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;~~.~~

~~2. The cell of claim 1,~~ 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~~3~~. The cell of claim 1~~ or 2~~, 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~~4~~. The cell of ~~any one of~~ claim~~s~~ 1~~-3~~ or 2, wherein the exogenous CCL21 is constitutively expressed.

4~~5~~. The cell of ~~any one of~~ claim~~s~~ 1~~-3~~ 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~~6~~. The cell of any one of claims 1-4~~5~~, 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~~7~~. The cell of any one of claims 1-4~~5~~, wherein the exogenous IL-7R-binding protein or exogenous IL-7 is constitutively expressed.

7~~8~~. The cell of any one of claims 1-4~~5~~, 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~~9~~. The cell of any one of claims 1-7~~8~~, 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~~10~~. The cell of claim 1, wherein the target antigen is a tumor antigen and / or a pathogen antigen; preferably, a tumor antigen.

10~~11~~. The cell of claim 9~~10~~, 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~~12~~. The cell of any one of claims 1-10~~11~~, 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~~13~~. The cell of claim 11~~12~~, 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~~14~~. The cell of claim 12~~13~~, 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~~15~~. The cell of claim 11~~12~~, 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~~16~~. The cell of claim 14~~15~~, 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~~17~~. The cell of any one of claims 1-15~~16~~, 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~~18~~. 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~~19~~. The expression construct of claim 17~~18~~,~~.~~ wherein said expression cassette 2 comprises a nucleic acid sequence as shown in SEQ ID NO: 17.

19~~20~~. The expression construct of claim 17~~18~~,~~.~~ wherein said expression cassette 3 comprises a nucleic acid sequence as shown in SEQ ID NO: 20.

20~~21~~. An expression vector, comprising the expression construct of any one of

claims 17~~18~~-19~~20~~.

21~~22~~. A virus, comprising the expression vector of claim 20~~21~~.

22~~23~~. Use of the combination of CCL21 and IL-7R binding protein or IL-7 in the preparation of a medicament~~A method~~ for improving the viability of immune response cells in an individual~~, wherein an exogenous CCL21, exogenous IL-7R binding protein or exogenous IL-7 are co-expressed in the immune response cells~~; and preferably, the~~w~~ chimeric receptor is an chimeric antigen receptor;~~.~~

~~24. The method of claim 23,~~ wherein the ~~exogenous~~ 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.

23~~25~~. The use~~method~~ of claim 22~~23 or 24~~, 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.

24~~26~~. The use~~method~~ of ~~any one of~~ claim~~s~~ 22~~23-25~~ or 23, wherein the ~~exogenous~~ CCL21 is constitutively expressed.

25~~27~~. The use~~method~~ of ~~any one of~~ claim~~s~~ 22~~23-25~~ or 23, 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.

26~~28~~. The use~~method~~ of any one of claims 22~~23~~-25~~27~~, 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;

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~~29~~. The ~~method~~ use of any one of claims 22~~23~~-25~~27~~, wherein the ~~exogenous~~ IL-7R-binding protein or ~~exogenous~~ IL-7 is constitutively expressed.

28~~30~~. The use~~method~~ of any one of claims 22~~23~~-25~~27~~, 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.

29~~31~~. The use~~method~~ of any one of claims 22~~23~~-28~~30~~, wherein the immune effector cells are T cells, NK cells or NKT cells.

30~~32~~. Use of the cell of any one of claims 1-16~~17~~, or the expression construct of any one of claims 17~~18~~-19~~20~~, or the expression vector of claim 20~~21~~, or the virus of claim 21~~22~~ for preparing a drug for inhibiting tumors, inhibiting pathogens; preferably, a drug for inhibiting tumors.

31~~33~~. The use of claim 30~~32~~, wherein the drug for inhibiting tumors is used in combination with a chemotherapeutic drug.

32~~34~~. A pharmaceutical composition, comprising the cell of any one of claims 1-16~~17~~ and a pharmaceutically acceptable carrier or excipient.

33~~35~~. 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;~~.~~

~~36. The kit of claim 35,~~ 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~~37~~. The kit of claim 33~~35 or 36~~, 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~~38~~. The kit of ~~any one of~~ claim~~s~~ 33~~35-37~~ 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~~39~~. The kit of claim 33~~35~~, wherein the kit A comprises immune effector cells modified by chimeric receptors;

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

37~~40~~. The kit of claim 33~~35~~, wherein the immune effector cells are T cells, NK cells or NKT cells.