

CLAIMS

1. An antibody or an antigen-binding fragment thereof that specifically binds to CD47, wherein

5 the antibody comprises CDR sequences selected from the following CDR sequences contained in heavy chain variable regions and light chain variable regions:

(1) an HCDR1, an HCDR2 and an HCDR3 contained in a heavy chain variable region set forth in SEQ ID NO: 2, and

10 an LCDR1, an LCDR2 and an LCDR3 contained in a light chain variable region set forth in SEQ ID NO: 4; or

(2) an HCDR1, an HCDR2 and an HCDR3 contained in a heavy chain variable region set forth in SEQ ID NO: 12, and

an LCDR1, an LCDR2 and an LCDR3 contained in a light chain variable region set forth in SEQ ID NO: 14; or

15 (3) an HCDR1, an HCDR2 and an HCDR3 contained in a heavy chain variable region set forth in SEQ ID NO: 16, and

an LCDR1, an LCDR2 and an LCDR3 contained in a light chain variable region set forth in SEQ ID NO: 18; or

20 (4) an HCDR1, an HCDR2 and an HCDR3 contained in a heavy chain variable region set forth in SEQ ID NO: 20, and

an LCDR1, an LCDR2 and an LCDR3 contained in a light chain variable region set forth in SEQ ID NO: 22;

preferably, the antibody comprises:

25 an HCDR1 comprising or consisting of a sequence set forth in SEQ ID NO: 5, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2 or 3) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence;

an HCDR2 comprising or consisting of a sequence set forth in SEQ ID NO: 6, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2 or 3) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence; and

an HCDR3 comprising or consisting of a sequence set forth in SEQ ID NO: 7, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2 or 3) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence;:-

theThe antibody further comprises:

an LCDR1 comprising or consisting of an amino acid sequence set forth in SEQ ID NO: 8, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2 or 3) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence;

an LCDR2 comprising or consisting of an amino acid sequence set forth in SEQ ID NO: 9, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2 or 3) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence; and

an LCDR3 comprising or consisting of a sequence set forth in SEQ ID NO: 10, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or

99% or more sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2 or 3) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence.

- 5 2. The antibody or the antigen-binding fragment thereof according to claim 1, wherein the antibody further comprises a combination of FRs in a heavy chain variable region and FRs in a light chain variable region selected from the group consisting of the following:

- 10 (1) the FRs in the heavy chain variable region include FR-H1, FR-H2, FR-H3 and FR-H4, wherein the FR-H1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 23, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 23, or an amino acid sequence having one or
15 more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 23; the FR-H2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 24, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%,
20 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 24, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 24; the FR-H3 comprises or consists of an
25 amino acid sequence set forth in SEQ ID NO: 25, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 25, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations
30 (preferably substitutions, insertions or deletions) compared to the amino acid

sequence set forth in SEQ ID NO: 25; and the FR-H4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 26, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the

5 sequence set forth in SEQ ID NO: 26, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 26;

the FRs in the light chain variable region include FR-L1, FR-L2, FR-L3

10 and FR-L4, wherein the FR-L1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 27, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in

SEQ ID NO: 27, or an amino acid sequence having one or more (preferably 1, 2,

15 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 27; the FR-L2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 28, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%,

20 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 28, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 28; the FR-L3 comprises or consists of an

25 amino acid sequence set forth in SEQ ID NO: 29, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 29, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations

30 (preferably substitutions, insertions or deletions) compared to the amino acid

sequence set forth in SEQ ID NO: 29; and the FR-L4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 30, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 30, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 30;

(2) the FRs in the heavy chain variable region include FR-H1, FR-H2, FR-H3 and FR-H4, wherein the FR-H1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 31, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 31, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 31; the FR-H2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 32, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 32, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 32; the FR-H3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 33, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 33, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid

sequence set forth in SEQ ID NO: 33; and the FR-H4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 34, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the

5 sequence set forth in SEQ ID NO: 34, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 34;

the FRs in the light chain variable region include FR-L1, FR-L2, FR-L3

10 and FR-L4, wherein the FR-L1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 35, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in

SEQ ID NO: 35, or an amino acid sequence having one or more (preferably 1, 2,

15 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 35; the FR-L2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 36, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%,

20 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 36, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 36; the FR-L3 comprises or consists of an

25 amino acid sequence set forth in SEQ ID NO: 37, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 37, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations

30 (preferably substitutions, insertions or deletions) compared to the amino acid

sequence set forth in SEQ ID NO: 37; and the FR-L4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 38, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 38, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 38;

(3) the FRs in the heavy chain variable region include FR-H1, FR-H2, FR-H3 and FR-H4, wherein the FR-H1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 39, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 39, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 39; the FR-H2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 40, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 40, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 40; the FR-H3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 41, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 41, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid

sequence set forth in SEQ ID NO: 41; and the FR-H4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 42, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the

5 sequence set forth in SEQ ID NO: 42, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 42;

the FRs in the light chain variable region include FR-L1, FR-L2, FR-L3

10 and FR-L4, wherein the FR-L1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 43, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in

SEQ ID NO: 43, or an amino acid sequence having one or more (preferably 1, 2,

15 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 43; the FR-L2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 44, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%,

20 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 44, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 44; the FR-L3 comprises or consists of an

25 amino acid sequence set forth in SEQ ID NO: 45, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 45, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations

30 (preferably substitutions, insertions or deletions) compared to the amino acid

sequence set forth in SEQ ID NO: 45; and the FR-L4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 46, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 46, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 46; and

(4) the FRs in the heavy chain variable region include FR-H1, FR-H2, FR-H3 and FR-H4, wherein the FR-H1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 47, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 47, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 47; the FR-H2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 48, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 48, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 48; the FR-H3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 49, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 49, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid

sequence set forth in SEQ ID NO: 49; and the FR-H4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 50, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 50, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 50;

the FRs in the light chain variable region include FR-L1, FR-L2, FR-L3 and FR-L4, wherein the FR-L1 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 51, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 51, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 51; the FR-L2 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 52, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 52, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 52; the FR-L3 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 53, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 53, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid

sequence set forth in SEQ ID NO: 53; and the FR-L4 comprises or consists of an amino acid sequence set forth in SEQ ID NO: 54, a sequence having at least 80%, preferably 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 54, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 54.

5

10 3. The antibody or the antigen-binding fragment thereof according to claim 1 or 2, wherein the antibody comprises:

(1) a heavy chain variable region comprising or consisting of:

an amino acid sequence set forth in SEQ ID NO: 2, or

a sequence having at least 85%, preferably 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 2, or

15 an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 2, and

20 a light chain variable region comprising or consisting of:

an amino acid sequence set forth in SEQ ID NO: 4, or

a sequence having at least 85%, preferably 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 4, or

25 an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 4;

30

- (2) a heavy chain variable region comprising or consisting of:
an amino acid sequence set forth in SEQ ID NO: 12, or
a sequence having at least 85%, preferably 86%, 87%, 88%, 89%, 90%,
91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity
5 to the sequence set forth in SEQ ID NO: 12, or
an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7,
8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29
or 30) conservative amino acid mutations (preferably substitutions, insertions or
deletions) compared to the amino acid sequence set forth in SEQ ID NO: 12; and
10 a light chain variable region comprising or consisting of:
an amino acid sequence set forth in SEQ ID NO: 14, or
a sequence having at least 85%, preferably 86%, 87%, 88%, 89%,
90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more
sequence identity to the sequence set forth in SEQ ID NO: 14, or
15 an amino acid sequence having one or more (preferably 1, 2, 3, 4,
5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25,
26, 27, 28, 29 or 30) conservative amino acid mutations (preferably
substitutions, insertions or deletions) compared to the amino acid
sequence set forth in SEQ ID NO: 14;
20 (3) a heavy chain variable region comprising or consisting of:
an amino acid sequence set forth in SEQ ID NO: 16, or
a sequence having at least 85%, preferably 86%, 87%, 88%, 89%, 90%,
91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity
to the sequence set forth in SEQ ID NO: 16, or
25 an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7,
8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29
or 30) conservative amino acid mutations (preferably substitutions, insertions or
deletions) compared to the amino acid sequence set forth in SEQ ID NO: 16; and
a light chain variable region comprising or consisting of:
30 an amino acid sequence set forth in SEQ ID NO: 18, or

a sequence having at least 85%, preferably 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 18, or

an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 18; and

(4) a heavy chain variable region comprising or consisting of:

an amino acid sequence set forth in SEQ ID NO: 20, or

a sequence having at least 85%, preferably 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 20, or

an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 20; and

a light chain variable region comprising or consisting of:

an amino acid sequence set forth in SEQ ID NO: 22, or

a sequence having at least 85%, preferably 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence set forth in SEQ ID NO: 22, or

an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the amino acid sequence set forth in SEQ ID NO: 22.

4. The antibody or the antigen-binding fragment thereof according to any one of claims 1–3, comprising HCDR1–3 and LCDR1–3 as shown below, wherein

the amino acid sequences of the 3 CDR regions of the heavy chain variable region are as follows:

HCDR1: GYTFTSYW (SEQ ID NO: 5),

HCDR2: IDPSDSET (SEQ ID NO: 6), and

5 HCDR3: ARLYRWYFDV (SEQ ID NO: 7); and

the amino acid sequences of the 3 CDR regions of the light chain variable region are as follows:

LCDR1: EIVGTY (SEQ ID NO: 8),

LCDR2: GAS (SEQ ID NO: 9), and

10 LCDR3: GQSYNFPYT (SEQ ID NO: 10).

5. The antibody or the antigen-binding fragment thereof according to any one of claims 1–4, wherein the antibody further comprises a heavy chain constant region and a light chain constant region, and the constant regions are derived from species other than murine, e.g., from a human antibody, preferably from a human IgG or IgM, more preferably from IgG1; preferably, the heavy chain constant region is Ig gamma-1 chain C region, ACCESSION No. P01857 (SEQ ID NO: 58) or Ig gamma-4 chain C region, ACCESSION No. P01861.1 (SEQ ID NO: 56); the light chain constant region is Ig kappa chain C region, ACCESSION No. P01834 (SEQ ID NO: 57).

20

6. The antibody or the antigen-binding fragment thereof according to any one of claims 1–5, wherein the antibody comprises a combination of a heavy chain and a light chain selected from the group consisting of the following:

(1) a heavy chain set forth in SEQ ID NO: 59 and a light chain set forth in SEQ ID NO: 60;

(2) a heavy chain set forth in SEQ ID NO: 61 and a light chain set forth in SEQ ID NO: 62;

(3) a heavy chain set forth in SEQ ID NO: 63 and a light chain set forth in SEQ ID NO: 64;

- (4) a heavy chain set forth in SEQ ID NO: 65 and a light chain set forth in SEQ ID NO: 66;
- (5) a heavy chain set forth in SEQ ID NO: 67 and a light chain set forth in SEQ ID NO: 68; and
- 5 (6) a heavy chain set forth in SEQ ID NO: 69 and a light chain set forth in SEQ ID NO: 70.
7. The antibody or the antigen-binding fragment thereof according to any one of claims 1–6, wherein the antibody further comprises an amino acid mutation introduced
- 10 at position 234 and/or 235 according to the EU numbering system.
8. The antibody or the antigen-binding fragment thereof according to any one of claims 1–7, wherein the antibody comprises mutation L234A and/or L235A according to the EU numbering system.
- 15
9. The antibody or the antigen-binding fragment thereof according to claim 8, wherein the antibody comprises a combination of a heavy chain and a light chain selected from the group consisting of the following:
- (1) a heavy chain set forth in SEQ ID NO: 59 and a light chain set forth in
- 20 SEQ ID NO: 60;
- (2) a heavy chain set forth in SEQ ID NO: 61 and a light chain set forth in SEQ ID NO: 62; and
- (3) a heavy chain set forth in SEQ ID NO: 63 and a light chain set forth in
- 25 SEQ ID NO: 64.
10. An isolated polypeptide comprising:
- (1) sequences set forth in SEQ ID NOs: 5, 6 and 7, wherein the polypeptide, as part of an anti-human CD47 antibody, specifically binds to human CD47, the antibody further comprising sequences set forth in SEQ ID NOs: 8, 9 and 10;

(2) sequences set forth in SEQ ID NOs: 8, 9 and 10, wherein the polypeptide, as part of an anti-human CD47 antibody, specifically binds to human CD47, the antibody further comprising sequences set forth in SEQ ID NOs: 5, 6 and 7;

5 (3) a sequence selected from sequences set forth in SEQ ID NOs: 2, 12, 16 and 20, a sequence having at least 85%, preferably 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 10 27, 28, 29 or 30) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence, wherein the polypeptide, as part of an anti-human CD47 antibody, specifically binds to human CD47, the antibody further comprising a sequence selected from sequences set forth in SEQ ID NOs: 4, 14, 18 and 22, a sequence having at least 85%, preferably 86%, 15 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence; or

20 (4) a sequence selected from sequences set forth in SEQ ID NOs: 4, 14, 18 and 22, a sequence having at least 85%, preferably 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 25 27, 28, 29 or 30) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence, wherein the polypeptide, as part of an anti-human CD47 antibody, specifically binds to human CD47, the monoclonal antibody further comprising a sequence selected from sequences set forth in SEQ ID NOs: 2, 12, 16 and 20, a sequence having at least 85%, 30 preferably 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%,

98% or 99% or more sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence.

11. The antibody or the antigen-binding fragment thereof according to any one of claims 1–10, wherein the antigen-binding fragment is selected from Fab, Fab', F(ab')₂, Fd, Fv, dAb, Fab/c, complementarity determining region (CDR) fragment, single chain antibody (e.g., scFv), bivalent antibody and domain antibody.

12. The antibody or the antigen-binding fragment thereof according to any one of claims 1–11, wherein the antibody is a humanized antibody, a chimeric antibody or a multispecific antibody (e.g., a bispecific antibody).

13. The antibody or the antigen-binding fragment thereof according to any one of claims 1–12, wherein the antibody binds to human CD47 protein with a KD less than about 10⁻⁵ M, e.g., less than about 10⁻⁶ M, 10⁻⁷ M, 10⁻⁸ M, 10⁻⁹ M or 10⁻¹⁰ M or less.

14. The antibody or the antigen-binding fragment thereof according to any one of claims 1–13, wherein the antibody binds to human CD47 protein with an EC50 less than about 100 nM, e.g., less than about 10 nM, 1 nM, 0.9 nM, 0.8 nM, 0.7 nM, 0.6 nM, 0.5 nM, 0.4 nM, 0.3 nM, 0.2 nM, or 0.1 nM or less.

15. An isolated polynucleotide encoding a polypeptide selected from:
(1) a polypeptide comprising sequences set forth in SEQ ID NOs: 5, 6 and 7, wherein the polypeptide, as part of an anti-human CD47 antibody, specifically binds to human CD47, the antibody further comprising sequences set forth in SEQ ID NOs: 8, 9 and 10;

(2) a polypeptide comprising sequences set forth in SEQ ID NOs: 8, 9 and 10, wherein the polypeptide, as part of an anti-human CD47 antibody, specifically binds to human CD47, the antibody further comprising sequences set forth in SEQ ID NOs: 5, 6 and 7;

- 5 (3) a polypeptide comprising a sequence selected from sequences set forth in SEQ ID NOs: 2, 12, 16 and 20, a sequence having at least 85%, preferably 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence, or a polypeptide of an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13,
10 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence, wherein the polypeptide, as part of an anti-human CD47 antibody, specifically binds to human CD47, the antibody further comprising a sequence selected from sequences set forth in SEQ ID NOs: 4, 14,
15 18 and 22, a sequence having at least 85%, preferably 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) conservative amino acid mutations
20 (preferably substitutions, insertions or deletions) compared to the sequence; or
(4) a polypeptide comprising a sequence selected from sequences set forth in SEQ ID NOs: 4, 14, 18 and 22, a sequence having at least 85%, preferably 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence, or a polypeptide of an amino acid
25 sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence, wherein the polypeptide, as part of an anti-human CD47 antibody, specifically binds to human CD47, the antibody further
30 comprising a sequence selected from sequences set forth in SEQ ID NOs: 2, 12,

16 and 20, a sequence having at least 85%, preferably 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence, or an amino acid sequence having one or more (preferably 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30) conservative amino acid mutations (preferably substitutions, insertions or deletions) compared to the sequence.

16. The isolated polynucleotide according to claim 15, wherein
(1) the polynucleotide molecule comprises or consists of a nucleotide sequence set forth in SEQ ID NO: 1, 11, 15 or 19, or a sequence having at least 85%, preferably 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence;
(2) the polynucleotide molecule comprises or consists of a nucleotide sequence set forth in SEQ ID NO: 3, 13, 17 or 21, or a sequence having at least 85%, preferably 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or more sequence identity to the sequence.

17. A vector, comprising the polynucleotide molecule according to claim 15 or 16.

18. A host cell, comprising the polynucleotide molecule according to claim 15 or 16 or the vector according to claim 17.

19. A method for preparing the antibody or the antigen-binding fragment thereof according to any one of claims 1–14, comprising: culturing the host cell according to claim 18 in a suitable condition, and isolating the antibody or the antigen-binding fragment thereof from the cell cultures.

20. An antibody conjugate, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1–14 and a conjugated moiety coupled thereto, wherein the conjugated moiety is a purification tag (e.g., a His tag), a cytotoxic agent or

a detectable label; preferably, the conjugated moiety is a radioisotope, a luminescent substance, a colored substance, an enzyme or polyethylene glycol.

21. A multispecific antibody, preferably a bispecific antibody, comprising the
5 antibody or the antigen-binding fragment thereof according to any one of claims 1–14, and an antibody or an antigen-binding fragment against another antigen and/or another antigenic epitope.

22. A fusion protein, comprising the antibody or the antigen-binding fragment
10 thereof according to any one of claims 1–14.

23. A kit, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1–14, or the antibody conjugate according to claim 20, the multispecific antibody according to claim 21 or the fusion protein according to
15 claim 22.

24. The kit according to claim 23, further comprising a second antibody that specifically identifies the antibody or the antigen-binding fragment thereof; optionally, the second antibody further comprising a detectable label, such as a radioisotope, a
20 luminescent substance, a colored substance, an enzyme or polyethylene glycol.

25. A hybridoma cell line and a monoclonal antibody produced by the hybridoma cell line, wherein the hybridoma cell line is hybridoma cell line LT012 under CCTCC NO. 2018135.

26. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1–14, the antibody conjugate according to claim 20, the multispecific antibody according to claim 21 or the fusion protein according to claim 22 in detecting the presence or level of human CD47 in a sample, or in preparing a kit for detecting the
30 presence or level of human CD47 in a sample.

27. A pharmaceutical composition, comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1–14, the antibody conjugate according to claim 20, the multispecific antibody according to claim 21 or the fusion protein
5 according to claim 22, and optionally, a pharmaceutically acceptable carrier and/or excipient.

28. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1–14, the antibody conjugate according to claim 20, the multispecific
10 antibody according to claim 21 or the fusion protein according to claim 22 in preparing:
a medicament for blocking the binding of human CD47 to human SIRP α ,
a medicament for blocking the activity of human CD47 or down-regulating the level of human CD47, or
a medicament for blocking cellular response mediated by the binding of human
15 SIRP α to CD47, or.

~~29. Use of the antibody or the antigen-binding fragment thereof according to any one of claims 1–14, the antibody conjugate according to claim 20, the multispecific antibody according to claim 21 or the fusion protein according to claim 22 in treating a tumor, or~~
20 ~~in preparing~~ a medicament for treating a tumor, wherein the tumor is preferably a tumor expressing CD47, preferably cancer, e.g., a hematological malignancy or a solid tumor, more preferably lymphoma, colon cancer or breast cancer, more preferably non-Hodgkin lymphoma, and even more preferably B cell lymphoma cells.

25 ~~30~~29. The use according to claim ~~29~~28, wherein the medicament is in a form suitable for injection, preferably in a form suitable for administration by subcutaneous injection, intradermal injection, intravenous injection, intramuscular injection or intralesional injection.

3430. An ~~*in vivo*~~ or *in vitro* method, comprising administering a cell comprising the antibody or the antigen-binding fragment thereof according to any one of claims 1–14, the antibody conjugate according to claim 20, the multispecific antibody according to claim 21 or the fusion protein according to claim 22, or administering to a subject in need an effective amount of the antibody or the antigen-binding fragment thereof, the antibody conjugate, the multispecific antibody or the fusion protein, wherein the method is selected from:

a method for blocking the binding of CD47 to human SIRP α ,

a method for blocking the activity of human CD47 or down-regulating the level of human CD47, and

a method for blocking cellular response mediated by the binding of human SIRP α to CD47.