

Claims

1. A T cell receptor (TCR), which has an activity of binding to SLLMWITQC-HLA A2 complex and comprises a TCR α chain variable domain and a TCR β chain variable domain, the

5 TCR α chain variable domain comprises three CDR regions, and

the TCR β chain variable domain comprises three CDR regions,

wherein the TCR has a CDR selected from the group consisting of:

TCR No.	CDR1 α	CDR2 α	CDR3 α	CDR1 β	CDR2 β	CDR3 β
1	TSINN	IRSNERE	ATDAFAWWI	SGHDY	FNNNVP	ASSLGSNEQY
2	GWAQN	IRTGEQE	ATDANARWN	SGHDY	FNHGAV	ASSLGSNEQY
3	GSIQN	IRTGEQE	ATDANARWE	SGHDY	FNHGAV	ASSLGSNEQY
4	GSIQN	IRTGEQE	ATDANARWE	SGHDY	FNHGAV	ASQRGANEQY
5	GSIQN	IRTGEQE	ATDANARWE	SGHDY	FNHGAV	ASQKGSNEQY
6	GSIQN	IRTGEQE	ATDANARWD	SGHDY	FNHGAV	ASQLGSNEQY
7	GWAQN	IRSNERE	ATDANARWN	SGHDY	FNHGAV	ASQLGSNEQY
8	GWVQN	IRTGEQE	ATDANARWD	SGHDY	FNHGAV	ASSLGSNEQY
9	GSIQN	IRSNERE	ATDANARWD	SGHDY	FNHGAV	ASQLGSNEQY
10	GWAQN	IRSNERE	ATDANARWD	SGHDY	FNHGAV	ASQLGSNEQY
11	GSIQN	IRSNERE	ATDANARWE	SGHDY	FNHGAV	ASQKGSNEQY
12	TSINN	IRSNERE	ATDANGKII	SGHDY	FNNNVP	ASQLGGNEQY
13	TSINN	IRSNERE	ATDANGKII	SGHDY	FNNNVP	ASQKGSNEQY
14	TSINN	IRSNERE	ATDANGKII	SGHDY	FNNNVP	ASQLGPNEQY
15	TSINN	IRSNERE	ATDANGKII	SGHDY	FNNNVP	ASQRGANEQY
16	TSINN	IRSNERE	ATDANGKII	SGHDY	FNNNVP	ASQMGSNEQY
17	TSINN	IRSNERE	ATDANGKII	SGHDY	FNNNVP	ASQLGSNEQY
18	TSINN	IRSNERE	ATDANGKII	SGHDY	FNNNVP	ASQLGSNEQY
19	TSINN	IRSNERE	MYDENGKII	SGHDY	FNNNVP	ASSLGSNEQY
20	TSINN	IRSNERE	MYDQNGKII	SGHDY	FNNNVP	ASSLGSNEQY
21	TSINN	IRSNERE	ATDAYGTVQ	SGHDY	FNNNVP	ASSLGSNEQY
22	TSINN	IRSNERE	ATDANGTVQ	SGHDY	FNNNVP	ASSLGSNEQY
23	TSINN	IRSNERE	ATDANGSVQ	SGHDY	FNNNVP	ASSLGSNEQY
24	TSINN	IRSNERE	ATDAYGRYI	SGHDY	FNNNVP	ASSLGSNEQY
25	TSINN	IRSNERE	ATDANQMWK	SGHDY	FNNNVP	ASSLGSNEQY
26	TSINN	IRSNERE	ATDAYGLPI	SGHDY	FNNNVP	ASSLGSNEQY
27	TSINN	IRSNERE	ATDANGLPV	SGHDY	FNNNVP	ASSLGSNEQY
28	TSINN	IRSNERE	ATDANGRWE	SGHDY	FNNNVP	ASSLGSNEQY
29	TSINN	IRSNERE	ATDANGTVG	SGHDY	FNNNVP	ASSLGSNEQY
30	TSINN	IRSNERE	ATDANGRWM	SGHDY	FNNNVP	ASSLGSNEQY
31	TSINN	IRSNERE	ATDANGLWS	SGHDY	FNNNVP	ASSLGSNEQY
32	GWAQN	IRTGEQE	ATDANARWD	SGHDY	FNNNVP	ASSLGSNEQY
33	GWAQN	IRTGQAE	ATDANARWE	SGHDY	FNNNVP	ASSLGSNEQY
34	GSIQN	IRSNERE	ATDAFAWWI	SGHDY	FNNNVP	ASSLGSNEQY
35	GWVQN	IRTGEQE	ATDANARWN	SGHDY	FNNNVP	ASSLGSNEQY
36	GWAQN	IRTGEQE	ATDANARWN	SGHDY	FNNNVP	ASSLGSNEQY
37	GWVQN	IRTGEQE	ATDANARWD	SGHDY	FNNNVP	ASSLGSNEQY
38	GSIQN	IRTGEQE	ATDAWARWI	SGHDY	FNNNVP	ASSLGSNEQY
39	GWVQN	IRTGQAE	ATDANARWE	SGHDY	FNNNVP	ASSLGSNEQY
40	GSIQN	IRTGEQE	ATDANARWN	SGHDY	FNNNVP	ASSLGSNEQY
41	TSINN	IRSNERE	ATDANGKII	SGHDY	FNNNVP	ASQMGSNEQY
42	TSINN	IRSNERE	ATDANGKII	SGHDY	FNNNVP	ASQRGANEQY
43	TSINN	IRSNERE	ATDANGKII	SGHDY	FNNNVP	ASQMGSNEQY
44	TSINN	IRSNERE	ATDANGKII	SGHDY	FNNNVP	ASMLGSNEQY.

2. The TCR of claim 1, wherein the TCR is in a soluble form.

3. The TCR of claim 1, wherein the TCR is an $\alpha\beta$ heterodimeric TCR.

4. The TCR of claim 1, wherein the TCR comprises (i) all or part of the TCR α chain other than its transmembrane domain, and (ii) all or part of the TCR β chain other than its

5 transmembrane domain, wherein both of (i) and (ii) comprise the variable domain and at least a portion of the constant domain of the TCR chain.

5. The TCR of claim 4, wherein an artificial interchain disulfide bond is contained between the α chain constant region and the β chain constant region of the TCR.

6. The TCR of claim 5, wherein cysteine residues forming an artificial interchain disulfide bond between the TCR α chain constant region and β chain constant region 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;

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

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.

20 7. The TCR of claim 1, wherein the amino acid sequence of the α chain variable domain of the TCR is selected from the group consisting of: SEQ ID NOs: 58-86; and/or the amino acid sequence of the β chain variable domain of the TCR is selected from the group consisting of: SEQ ID NOs: 87-102.

8. The TCR of claim 1, wherein the TCR is selected from the group consisting of:

TCR number	Sequence of α chain variable domain SEQ ID NO:	Sequence of β chain variable domain SEQ ID NO:
1	58	2
2	59	87
3	60	87
4	60	88
5	60	89
6	61	90
7	62	90
8	63	87
9	64	91
10	65	90
11	66	89
12	1	92
13	1	93

14	1	94
15	1	95
16	1	96
17	1	97
18	1	98
19	67	2
20	68	2
21	69	2
22	70	2
23	71	2
24	72	2
25	73	2
26	74	2
27	75	2
28	76	2
29	77	2
30	78	2
31	79	2
32	80	2
33	81	2
34	82	2
35	83	2
36	59	2
37	63	2
38	84	2
39	85	2
40	86	2
41	1	99
42	1	100
43	1	101
44	1	102.

9. The TCR of claim 1, wherein the TCR is a single chain TCR;

or

the TCR is a single-chain TCR consisting of an α chain variable domain and a β chain variable domain, and the α chain variable domain and the β chain variable domain are connected

5 by a flexible short peptide sequence (linker);

or

the amino acid sequence of the α chain variable domain of the TCR is selected from the group consisting of: SEQ ID NOs: 9-37; and/or the amino acid sequence of the β chain variable domain of the TCR is selected from the group consisting of: SEQ ID NOs: 38-53;

10 or

the TCR is selected from the group consisting of:

TCR Number	Sequence of α chain variable domain SEQ ID NO:	Sequence of β chain variable domain SEQ ID NO:
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s-1	9	4
s-2	10	38
s-3	11	38
s-4	11	39
s-5	11	40
s-6	12	41
s-7	13	41
s-8	14	38
s-9	15	42
s-10	16	41
s-11	17	40
s-12	3	43
s-13	3	44
s-14	3	45
s-15	3	46
s-16	3	47
s-17	3	48
s-18	3	49
s-19	18	4
s-20	19	4
s-21	20	4
s-22	21	4
s-23	22	4
s-24	23	4
s-25	24	4
s-26	25	4
s-27	26	4
s-28	27	4
s-29	28	4
s-30	29	4
s-31	30	4
s-32	31	4
s-33	32	4
s-34	33	4
s-35	34	4
s-36	10	4
s-37	14	4
s-38	35	4
s-39	36	4
s-40	37	4
s-41	3	50
s-42	3	51
s-43	3	52
s-44	3	53.

10. The TCR of claim 9, wherein the hydrophobic core of the TCR α chain variable domain and/or β chain variable domain is mutated.

11. The TCR of any one of preceding claims, wherein a conjugate binds to the α chain and/or β chain of the TCR at C- or N-terminus.

12. The TCR of claim 11, wherein the conjugate that binds to the TCR is a detectable label, a therapeutic agent, a PK modified moiety, or a combination of any of these.

13. The TCR of claim 12, wherein the therapeutic agent that binds to the TCR is an anti-CD3 antibody linked to the α or β chain of the TCR at C- or N-terminus.

5 14. A multivalent TCR complex comprising at least two TCR molecules, and at least one TCR molecule is the TCR of any one of preceding claims.

15. A nucleic acid molecule comprising a nucleic acid sequence encoding the TCR of any one of claims 1-13, or a complement sequence thereof.

16. A vector comprising the nucleic acid molecule of claim 15.

10 17. A host cell comprising the vector of claim 16 or having the exogenous nucleic acid molecule of claim 15 integrated into its genome.

18. An isolated T cell expressing the TCR of any one of claims 1-13.

19. A pharmaceutical composition comprising a pharmaceutically acceptable carrier, and a TCR of any one of claims 11-13, or the T cell of claim 18.

15 20. Use of the TCR of any one of claims 11-13, or the T cell of claim 18 for preparing a medicament for treating tumor.

21. A method for preparing the TCR of any one of claims 1-13, comprising the steps of:

(i) culturing the host cell of claim 17 to express the TCR of any one of claims 1-13;

(ii) isolating or purifying the TCR.