forth in SEQ ID NO: 15, and the LCDR3 consists of the amino acid sequence as set forth in SEQ ID NO: 16.

4. The antibody or antigen-binding fragment thereof of any of the preceding claims, comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH and VL are selected from

(1) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 1; and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 2;

(2) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 3; and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 4;

(3) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 5; and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 8, 9 or 10;

(4) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 6; and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 9 or 10; or

(5) a VH comprising the amino acid sequence as set forth in SEQ ID NO: 7; and a VL comprising the amino acid sequence as set forth in SEQ ID NO: 8, 9 or 10.

5. The antibody or antigen-binding fragment thereof of claim 4, comprising a heavy chain variable region (VH) and a light chain variable region (VL), wherein the VH comprises the amino acid sequence as set forth in SEQ ID NO: 7, and the VL comprises the amino acid sequence as set forth in SEQ ID NO: 8.

6. The antibody or antigen-binding fragment thereof of any of the preceding claims, comprising a heavy chain constant region, such as a human IgG1 constant region, a human IgG1TM constant region, a human IgG4 constant region or a human IgG4P constant region.

7. The antibody or antigen-binding fragment thereof of any of the preceding claims, comprising a light chain constant region, such as a human κ light chain constant region.

8. The antibody or antigen-binding fragment thereof of any of the preceding claims, which is a murine antibody, a chimeric antibody or a humanized antibody.

9. The antibody or antigen-binding fragment thereof of any of the preceding claims, which is a full-length antibody, a Fab, a Fab', a Fab'-SH, a (Fab')₂, a scFv, a Fv, or a bis (multi) -specific antibody.

10. An isolated nucleic acid, encoding the antibody or antigen-binding fragment thereof of any one of claims 1-9.

11. A recombinant vector or an expression vector, comprising one or more nucleic acids of claim 10, wherein the vector is suitable for the recombinant production of the antibody or antigen-binding fragment thereof of any one of claims 1-9.

12. A host cell, comprising one or more nucleic acids of claim 10 or one or more recombinant vectors or expression vectors of claim 11.

13. An immunoconjugate, comprising the antibody or antigen-binding fragment thereof of any one of claims 1-9.

14. A pharmaceutical composition, comprising the antibody or antigen-binding fragment thereof of any one of claims 1-9, the nucleic acid of claim 10, the vector of claim 11, the host cell of claim 12, or the immunoconjugate of claim 13, and optionally comprising a pharmaceutically acceptable excipient.

15. A use of the antibody of any one of claims 1-9, the immunoconjugate of claim 13, or the pharmaceutical composition of claim 14 in the manufacture of a medicament for treating or preventing cancer

(i) with abnormal CD47 expression, activity and/or signal transmission; or
(ii) with CD47 expression increased, or
(iii) with CD47 protein level increased, or activity increased, or activity signal transmission increased.

16. The use of claim 15, wherein the cancer is a hematological cancer or a solid tumor.

17 The use of claim 15 or 16, wherein the cancer is selected from bladder cancer, pancreatic cancer, lymphoma, leukemia, multiple myeloma, (malignant) melanoma, leiomyoma, leiomyosarcomas, glioma, glioblastoma, myeloma, endometrial cancer, renal carcinoma, (benign) melanoma, prostate cancer, thyroid carcinoma, cervical cancer, gastric cancer, liver cancer, colon cancer, ovarian cancer, urothelial carcinoma, and so on.

18. A method for detecting CD47 protein in a sample, comprising:
(a) contacting a sample with the isolated antibody or antigen-binding fragment thereof of any one of claims 1-9 or the immunoconjugate of claim 13; and

(b) detecting the formation of the complex between the antibody or antigen-binding fragment thereof or the immunoconjugate and the CD47 protein.