Claims

1. A genetically engineered cell, wherein the cell expresses an exogenous receptor specifically binding to a target antigen and exogenous CCL21; and preferably, further expresses a protein promoting the proliferation of the cell; and more preferably, the protein promoting the proliferation of the cell is a IL-7R-binding protein or exogenous IL-7;

wherein the IL-7R-binding protein is an exogenous IL-7R-binding protein, and the exogenous IL-7R-binding protein can specifically bind to IL-7R and improve activities of IL-7R;

preferably, the amino acid sequence of the exogenous IL-7R is shown in SEQ ID NO: 19.

2. The cell of claim 1, wherein the exogenous CCL21 is natural CCL21, or a truncated fragment of natural CCL21, or a mutant of natural CCL21 having the same function as natural CCL21;

and preferably, the natural CCL21 has at least 90% sequence identity with the amino acid sequence as shown in SEQ ID NO: 21, or is a truncated fragment of the amino acid sequence as shown in SEQ ID NO: 21; or has at least 90% sequence identity with the amino acid sequence encoded by the nucleotide sequence as shown in SEQ ID NO: 14 or 15, or is a truncated fragment of an amino acid sequence encoded by the nucleotide sequence as shown in SEQ ID NO: 14 or 15.

3. The cell of claim 1 or 2, wherein the exogenous CCL21 is constitutively expressed.

4. The cell of claim 1 or 2, wherein the exogenous CCL21 is inducibly expressed; preferably, the inducible expression is initiated by an immune cell inducible promoter; and more preferably, the immune cell inducible promoter is NFAT promoter.

5. The cell of any one of claims 1-4, wherein the exogenous IL-7 is natural IL-7, or a truncated fragment of natural IL-7, or a mutant of natural IL-7 having the same function

as natural IL-7;

preferably, the natural IL-7 has at least 90% sequence identity with the amino acid sequence as shown in SEQ ID NO: 18, or is a truncated fragment of the amino acid sequence as shown in SEQ ID NO: 18; or has at least 90% sequence identity with the amino acid sequence encoded by the nucleotide sequence as shown in SEQ ID NO: 13, or is a truncated fragment of an amino acid sequence encoded by the nucleotide sequence as shown in SEQ ID NO: 13.

6. The cell of any one of claims 1-4, wherein the exogenous IL-7R-binding protein or exogenous IL-7 is constitutively expressed.

7. The cell of any one of claims 1-4, wherein the exogenous IL-7R-binding protein or exogenous IL-7 is inducibly expressed; preferably, the inducible expression is initiated by an immune cell inducible promoter; and more preferably, the immune cell inducible promoter is NFAT promoter.

8. The cell of any one of claims 1-7, wherein the cell is an immune effector cell;

preferably, the immune effector cells are T cells, NK cells or NKT cells;

and more preferably, the immune effector cells are T cells.

9. The cell of claim 1, wherein the target antigen is a tumor antigen and / or a pathogen antigen; preferably, a tumor antigen.

10. The cell of claim 9, wherein the target antigen is a solid tumor antigen;

and preferably, the solid tumor antigen is GPC3, EGFR or Claudin18.2; and more preferably, the solid tumor antigen is Claudin18.2.

11. The cell of any one of claims 1-10, wherein the exogenous receptor is a chimeric receptor, which includes an antigen-binding domain specifically binding to a target antigen, a transmembrane domain and an intracellular domain.

12. The cell of claim 11, wherein the exogenous receptor is selected from the group consisting of chimeric antigen receptor (CAR), modified T cell (antigen) receptor (TCR), T Cell fusion protein (TFP), T cell antigen coupler (TAC) or a combination thereof;

and preferably, the exogenou s receptor is a chimeric antigen receptor.

13. The cell of claim 12, wherein the chimeric antigen receptor includes:

(i) an antibody or a fragment thereof specifically binding to a target antigen, a

transmembrane domain of CD28 or CD8, a costimulatory signal domain of CD28, and CD3ζ; or

(ii) an antibody or a fragment thereof specifically binding to a target antigen, the transmembrane domain of CD28 or CD8, the costimulatory signal domain of 4-1BB, and CD3ζ; or

(iii) an antibody or a fragment thereof specifically binding to the target antigen, the transmembrane domain of CD28 or CD8, the costimulatory signal domain of CD28, the costimulatory signal domain of 4-1BB and CD3ζ.

14. The cell of claim 11, wherein the amino acid sequence of the antigen binding domain of the exogenous receptor has at least 90% identity with the sequence as shown in SEQ ID NO: 2.

15. The cell of claim 14, wherein the amino acid sequence of the exogenous receptor has at least 90% identity with the sequence as shown in SEQ ID NO: 26, 27 or 35.

16. The cell of any one of claims 1-15, wherein the exogenous receptor, and/or exogenous IL-7R binding protein or exogenous IL-7, and/or exogenous CCL21 are expressed by using a viral vector;

and preferably, the viral vectors include: lentiviral vectors, retroviral vectors or adenovirus vectors.

17. An expression construct, comprising sequentially connected: an expression cassette 1 for an exogenous receptor specifically binding to a target antigen, an expression cassette 2 for exogenous IL-7R binding protein or exogenous IL-7, and an expression cassette 3 exogenous for CCL21; and preferably, the expression cassettes are connected by tandem fragments, selected from F2A, PA2, T2A, and/or E2A.

18. The expression construct of claim 17, wherein said expression cassette 2 comprises a nucleic acid sequence as shown in SEQ ID NO: 17.

19. The expression construct of claim 17, wherein said expression cassette 3 comprises a nucleic acid sequence as shown in SEQ ID NO: 20.

20. An expression vector, comprising the expression construct of any one of claims 17-19.

21. A virus, comprising the expression vector of claim 20.

22. Use of the combination of CCL21 and IL-7R binding protein or IL-7 in the

preparation of a medicament for improving the viability of immune response cells in an individual; and preferably, the chimeric receptor is an chimeric antigen receptor;

wherein the IL-7R binding protein can specifically bind to IL-7R and enhance activities of IL-7R;

and preferably, the amino acid sequence of the IL-7R is shown in SEQ ID NO: 19.

23. The use of claim 22, wherein the CCL21 is natural CCL21, or a truncated fragment of natural CCL21, or a mutant of natural CCL21 having the same function as natural CCL21;

and preferably, the natural CCL21 has at least 90% sequence identity with the amino acid sequence as shown in SEQ ID NO: 21, or is a truncated fragment of the amino acid sequence as shown in SEQ ID NO: 21; or has at least 90% sequence identity with the amino acid sequence encoded by the nucleotide sequence as shown in SEQ ID NO: 14 or 15, or is a truncated fragment of an amino acid sequence encoded by the nucleotide sequence as shown in SEQ ID NO: 14 or 15.

24. The use of claim 22 or 23, wherein the CCL21 is constitutively expressed.

25. The use of claim 22 or 23, wherein the CCL21 is inducibly expressed; preferably, the inducible expression is initiated by an immune cell inducible promoter; and more preferably, the immune cell inducible promoter is NFAT promoter.

26. The use of any one of claims 22-25, wherein the IL-7 is natural IL-7, or a truncated fragment of natural IL-7, or a mutant of natural IL-7 having the same function as natural IL-7;

and preferably, the natural IL-7 has at least 90% sequence identity with the amino acid sequence as shown in SEQ ID NO: 18, or is a truncated fragment of the amino acid sequence as shown in SEQ ID NO: 18; or has at least 90% sequence identity with the amino acid sequence encoded by the nucleotide sequence as shown in SEQ ID NO: 13, or is a truncated fragment of an amino acid sequence encoded by the nucleotide sequence as shown in SEQ ID NO: 13.

27. The use of any one of claims 22-25, wherein the IL-7R-binding protein or IL-7 is constitutively expressed.

28. The use of any one of claims 22-25, wherein the IL-7R-binding protein or IL-7 is inducibly expressed; preferably, the inducible expression is initiated by an immune cell

inducible promoter; and more preferably, the immune cell inducible promoter is NFAT promoter.

29. The use of any one of claims 22-28, wherein the immune effector cells are T cells, NK cells or NKT cells.

30. Use of the cell of any one of claims 1-16, or the expression construct of any one of claims 17-19, or the expression vector of claim 20, or the virus of claim 21 for preparing a drug for inhibiting tumors, inhibiting pathogens; preferably, a drug for inhibiting tumors.

31. The use of claim 30, wherein the drug for inhibiting tumors is used in combination with a chemotherapeutic drug.

32. A pharmaceutical composition, comprising the cell of any one of claims 1-16 and a pharmaceutically acceptable carrier or excipient.

33. A kit, comprising kit A and kit B, wherein the kit A comprises genetically engineered cells, and the cells expresses an exogenous receptor specifically binding to a target antigen; and the kit B comprises CCL21, and/or a protein that promotes the proliferation of the cells; preferably, the protein that promotes the proliferation of the cells is IL-7R binding protein or IL-7; and more preferably, the kit A and the kit B are administered in any order;

wherein the IL-7R binding protein can specifically bind to IL-7R and enhance activities of IL-7R; and preferably, the amino acid sequence of the exogenous IL-7R is shown in SEQ ID NO: 19.

34. The kit of claim 33, wherein the CCL21 is natural CCL21, or a truncated fragment of natural CCL21, or a mutant of natural CCL21 having the same function as natural CCL21;

and preferably, the natural CCL21 has at least 90% sequence identity with the amino acid sequence as shown in SEQ ID NO: 21, or is a truncated fragment of the amino acid sequence as shown in SEQ ID NO: 21; or has at least 90% sequence identity with the amino acid sequence encoded by the nucleotide sequence as shown in SEQ ID NO: 14 or 15, or is a truncated fragment of an amino acid sequence encoded by the nucleotide sequence as shown in SEQ ID NO: 14 or 15.

35. The kit of claim 33 or 34, wherein the IL-7 is natural IL-7, or a truncated fragment

of natural IL-7, or a mutant of natural IL-7 having the same function as natural IL-7;

and preferably, the natural IL-7 has at least 90% sequence identity with the amino acid sequence as shown in SEQ ID NO: 18, or is a truncated fragment of the amino acid sequence as shown in SEQ ID NO: 18; or has at least 90% sequence identity with the amino acid sequence encoded by the nucleotide sequence as shown in SEQ ID NO: 13, or is a truncated fragment of an amino acid sequence encoded by the nucleotide sequence as shown in SEQ ID NO: 13.

36. The kit of claim 33, wherein the kit A comprises immune effector cells modified by chimeric receptors;

and preferably, the chimeric receptor is a chimeric antigen receptor.

37. The kit of claim 33, wherein the immune effector cells are T cells, NK cells or NKT cells.