

CLAIMS

1. An isolated antigen-binding polypeptide that binds to CD47 or an antigen-binding portion thereof, wherein the antigen-binding polypeptide comprises:
 - a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 5;
 - a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 10;
 - a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 15;
 - a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 20;
 - a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 25; and
 - a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 30.
2. The antigen-binding polypeptide or the antigen-binding portion thereof according to claim 1, wherein the antigen-binding polypeptide comprises a heavy chain variable region comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 41, and a light chain variable region comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 42; or comprises a heavy chain variable region comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 87, and a light chain variable region comprising an amino acid sequence having at least 80% identity to the amino acid sequence of SEQ ID NO: 88.
3. The antigen-binding polypeptide or the antigen-binding portion thereof according to claim 1 or 2, wherein the antigen-binding polypeptide comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 41, and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 42; the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 87, and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 88; the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 81, and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 82; or the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 79, and the light chain variable region comprises the amino acid sequence of SEQ ID NO: 80.
4. The antigen-binding polypeptide or the antigen-binding portion thereof according to any one of claims 1–3, wherein the antigen-binding polypeptide comprises a heavy chain variable region with the amino acid sequence of SEQ ID NO: 79 and a light chain variable region with the amino acid sequence of SEQ ID NO: 80.
5. The antigen-binding polypeptide or the antigen-binding portion thereof according to any one of claims 1–4, wherein the antigen-binding polypeptide comprises:
 - a heavy chain having an amino acid sequence having at least 80% identity to an amino acid sequence of SEQ ID NO: 105, and a light chain having an amino acid sequence having at least 80% identity to an amino acid sequence of SEQ ID NO: 107;
 - a heavy chain having an amino acid sequence having at least 80% identity to an amino acid sequence of SEQ ID NO: 181, and a light chain having an amino acid sequence having at least 80% identity to an amino acid sequence of SEQ ID NO: 183; or
 - a heavy chain having an amino acid sequence having at least 80% identity to an amino acid sequence of SEQ ID NO: 185, and a light chain having an amino acid sequence having at least 80% identity to an amino acid sequence of SEQ ID NO: 187.
6. The antigen-binding polypeptide or the antigen-binding portion thereof according to any one of claims 1–5, wherein
 - the antigen-binding polypeptide comprises a heavy chain according to SEQ ID NO: 105 and a light chain according to SEQ ID NO: 107;
 - the antigen-binding polypeptide comprises a heavy chain according to SEQ ID NO: 181 and a light chain according to SEQ ID NO: 183; or
 - the antigen-binding polypeptide comprises a heavy chain according to SEQ ID NO: 185 and a light chain according to SEQ ID NO: 187.
7. The antigen-binding polypeptide or the antigen-binding portion thereof according to any one of claims 1–6, wherein the antigen-binding polypeptide comprises a heavy chain according to SEQ ID NO: 181 and a light chain according to SEQ ID NO: 183.
8. The antigen-binding polypeptide or the antigen-binding portion thereof according to any one of claims 1–7, wherein the antigen-binding polypeptide is chimeric or humanized.
9. The antigen-binding polypeptide or the antigen-binding portion thereof according to any one of claims 1–8, wherein the antigen-binding polypeptide or the antigen-binding portion thereof is selected from the group consisting of monoclonal antibodies, fusion proteins, multispecific antibodies, Fab fragments, Fab' fragments, F(ab')₂ fragments, Fv fragments, and scFv.
10. The antigen-binding polypeptide or the antigen-binding portion thereof according to any one of claims 1–9, wherein the antigen-binding polypeptide is of IgG1, IgG2, IgG3 or IgG4 subclass.
11. The antigen-binding polypeptide or the antigen-binding portion thereof according to claim 10, wherein the

antigen-binding polypeptide of IgG4 subclass has an S228P mutation according to the EU numbering index.

12. The antigen-binding polypeptide or the antigen-binding portion thereof according to any one of claims 1–11, wherein the antigen-binding polypeptide or the antigen-binding portion thereof has one of, or a combination of several of, the following properties:

(a) binding to CD47 with a K_D value of 1.89×10^{-8} or less;

(b) blocking binding of CD47 to SIRP α ;

(c) promoting macrophage-mediated phagocytosis of CD47-expressing cells;

(d) not significantly inducing apoptosis of CD4⁺ T cells;

(e) not causing substantial hematocytopenia, anemia or red cell agglutination; and

(f) the antigen-binding polypeptide or the antigen-binding portion thereof having a melting temperature $T \geq 62$ °C and an aggregation temperature $T_{agg} \geq 61$ °C.

13. An immunoconjugate comprising the antigen-binding polypeptide or the antigen-binding portion thereof according to any one of claims 1–12 and a therapeutic agent linked or conjugated to the antigen-binding polypeptide or the antigen-binding portion thereof.

14. The immunoconjugate according to claim 13, wherein the therapeutic agent is a cytotoxic drug, a radioisotope, an immunomodulator or an antibody.

15. A composition comprising a component A and a pharmaceutically acceptable carrier, wherein the component A is the antigen-binding polypeptide or the antigen-binding portion thereof according to any one of claims 1–12 or the immunoconjugate according to claim 13 or 14.

16. An isolated nucleic acid encoding the antigen-binding polypeptide or the antigen-binding portion thereof according to any one of claims 1–12.

17. A vector comprising the isolated nucleic acid according to claim 16.

18. A host cell comprising the vector according to claim 17 or into whose genome the isolated nucleic acid according to claim 16 is integrated.

19. A method for preparing the antigen-binding polypeptide or the antigen-binding portion thereof according to any one of claims 1–12, comprising: culturing the host cell according to claim 18 under conditions suitable for expression of the nucleic acid encoding the antigen-binding polypeptide or the antigen-binding portion thereof according to any one of claims 1–12, and isolating the antigen-binding polypeptide or the antigen-binding portion thereof expressed.

20. Use of the antigen-binding polypeptide or the antigen-binding portion thereof according to any one of claims 1–12, the immunoconjugate according to claim 13 or 14, or the composition according to claim 15 in the preparation of a medicament for reducing a tumor or inhibiting tumor cell growth in a subject.

21. Use of the antigen-binding polypeptide or the antigen-binding portion thereof according to any one of claims 1–12, the immunoconjugate according to claim 13 or 14, or the composition according to claim 15 in the preparation of a medicament for treating cancer in a subject in need thereof.

22. The use according to claim 21, wherein the cancer is selected from the group consisting of leukemia, lymphoma, ovarian cancer, breast cancer, endometrial cancer, colon cancer, rectal cancer, bladder cancer, urothelial cancer, lung cancer, bronchial cancer, bone cancer, prostate cancer, pancreatic cancer, gastric cancer, hepatocellular cancer, gallbladder cancer, bile duct cancer, esophageal cancer, renal cell cancer, thyroid cancer, head and neck cancer, testicular cancer, endocrine adenocarcinoma, adrenal cancer, pituitary gland cancer, skin cancer, soft tissue cancer, vascular cancer, brain cancer, neural cancer, eye cancer, meningeal cancer, oropharyngeal cancer, hypopharynx cancer, cervical cancer, and uterine cancer, glioblastoma, medulloblastoma, astrocytoma, glioma, meningioma, gastrinoma, neuroblastoma, melanoma, acute myeloid leukemia, myelodysplastic syndrome and sarcoma.

23. Use of the antigen-binding polypeptide or the antigen-binding portion thereof according to any one of claims 1–12, the immunoconjugate according to claim 13 or 14, or the composition according to claim 15 in the preparation of a medicament for promoting macrophage phagocytosis in a subject.