

WHAT IS CLAIMED IS

1. A nucleic acid molecule encoding a chimeric antigen receptor, wherein the chimeric antigen receptor comprises an scFv targeted to BAFF-R, wherein the scFv comprises a light chain variable region and a heavy chain variable region, wherein

the light chain variable region comprises CDR L1 (SEQ ID NO:1), CDR L2 (SEQ ID NO:2) and CDR L3 (SEQ ID NO:3) and the heavy chain variable region comprises CDR H1 (SEQ ID NO:4), CDR H2 (SEQ ID NO:5), and CDR H3 (SEQ ID NO:6), or

the light chain variable region comprises CDR L1 (SEQ ID NO:7), CDR L2 (SEQ ID NO:8) and CDR L3 (SEQ ID NO:9) and the heavy chain variable region comprises CDR H1 (SEQ ID NO:10), CDR H2 (SEQ ID NO:11), and CDR H3 (SEQ ID NO:12),

wherein the chimeric antigen receptor further comprises:

(i) a transmembrane domain selected from the group consisting of: a CD4 transmembrane domain or variant thereof comprising 1-5 amino acid modifications, a CD8 transmembrane domain or variant thereof comprising 1-5 amino acid modifications, a CD28 transmembrane domain or a variant thereof comprising 1-5 amino acid modifications, and a CD3 ζ transmembrane domain or a variant thereof comprising 1- 5 amino acid modifications;

(ii) a costimulatory domain; and

(iii) CD3 ζ signaling domain or a variant thereof comprising 1-5 amino acid modifications.

2. The nucleic acid molecule of claim 1, wherein the costimulatory domain is selected from the group consisting of a CD28 costimulatory domain or a variant thereof comprising 1-5 amino acid modifications, a 4-1BB costimulatory domain or a variant thereof comprising 1-5 amino acid modifications and an OX40 costimulatory domain or a variant thereof comprising 1-5 amino acid modifications.

3. The nucleic acid molecule of claim 1 or claim 2, wherein the light chain variable region comprises CDR L1 (SEQ ID NO:1), CDR L2 (SEQ ID NO:2) and CDR L3 (SEQ ID NO:3); and

the heavy chain variable region comprises CDR H1 (SEQ ID NO:4), CDR H2 (SEQ ID NO:5), and CDR H3 (SEQ ID NO:6).

4. The nucleic acid molecule of claim 1 or claim 2, wherein the light chain variable region comprises CDR L1 (SEQ ID NO:7), CDR L2 (SEQ ID NO:8) and CDR L3 (SEQ ID NO:9); and the heavy chain variable region comprises CDR H1 (SEQ ID NO:10), CDR H2 (SEQ ID NO:11), and CDR H3 (SEQ ID NO:12).

5. The nucleic acid molecule of any one of claims 1 to 4, wherein the scFv comprises a spacer between the heavy chain variable domain and the light chain variable domain.

6. The nucleic acid molecule of any one of claims 1 to 5, wherein the chimeric antigen receptor comprises a spacer region located between the scFv and the transmembrane domain.

7. The nucleic acid molecule of any one of claims 2 to 6, wherein the 4-1BB costimulatory domain comprises the amino acid sequence of SEQ ID NO:41.

8. The nucleic acid molecule of any one of claims 1 to 7, wherein the CD3 ζ signaling domain comprises the amino acid sequence of SEQ ID NO:42.

9. The nucleic acid molecule of any one of claims 1 to 8, wherein a linker of 3 to 15 amino acids is located between the co-stimulatory domain and the CD3 ζ signaling domain or variant thereof.

10. The nucleic acid molecule of claim 1, wherein the scFv comprises:

(i) a light chain variable domain comprising an amino acid sequence of SEQ ID NO:14 and a heavy chain variable domain comprising an amino acid sequence of SEQ ID NO:16;

(ii) a light chain variable domain comprising an amino acid sequence of SEQ ID NO:18 and a heavy chain variable domain comprising an amino acid sequence of SEQ ID NO:24;

(iii) a light chain variable domain comprising an amino acid sequence of SEQ ID NO:20 and a heavy chain variable domain comprising an amino acid sequence of SEQ ID NO:26;

- (iv) a light chain variable domain comprising an amino acid sequence of SEQ ID NO:22 and a heavy chain variable domain comprising an amino acid sequence of SEQ ID NO:28;
- (v) a light chain variable domain comprising an amino acid sequence of SEQ ID NO:30 and a heavy chain variable domain comprising an amino acid sequence of SEQ ID NO:32;
- (vi) a light chain variable domain comprising an amino acid sequence of SEQ ID NO:36 and a heavy chain variable domain comprising an amino acid sequence of SEQ ID NO:33;
- (vii) a light chain variable domain comprising an amino acid sequence of SEQ ID NO:37 and a heavy chain variable domain comprising an amino acid sequence of SEQ ID NO:34; or
- (viii) a light chain variable domain comprising an amino acid sequence of SEQ ID NO:38 and a heavy chain variable domain comprising an amino acid sequence of SEQ ID NO:35.

11. The nucleic acid molecule of claim 1, wherein the scFv comprises an amino acid sequence selected from SEQ ID NOs: 43 and 44.

12. A population of human T cells transduced by a vector comprising an expression cassette comprising the nucleic acid molecule of any one of claims 1 to 11.

13. The population of human T cells of claim 12, wherein the T cells comprise CD4⁺ T_N cells and CD8⁺ T_N cells.

14. Use of the population of human T cells of claim 12 or claim 13 in the manufacture of a medicament for treating cancer in a subject in need thereof.

15. The use of claim 14, wherein the cancer is lymphoma, leukemia or myeloma.

16. The use of claim 15, wherein the lymphoma is mantle cell lymphoma, follicular lymphoma, diffuse large B-cell lymphoma, marginal zone lymphoma or Burkitt's lymphoma.

17. The use of claim 15, wherein the leukemia is lymphoblastic leukemia, chronic lymphocytic leukemia or hairy cell leukemia.

18. The use of claim 15, wherein the myeloma is multiple myeloma.

19. The use of any one of claims 14 to 18, wherein the subject is to be administered a second therapeutic agent.

20. The use of any one of claims 14 to 19, wherein the population of T cells are autologous or allogeneic to the patient.

21. Use of the population of human T cells of claim 12 or claim 13 in the manufacture of a medicament for treating an autoimmune disease in a subject in need thereof.

22. The use of claim 21, wherein the autoimmune disease is rheumatoid arthritis, systemic Lupus erythematosus, multiple sclerosis, glomerulonephritis, Sjögren's Syndrome or autoimmune hemolytic anemia.