

Claims

1. A fusion protein, comprising: a first binding domain that specifically binds a tumor-associated antigen; and a second binding domain that specifically binds a CD47 protein; wherein said second binding domain comprises a mutant of a human SIRP α variant 1, said mutant comprises substitution, deletion or addition of the amino acid residue at one or more positions from site 33 to site 149, compared to the sequence as shown in SEQ ID NO: 50, wherein said mutant comprises amino acid substitutions at one or more amino acid residues selected from the group consisting of: R22, I29, I61, V63, E77, Q82, K83, E84, V93, D95, D96, K98, N100, R107, G109 and V132.

2. The fusion protein according to claim 1, wherein said mutant comprises amino acid substitutions at amino acid residues selected from the group consisting of:

- (1) I61, V63, E77, E84, V93, L96, K98, N100 and V132;
- (2) I61, E77, Q82, K83 and E84;
- (3) I61, V63, K83, E84 and V132;
- (4) I61, E77, E84, R107 and V132;
- (5) I61, V63, E77, K83, E84 and N100;
- (6) I61, E77, Q82, K83, E84 and R107;
- (7) I61, E77, Q82, E84, V93, L96, N100, R107, G109 and V132;
- (8) I61, E77, Q82, K83, E84 and V132;
- (9) I61;
- (10) I61, D95, L96, G109 and V132;
- (11) I61, D95, L96, K98, G109 and V132;
- (12) I61, E77, E84, V93, R107 and V132;
- (13) E77, L96, N100, G109 and V132;
- (14) I61, V63, Q82, E84, D95, L96, N100 and V132;
- (15) I61, E77, Q82, K83, E84, V93, D95, L96, K98, N100 and V132;
- (16) I61, E77, Q82, K83, E84 and V93;
- (17) I61, V63, E77, K83, E84, D95, L96, K98 and N100;
- (18) I61, V63, E77, K83, D95, L96, K98, N100 and G109;
- (19) I61, E77, Q82, E84, V93, D95, L96, K98 and N100; and
- (20) I61, V63, E77, Q82 and E84.

3. The fusion protein according to any one of claims 1-2, wherein said mutant comprises one or more amino acid substitutions selected from the group consisting of: R22C, I29L, I61L/V/F, V63I, E77I/N/Q/K/H/M/R/N/V/L, Q82S/R/G/N, K83R, E84K/H/D/R/G, V93L/A, D95H/R/E, D96S/T, K98R, N100G/K/D/E, R107N/S, G109R/H and V132L/R/I/S.

4. The fusion protein according to any one of claims 1-3, wherein said mutant comprises an amino acid sequence as shown in any one of SEQ ID NOs: 51-70.

5. The fusion protein according to any one of claims 1-4, wherein said first binding domain comprises an antibody or an antigen-binding fragment or a variant thereof.

6. The fusion protein according to any one of claims 1-5, wherein said tumor-associated antigen is selected from the group consisting of: CD38, AXL and Trop2.

7. The fusion protein according to claim 6, wherein the first binding domain comprises an anti-CD38 antibody or an antigen-binding fragment or a variant thereof.

8. The fusion protein according to claim 7, wherein said antibody comprises a heavy chain of the antibody or a fragment thereof, the heavy chain of the antibody or the fragment thereof comprises HCDR1-3, the amino acid sequences of the HCDR1-3 are SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6, successively.

9. The fusion protein according to any one of claims 7-8, wherein the antibody comprises a light chain of the antibody or a fragment thereof, the light chain of the antibody or the fragment thereof comprises LCDR1-3, the amino acid sequences of said LCDR1-3 are SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, successively.

10. The fusion protein according to claim 6, wherein the first binding domain comprises an anti-AXL antibody or an antigen-binding fragment or a variant thereof.

11. The fusion protein according to claim 10, wherein the antibody comprises a heavy chain of the antibody or a fragment thereof, the heavy chain of the antibody or the fragment thereof comprises HCDR1-3, the amino acid sequences of the HCDR1-3 are SEQ ID NO: 25, SEQ ID NO: 26 and SEQ ID NO: 27, successively.

12. The fusion protein according to any one of claims 10-11, wherein the antibody comprises a light chain of the antibody or a fragment thereof, the light chain of the antibody or the fragment thereof comprises LCDR1-3, the amino acid sequences of the LCDR1-3 are SEQ ID NO: 22, SEQ ID NO: 23 and SEQ ID NO: 24, successively.

13. The fusion protein according to claim 6, wherein the first binding domain comprises

an anti-Trop2 antibody or an antigen-binding fragment or a variant thereof.

14. The fusion protein according to claim 13, wherein the antibody comprises a heavy chain of the antibody or a fragment thereof, the heavy chain of the antibody or the fragment thereof comprises HCDR1-3, the amino acid sequences of the HCDR1-3 are SEQ ID NO: 39, SEQ ID NO: 40 and SEQ ID NO: 41, successively.

15. The fusion protein according to any one of claims 13-14, wherein the antibody comprises a light chain of the antibody or a fragment thereof, the light chain of the antibody or the fragment thereof comprises LCDR1-3, the amino acid sequences of the LCDR1-3 are SEQ ID NO: 36, SEQ ID NO: 37 and SEQ ID NO: 38, successively.

16. The fusion protein according to any one of claims 1-15, wherein the first binding domain is located at N-terminal of the second binding domain.

17. The fusion protein according to any one of claims 1-16, wherein the fusion protein further comprises a linker, the linker is located at C-terminal of the first binding domain and located at N-terminal of the second binding domain.

18. The fusion protein according to any one of claims 1-17, comprising at least two of the second binding domain, and each of the second binding domains is located at C-terminal of the first binding domain respectively.

19. The fusion protein according to any one of claims 1-18, comprising a first polypeptide chain and a second polypeptide chain, wherein,

the first polypeptide chain comprises the amino acid sequences as set forth in SEQ ID NO: 11, and the second polypeptide chain comprises the amino acid sequences as set forth in SEQ ID NO: 75,

the first polypeptide chain comprises the amino acid sequences as set forth in SEQ ID NO: 11, and the second polypeptide chain comprises the amino acid sequences as set forth in SEQ ID NO: 76,

the first polypeptide chain comprises the amino acid sequences as set forth in SEQ ID NO: 46, and the second polypeptide chain comprises the amino acid sequences as set forth in SEQ ID NO: 78, or

the first polypeptide chain comprises the amino acid sequences as set forth in SEQ ID NO: 32, and the second polypeptide chain comprises the amino acid sequences as set forth in SEQ ID NO: 77.

20. A composition, comprising the fusion protein according to any one of claims 1-19, and optionally, a pharmaceutically acceptable excipient.

21. A use of the fusion protein according to any one of claims 1-19, or the composition according to claim 20 in the preparation of a medicament, wherein the medicament is used for treating a tumor or an autoimmune disease.