

Claims

1. A T cell receptor (TCR), wherein the TCR can bind to KASEKIFYV-HLA A0201 complex; and preferably, the TCR comprises a TCR α chain variable domain and a TCR β chain variable domain, wherein 3 complementarity determining regions (CDR) of the TCR α chain variable domain are:

α CDR1- DSSSTY (SEQ ID NO: 10)

α CDR2- IFSNMDM (SEQ ID NO: 11)

α CDR3- AEPNQAGTALI (SEQ ID NO: 12); and

3 complementarity determining regions of the TCR β chain variable domain are:

β CDR1- MNHEY (SEQ ID NO: 13)

β CDR2- SVGEGT (SEQ ID NO: 14)

β CDR3- ASSSLEDPYEQY (SEQ ID NO: 15).

2. The TCR of claim 1, wherein the TCR comprises a TCR α chain variable domain and a TCR β chain variable domain, and the TCR α chain variable domain is an amino acid sequence having at least 90% sequence identity with SEQ ID NO: 1; and/ or the TCR β chain variable domain is an amino acid sequence with at least 90% sequence identity with SEQ ID NO: 5.

3. The TCR of claim 1, wherein the TCR comprises a TCR α chain variable domain, the amino acid sequence of which is SEQ ID NO: 1.

4. The TCR of claim 1, wherein the TCR comprises a TCR β chain variable domain, the amino acid sequence of which is SEQ ID NO: 5.

5. The TCR of claim 1, wherein the TCR is a $\alpha\beta$ heterodimer, which comprises a TCR α chain constant region TRAC*01 and a TCR β chain constant region TRBC1*01 or TRBC2*01.

6. The TCR of claim 5, wherein the amino acid sequence of the TCR α chain is SEQ ID NO: 3 and / or the amino acid sequence of the TCR β chain is SEQ ID NO: 7.

7. The TCR of any one of claims 1-4, wherein the TCR is soluble.

8. The TCR of claim 7, wherein the TCR is a single-chain TCR.

9. The TCR of claim 8, wherein the TCR is formed by connecting the α chain variable domain and the β chain variable domain through a peptide linking sequence.

10. The TCR of claim 9, wherein the TCR has one or more mutations at amino acid position 11, 13, 19, 21, 53, 76, 89, 91, or 94 of the α chain variable region, and/or at the last 3, 5 or 7 amino acid position of the short peptide of the α chain J gene; and/or the TCR has one or more mutations at amino acid position 11, 13, 19, 21, 53, 76, 89, 91, or 94 of the β chain variable region, and / or at the last 2, 4, or 6 amino acid position of the short peptide of the β chain J gene, wherein the amino acid position number is based on the position number listed in IMGT

(International Immunogenetics Information System).

11. The TCR of claim 10, wherein the amino acid sequence of the α chain variable domain of the TCR comprises SEQ ID NO: 32 and/or the amino acid sequence of the β chain variable domain of the TCR comprises SEQ ID NO: 34.

5 12. The TCR of claim 11, wherein the amino acid sequence of the TCR is SEQ ID NO: 30.

13. The TCR of claim 7, wherein the TCR comprises (a) all or part of the TCR α chain except for its transmembrane domain, and (b) all or part of the TCR β chain except for its transmembrane domain;

10 and each of (a) and (b) comprise the functional variable domain, or the functional variable domain and at least a portion of the constant domain of the TCR chain, respectively.

14. The TCR of claim 13, wherein cysteine residues form an artificial disulfide bond between the α and β chain constant domains of the TCR.

15 15. The TCR of claim 14, wherein the cysteine residues forming the artificial interchain disulfide bond in the TCR are substituted for one or more groups of amino acids selected from the following:

Thr48 of TRAC*01 exon 1 and Ser57 of TRBC1*01 or TRBC2*01 exon 1;

Thr45 of TRAC*01 exon 1 and Ser77 of TRBC1*01 or TRBC2*01 exon 1;

Tyr10 of TRAC*01 exon 1 and Ser17 of TRBC1*01 or TRBC2*01 exon 1;

Thr45 of TRAC*01 exon 1 and Asp59 of TRBC1*01 or TRBC2*01 exon 1;

20 Ser15 of TRAC*01 exon 1 and Glu15 of TRBC1*01 or TRBC2*01 exon 1;

Arg53 of TRAC*01 exon 1 and Ser54 of TRBC1*01 or TRBC2*01 exon 1;

Pro89 of TRAC*01 exon 1 and Ala19 of TRBC1*01 or TRBC2*01 exon 1; and

Tyr10 of TRAC*01 exon 1 and Glu20 of TRBC1*01 or TRBC2*01 exon 1.

25 16. The TCR of claim 15, wherein the amino acid sequence of the TCR α chain is SEQ ID NO: 26 and/or the amino acid sequence of the TCR β chain is SEQ ID NO: 28.

17. The TCR of claim 13, wherein an artificial interchain disulfide bond is contained between α chain variable region and β chain constant region of the TCR.

30 18. The TCR of claim 17, wherein cysteine residues forming the artificial interchain disulfide bond in the TCR are substituted for one or more groups of amino acids selected from the following:

amino acid at position 46 of TRAV and amino acid at position 60 of TRBC1*01 or TRBC2*01 exon 1;

amino acid at position 47 of TRAV and amino acid at position 61 of TRBC1*01 or TRBC2*01 exon 1;

35 amino acid at position 46 of TRAV and amino acid at position 61 of TRBC1*01 or

TRBC2*01 exon 1; or

amino acid at position 47 of TRAV and amino acid at position 60 of TRBC1*01 or TRBC2*01 exon 1.

19. The TCR of claim 17 or 18, wherein the TCR comprises α chain variable domain and β chain variable domain as well as all or part of β chain constant domains except for its transmembrane domain, however it does not comprise α chain constant domain, and α chain variable domain and β chain of the TCR form a heterodimer.

20. The TCR of claim 1, wherein a conjugate binds to the α chain and/or β chain of the TCR at C- or N-terminal.

21. The TCR of claim 20, wherein the conjugate that binds to the TCR is a detectable label, a therapeutic agent, a PK modified moiety, or a combination thereof; and preferably, the therapeutic agent is an anti-CD3 antibody.

22. A multivalent TCR complex, wherein the multivalent TCR complex comprises at least two TCR molecules, and at least one TCR molecule is the TCR of any one of claims 1-21.

23. A nucleic acid molecule, comprising a nucleic acid sequence encoding the TCR molecule of any one of claims 1-21, or a complement sequence thereof.

24. The nucleic acid molecule of claim 23, wherein the nucleic acid molecule comprises the nucleotide sequence SEQ ID NO: 2 or SEQ ID NO: 33 encoding the variable domain of the TCR α chain.

25. The nucleic acid molecule of claim 23 or 24, wherein the nucleic acid molecule comprises the nucleotide sequence SEQ ID NO: 6 or SEQ ID NO: 35 encoding the variable domain of the TCR β chain.

26. The nucleic acid molecule of claim 23, wherein the nucleic acid molecule comprises the nucleotide sequence SEQ ID NO: 4 encoding the TCR α chain and / or the nucleotide sequence SEQ ID NO: 8 encoding the variable domain of the TCR β chain.

27. A vector, comprising the nucleic acid molecule of any one of the claims 23-26; preferably, the vector is a viral vector; and more preferably, the vector is a lentiviral vector.

28. An isolated host cell, comprising the vector of claim 27 or having the exogenous nucleic acid molecule of any one of claims 23-26 integrated into its genome.

29. A cell, which is transduced with the nucleic acid molecule of any one of claims 23-26 or the vector of claim 27; and preferably, the cell is a T cell or stem cell.

30. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier, and the TCR of any one of claims 1-21, or the TCR complex of claim 22, or the cell of claim 29.

31. Use of the TCR of any one of claims 1-21, or the TCR complex of claim 22, or the cell of claim 29 for preparing a medicament for treating tumor or autoimmune disease; preferably,

the tumor is a SSX2 antigen-positive tumor; and more preferably, the tumor is melanoma, head and neck cancer, lymphoma, multiple myeloma, pancreatic cancer, prostate cancer, sarcoma, hepatocellular carcinoma, and colon cancer.