Claims

1. A bispecific chimeric antigen receptor targeting BCMA-CD19, comprising an extracellular antigen recognition domain, a hinge region, a transmembrane region and an intracellular domain; wherein the extracellular antigen recognition domain comprises an anti-BCMA extracellular antigen recognition domain and an anti-CD19 extracellular antigen recognition domain;

the anti-BCMA extracellular antigen recognition domain comprises BCMA VH and BCMA VL, wherein amino acid sequences of BCMA VH complementarity-determining regions CDR1, CDR2 and CDR3 respectively comprise amino acid sequences as represented by SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, and amino acid sequences of BCMA VL complementarity-determining regions CDR1, CDR2 and CDR3 respectively comprise amino acid sequences as represented by SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6.

2. The bispecific chimeric antigen receptor according to claim 1, wherein the anti-CD19 extracellular antigen recognition domain comprises CD19 VH and CD19 VL, wherein amino acid sequences of CD19 VH complementarity-determining regions CDR1, CDR2 and CDR3 respectively comprise amino acid sequences as represented by SEQ ID NO: 7, SEQ ID NO: 8 and SEQ ID NO: 9, and amino acid sequences of CD19 VL complementarity-determining regions CDR1, CDR2 and CDR3 respectively comprise amino acid sequences as represented by SEQ ID NO: 10, SEQ ID NO: 11 and SEQ ID NO: 12.

3. The bispecific chimeric antigen receptor according to claim 1 or 2, wherein the BCMA VH sequence comprises the amino acid sequence as represented by SEQ ID NO: 13, and the BCMA VL sequence comprises the amino acid sequence as represented by SEQ ID NO: 14; or
the BCMA VH sequence comprises the amino acid sequence as represented by SEQ ID NO: 15, and the BCMA VL sequence comprises the amino acid sequence as represented by SEQ ID NO: 16.

4. The bispecific chimeric antigen receptor according to claim 2, wherein the CD19 VH sequence comprises the amino acid sequence as represented by SEQ ID NO: 17, and the CD19 VL sequence comprises the amino acid sequence as represented by SEQ ID NO: 18.

5. The bispecific chimeric antigen receptor according to claim 1, wherein the extracellular antigen recognition domain of the bispecific chimeric antigen receptor comprises any one structure selected from the group consisting of: CD19 VL sequence-1st linker sequence-CD19 VH sequence-2nd linker sequence-BCMA VL sequence-3rd linker sequence-BCMA VH sequence, BCMA VL sequence-4th linker

sequence-BCMA VH sequence-5th linker sequence-CD19 VL sequence-6th linker sequence-CD19 VH sequence, BCMA VL sequence-7th linker sequence-CD19 VL sequence-8th linker sequence-CD19 VH sequence-9th linker sequence-BCMA VH sequence, and CD19 VL sequence-10th linker sequence-BCMA VL sequence-11th linker sequence-BCMA VH sequence-12th linker sequence-CD19 VH sequence;

optionally, the extracellular antigen recognition domain of the bispecific chimeric antigen receptor comprises any one structure selected from the group consisting of: BCMA VL sequence-7th linker sequence-CD19 VL sequence-8th linker sequence-CD19 VH sequence-9th linker sequence-BCMA VH sequence, and CD19 VL sequence-10th linker sequence-BCMA VL sequence-11th linker sequence-BCMA VH sequence-12th linker sequence-CD19 VH sequence;

further optionally, the 1st linker sequence, the 2nd linker sequence, the 3rd linker sequence, the 4th linker sequence, the 5th linker sequence, the 6th linker sequence, the 7th linker sequence, the 8th linker sequence, the 9th linker sequence, the 10th linker sequence, the 11th linker sequence, and the 12th linker sequence are each independently selected from one or more of the following sequences: SEQ ID NO: 34, SEQ ID NO: 35, and SEQ ID NO: 36.

6. The bispecific chimeric antigen receptor according to claim 5, wherein the extracellular antigen recognition domain of the bispecific chimeric antigen receptor comprises the amino acid sequence as represented by SEQ ID NO: 19 or SEQ ID NO: 20.

7. The bispecific chimeric antigen receptor according to claim 1, wherein the hinge region is derived from one or more of IgG1, IgG4, CD4, CD7, CD28, CD84 and CD8α; optionally, the amino acid of the hinge region is derived from CD8α; further optionally, the amino acid sequence of the hinge region comprises the amino acid sequence as represented by SEQ ID NO: 21; and/or

wherein the transmembrane region is derived from one or more of CD3, CD4, CD7, CD8α, CD28, CD80, CD86, CD88, 4-1BB, CD152, OX40 and Fc70; optionally, the amino acid of the transmembrane region is derived from CD8α; further optionally, the amino acid sequence of the transmembrane region comprises the amino acid sequence as represented by SEQ ID NO: 22.

8. The bispecific chimeric antigen receptor according to claim 1, wherein the intracellular domain comprises an intracellular signal transduction region; optionally, the intracellular signal transduction region is derived from one or more of CD3ζ, CD3γ, CD3δ, CD3ε, CD5, CD22, CD79a, CD79b, FcRγ, FcRβ, CD66d, DAP10, DAP12 and Syk; further optionally, the intracellular signal transduction region is derived from CD3ζ; even further optionally, the amino acid sequence of the

intracellular signal transduction region comprises the amino acid sequence as represented by SEQ ID NO: 23.

9. The bispecific chimeric antigen receptor according to claim 1, wherein the intracellular domain further comprises a costimulatory signal transduction region; optionally, the costimulatory signal transduction region is derived from one, two or more of CD2, CD3, CD7, CD27, CD28, CD30, CD40, CD83, CD244, 4-1BB, OX40, LFA-1, ICOS, LIGHT, NKG2C, NKG2D, DAP10, B7-H3 and MyD88; further optionally, the costimulatory signal transduction region is derived from CD28 or 4-1BB; even further optionally, the amino acid sequence of the costimulatory signal transduction region comprises the amino acid sequence as represented by SEQ ID NO: 24.

10. The bispecific chimeric antigen receptor according to any one of claims 1-9, further comprising a guiding peptide located at the N-terminus of the amino acid sequence of the chimeric antigen receptor; optionally, the guiding peptide is derived from CD8α; further optionally, the amino acid sequence of the guiding peptide comprises the amino acid sequence as represented by SEQ ID NO: 25.

11. The bispecific chimeric antigen receptor according to any one of claims 1-10, wherein the bispecific chimeric antigen receptor comprises the amino acid sequence as represented by SEQ ID NO: 28 or SEQ ID NO: 29.

12. An isolated nucleic acid molecule comprising a nucleotide sequence encoding the bispecific chimeric antigen receptor according to any one of claims 1-11;

optionally, the nucleotide sequence encoding the bispecific chimeric antigen receptor comprises:

1) a nucleotide sequence encoding a BCMA VH amino acid sequence as represented by SEQ ID NO: 13, which is represented by SEQ ID NO: 37; and a nucleotide sequence encoding a BCMA VL amino acid sequence as represented by SEQ ID NO: 14, which is represented by SEQ ID NO: 38; and/or

2) a nucleotide sequence encoding a CD19 VH amino acid sequence as represented by SEQ ID NO: 17, which is represented by SEQ ID NO: 39; and a nucleotide sequence encoding a CD19 VL amino acid sequence as represented by SEQ ID NO: 18, which is represented by SEQ ID NO: 40.

13. A vector comprising the isolated nucleic acid molecule according to claim 12;

optionally, the vector is an expression vector;

further optionally, the vector is a viral vector;

even further optionally, the vector is a lentiviral vector.

14. An engineered immune effector cell comprising the chimeric antigen receptor according to any one of claims 1-11, the isolated nucleic acid molecule according to claim 12 or the vector according to claim 13.

15. The engineered immune effector cell according to claim 14, wherein the engineered immune effector cell is selected from one or more of T lymphocyte, natural killer cell (NK cell), peripheral blood mononuclear cell (PBMC cell), pluripotent stem cell, T cell differentiated from pluripotent stem cell, NK cell differentiated from pluripotent stem cell, induced pluripotent stem cell (iPSC), T cell differentiated from induced pluripotent stem cell (iPSC-T), NK cell differentiated from induced pluripotent stem cell (iPSC-NK) and embryonic stem cell;

optionally, the engineered immune effector cell is a T lymphocyte;

further optionally, the source of the T lymphocyte is autologous T lymphocyte or allogeneic T lymphocyte.

16. A pharmaceutical composition comprising the engineered immune effector cell according to claim 14 or 15, and a pharmaceutically acceptable adjuvant; optionally, the pharmaceutically acceptable adjuvant includes a protective agent; optionally, the pharmaceutically acceptable adjuvant includes a cell cryopreservation solution.

17. The pharmaceutical composition according to claim 16, wherein the pharmaceutical composition is an intravenous injection.

18. Use of the chimeric antigen receptor according to any one of claims 1-11, the isolated nucleic acid molecule according to claim 12, the vector according to claim 13 or the engineered immune effector cell according to claim 14 or 15 in the preparation of a medicament, wherein the medicament is used for treating a disease or condition associated with the expression of BCMA.

19. The use according to claim 18, wherein the disease or condition associated with the expression of BCMA is cancer; optionally, the cancer is multiple myeloma; further optionally, the cancer is refractory or relapsed multiple myeloma.

20. The use according to claim 18, wherein the disease or condition associated with the expression of BCMA is an autoimmune disease; optionally, the autoimmune disease is selected from the group consisting of systemic lupus erythematosus, rheumatoid arthritis, idiopathic thrombocytopenic purpura, myasthenia gravis, and

autoimmune hemolytic anemia.

21. The engineered immune effector cell according to claim 14 or 15 or the pharmaceutical composition according to claim 16 or 17, for use in treating a disease or condition associated with the expression of BCMA.

22. The engineered immune effector cell or the pharmaceutical composition according to claim 21, wherein the disease or condition associated with the expression of BCMA is cancer; optionally, the cancer is multiple myeloma; further optionally, the cancer is refractory or relapsed multiple myeloma.

23. The engineered immune effector cell or the pharmaceutical composition according to claim 21, wherein the disease or condition associated with the expression of BCMA is an autoimmune disease; optionally, the autoimmune disease is selected from the group consisting of systemic lupus erythematosus, rheumatoid arthritis, idiopathic thrombocytopenic purpura, myasthenia gravis, and autoimmune hemolytic anemia.