CLAIMS

1. An engineered T cell receptor (TCR) comprising at least one of the following amino acid residues, numbered according to the International ImMunoGeneTics information system (IMGT):

L96 of the α chain; R9 of the β chain; T24 of the α chain; T20 of the α chain; M50 of the α chain; T5 of the α chain; Q8 of the α chain; S86 of the α chain; F39 of the α chain; D55 of the α chain; R43 of the β chain; A66 of the α chain; L21 of the β chain; L103 of the β chain; T3 of the α chain; P9 of the α chain; A16 of the α chain; T18 of the α chain; L21 of the α chain; S22 of the α chain; D26 of the α chain; F40 of the α chain; S47 of the α chain; R48 of the α chain; Q49 of the α chain; I51 of the α chain; L52 of the α chain; V53 of the α chain; T67 of the α chain; E68 of the α chain; N74 of the α chain; F76 of the α chain; N79 of the α chain; Q81 of the α chain; A83 of the α chain; K90 of the α chain; S92 of the α chain; D93 of the α chain; and M101 of the α chain;

wherein the at least one amino acid residue is not present in the corresponding germline TCR amino acid sequence, preferably wherein the at least one amino acid residue is selected from:

L96 of the α chain;
R9 of the β chain;
T24 of the α chain;
T20 of the α chain;
M50 of the α chain;
T5 of the α chain;
Q8 of the α chain;
S86 of the α chain;
F39 of the α chain;
D55 of the α chain; or
R43 of the β chain.

2. An engineered cell surface expressed T cell receptor (TCR) comprising at least one of the following amino acid residues, numbered according to the IMGT system:

L96 of the α chain; R9 of the β chain; Y10 of the β chain; T24 of the α chain; V19 of the α chain; T20 of the α chain; M50 of the α chain; T5 of the α chain; Q8 of the α chain; S86 of the α chain; F39 of the α chain; D55 of the α chain; R43 of the β chain; A66 of the α chain; V19 of the β chain; L21 of the β chain; L103 of the β chain; T3 of the α chain; S7 of the α chain; P9 of the α chain; M11 of the α chain; A16 of the α

chain; T18 of the α chain; L21 of the α chain; S22 of the α chain; D26 of the α chain; F40 of the α chain; S47 of the α chain; R48 of the α chain; Q49 of the α chain; I51 of the α chain; L52 of the α chain; V53 of the α chain; T67 of the α chain; E68 of the α chain; N74 of the α chain; F76 of the α chain; N79 of the α chain; Q81 of the α chain; A83 of the α chain; K90 of the α chain; S92 of the α chain; D93 of the α chain; and M101 of the α chain;

wherein the cell is human, and the at least one amino acid residue is not present in the corresponding germline TCR amino acid sequence, preferably wherein the at least one amino acid residue is selected from:

L96 of the α chain;
R9 of the β chain;
Y10 of the β chain;
T24 of the α chain;
V19 of the α chain;
T20 of the α chain;
M50 of the α chain;
T5 of the α chain;
Q8 of the α chain;
S86 of the α chain;
F39 of the α chain;
D55 of the α chain; or
R43 of the β chain.

3. An engineered TCR according to any preceding claim which comprises:
(i) L96 of the α chain; and/or(ii) R9 of the β chain.

4. An engineered TCR according to claim 1 or claim 2 which comprises T24 of the α chain.

5. An engineered TCR according to any of claims 1 to 4 which comprises a plurality of amino acid residues as defined in claim 1 or claim 2.

6. An engineered TCR according to claim 5:
(i) further comprising V19 of the α chain; V19 of the β chain; S7 of the α chain; or M11 the α chain;
(ii) which comprises L96 of the α chain; R9 of the β chain and Y10 of the β chain; or(iii) which comprises V19 of the α chain; R9 of the β chain and Y10 of the β chain.

7. An engineered TCR according to any preceding claim which comprises:
(i) each of L96 of the α chain; R9 of the β chain; Y10 of the β chain; T24 of the α chain; V19 of the α chain; T20 of the α chain; M50 of the α chain; T5 of the α chain; Q8 of the α chain; S86 of the α chain; F39 of the α chain; D55 of the α chain; and R43 of the β chain;
(ii) each of L96 of the α chain; R9 of the β chain; Y10 of the β chain; T24 of the α chain; V19 of the α chain; T20 of the α chain; M50 of the α chain; T5 of the α chain; Q8 of the α chain; and S86 of the α chain; and/or(iii) each of:
L96 of the α chain; R9 of the β chain; Y10 of the β chain; T24 of the α chain; V19 of the α chain; T20 of the α chain; M50 of the α chain; T5 of the α chain; Q8 of the α chain; S86 of the α chain; F39 of the α chain; D55 of the α chain; R43 of the β chain; A66 of the α chain; V19 of the β chain; L21 of the β chain; L103 of the β chain; T3 of the α chain; S7 of the α chain; P9 of the α chain; M11 of the α chain; A16 of the α chain; T18 of the α chain; L21 of the α chain; S22 of the α chain; D26 of the α chain; F40 of the α chain; S47 of the α chain; R48 of the α chain; Q49 of the α chain; I51 of the α chain; L52 of the α chain; V53 of the α chain; T67 of the α chain; E68 of the α chain; N74 of the α chain; F76 of the α chain; N79 of the α chain; Q81 of the α chain; A83 of the α chain; K90 of the α chain; S92 of the α chain; D93 of the α chain; and M101 of the α chain.

8. A nucleic acid sequence encoding a TCR α chain and/or a β chain, wherein the α chain and/or a β chain is altered to comprise one or more amino acid residues as defined in any preceding claim, preferably
which comprises a nucleic acid sequence encoding an α chain and a nucleic acid sequence encoding a β chain linked by an internal self-cleaving sequence or an internal ribosome entry site.

9. A vector comprising a nucleic acid sequence according to claim 8, preferably wherein the vector is a retrovirus vector, lentivirus vector or a transposon.

10. A cell comprising a nucleic acid sequence according to claim 8 or a vector according to claim 9, , preferably wherein the cell is a T-cell, a natural killer cell or a stem cell, more preferably wherein the cell is derived from a T-cell, a natural killer cell or a stem cell isolated from a subject.

11. A pharmaceutical composition comprising a vector according to claim 9 or a cell which expresses a TCR as defined in any of claims 1 to 7.

12. A pharmaceutical composition according to claim 11 for use in treating and/or preventing a disease.

13. A vector according to claim 9 or a cell according to claim10 for use in the manufacture of a medicament for treating and/or preventing a disease.

14. A method for producing a cell according to claim10 which comprises the step of transducing a cell *in vitro* or *ex vivo* with a vector according to claim 9.

15. A method for increasing the cell surface expression of a TCR which comprises the steps of:

(i) providing a TCR α chain and/or β chain sequence;

(ii) determining an amino acid residue of the TCR α chain and/or β chain at one or more positions selected from:

96 of the α chain; 9 of the β chain; 10 of the β chain; 24 of the α chain; 19 of the α chain; 20 of the α chain; 50 of the α chain; 5 of the α chain; 8 of the α chain; 86 of the α chain; 39 of the α chain; 55 of the α chain; 43 of the β chain; 66 of the α chain; 19 of the β chain; 21 of the β chain; 103 of the β chain; 3 of the α chain; 7 of the α chain; 9 of the α chain; 11 of the α chain; 16 of the α chain; 18 of the α chain; 21 of the α chain; 22 of the α chain; 26 of the α chain; 40 of the α chain; 47 of the α chain; 48 of the α chain; 49 of the α chain; 51 of the α chain; 52 of the α chain; 53 of the α chain; 67 of the α chain; 68 of the α chain; 74 of the α chain; 76 of the α chain; 79 of the α chain; 81 of the α chain; 83 of the α chain; 90 of the α chain; 92 of the α chain; 93 of the α chain; and 101 of the α chain; and

(iii) altering the amino acid residue at one or more of the positions listed in step (ii) to an amino acid residue selected from:

L96 of the α chain; R9 of the β chain; Y10 of the β chain; T24 of the α chain; T20 of the α chain; M50 of the α chain; T5 of the α chain; Q8 of the α chain; S86 of the α chain; F39 of the α chain; D55 of the α chain; R43 of the β chain; A66 of the α chain; L21 of the β chain; L103 of the β chain; T3 of the α chain; S7 of the α chain; P9 of the α chain; M11 of the α chain; A16 of the α chain; T18 of the α chain; L21 of the α chain; S22 of the α chain; D26 of the α chain; F40 of the α chain; S47 of the α chain; R48 of the α chain; Q49 of the α chain; I51 of the α chain; L52 of the α chain; V53 of the α chain; T67 of the α chain; E68 of the α chain; N74 of the α chain; F76 of the α chain; N79 of the α chain; Q81 of the α chain; A83 of the α chain; K90 of the α chain; S92 of the α chain; D93 of the α chain; and M101 of the α chain,

wherein the amino acid positions are numbered according to the IMGT system, preferably wherein:
(i) the TCR amino acid is altered to comprise one or more amino acid residues as defined in any of claims 1-7; and/or
(ii) the TCR amino acid sequence is altered by mutagenesis of a nucleic acid sequence encoding the TCR.

16. A method for increasing the cell surface expression of a TCR which comprises the step of altering a TCR amino acid sequence such that it comprises a plurality of amino acid residues as defined in claim 15, preferably wherein:
(i) the TCR amino acid is altered to comprise one or more amino acid residues as defined in any of claims 1, 3, 4 or 7; and/or
(ii) the TCR amino acid sequence is altered by mutagenesis of a nucleic acid sequence encoding the TCR.

17. A method for selecting a high expression TCR which comprises the steps of:

(i) providing a group of TCR amino acid sequences; and

(ii) selecting a TCR amino acid sequence comprising at least one amino acid residue selected from:

L96 of the α chain; R9 of the β chain; Y10 of the β chain; T24 of the α chain; T20 of the α chain; M50 of the α chain; T5 of the α chain; Q8 of the α chain; S86 of the α chain; F39 of the α chain; D55 of the α chain; R43 of the β chain; A66 of the α chain; L21 of the β chain; L103 of the β chain; T3 of the α chain; S7 of the α chain; P9 of the α chain; M11 of the α chain; A16 of the α chain; T18 of the α chain; L21 of the α chain; S22 of the α chain; D26 of the α chain; F40 of the α chain; S47 of the α chain; R48 of the α chain; Q49 of the α chain; I51 of the α chain; L52 of the α chain; V53 of the α chain; T67 of the α chain; E68 of the α chain; N74 of the α chain; F76 of the α chain; N79 of the α chain; Q81 of the α chain; A83 of the α chain; K90 of the α chain; S92 of the α chain; D93 of the α chain; and M101 of the α chain,

wherein the amino acid residues are numbered according to the IMGT system.

18. A method for selecting a high expression TCR which comprises the steps of:

(i) providing a group of TCR amino acid sequences; and

(ii) selecting a TCR amino acid sequence comprising a plurality of amino acid residues as defined in claim 17.

19. A method for selecting a high expression TCR according to claim 17 or18 wherein the TCR amino acid sequence selected in step (ii) comprises one or more amino acid residues as defined in any of claims 1 , 3, 4 or 7.

20. A method for determining the strength of a TCR which comprises the steps of:

(i) providing a TCR α chain and/or β chain sequence; and

(ii) determining if the TCR sequence comprises at least one amino acid residue selected from:

L96 of the α chain; R9 of the β chain; Y10 of the β chain; T24 of the α chain; V19 of the α chain; T20 of the α chain; M50 of the α chain; T5 of the α chain; Q8 of the α chain; S86 of the α chain; F39 of the α chain; D55 of the α chain; R43 of the β chain; A66 of the α chain; V19 of the β chain; L21 of the β chain; L103 of the β chain; T3 of the α chain; S7 of the α chain; P9 of the α chain; M11 of the α chain; A16 of the α chain; T18 of the α chain; L21 of the α chain; S22 of the α chain; D26 of the α chain; F40 of the α chain; S47 of the α chain; R48 of the α chain; Q49 of the α chain; I51 of the α chain; L52 of the α chain; V53 of the α chain; T67 of the α chain; E68 of the α chain; N74 of the α chain; F76 of the α chain; N79 of the α chain; Q81 of the α chain; A83 of the α chain; K90 of the α chain; S92 of the α chain; D93 of the α chain; and M101 of the α chain;

wherein the amino acid residues are numbered according to the IMGT system, further wherein a sequence which comprises at least one of the recited amino acid residues is determined to be a high expression TCR and a sequence which does not comprise at least one of the recited amino acid sequences is determined to be a low expression TCR.

21. Use of an engineered TCR comprising at least one of the following amino acid residues, numbered according to the IMGT system:

L96 of the α chain; R9 of the β chain; Y10 of the β chain; T24 of the α chain; V19 of the α chain; T20 of the α chain; M50 of the α chain; T5 of the α chain; Q8 of the α chain; S86 of the α chain; F39 of the α chain; D55 of the α chain; R43 of the β chain; A66 of the α chain; V19 of the β chain; L21 of the β chain; L103 of the β chain; T3 of the α chain; S7 of the α chain; P9 of the α chain; M11 of the α chain; A16 of the α chain; T18 of the α chain; L21 of the α chain; S22 of the α chain; D26 of the α chain; F40 of the α chain; S47 of the α chain; R48 of the α chain; Q49 of the α chain; I51 of the α chain; L52 of the α chain; V53 of the α chain; T67 of the α chain; E68 of the α chain; N74 of the α chain; F76 of the α chain; N79 of the α chain; Q81 of the α chain; A83 of the α chain; K90 of the α chain; S92 of the α chain; D93 of the α chain; and M101 of the α chain;

wherein the at least one amino acid residue is not present in the corresponding germline TCR amino acid sequence or an engineered TCR according to any of claims 1 to 7; a nucleic acid sequence encoding the α chain and/or a β chain of said engineered TCR or a vector comprising said nucleic acid sequence encoding the α chain and/or a β chain of said engineered TCR to increase the cell surface expression of the TCR.

22. A cell, isolated from a human subject and transduced with a nucleic acid sequence or vector encoding an engineered TCR comprising at least one of the following residues, numbered according to the IMGT system:
L96 of the α chain; R9 of the β chain; Y10 of the β chain; T24 of the α chain; V19 of the α chain; T20 of the α chain; M50 of the α chain; T5 of the α chain; Q8 of the α chain; S86 of the α chain; F39 of the α chain; D55 of the α chain; R43 of the β chain; A66 of the α chain; V19 of the β chain; L21 of the β chain; L103 of the β chain; T3 of the α chain; S7 of the α chain; P9 of the α chain; M11 of the α chain; A16 of the α chain; T18 of the α chain; L21 of the α chain; S22 of the α chain; D26 of the α chain; F40 of the α chain; S47 of the α chain; R48 of the α chain; Q49 of the α chain; I51 of the α chain; L52 of the α chain; V53 of the α chain; T67 of the α chain; E68 of the α chain; N74 of the α chain; F76 of the α chain; N79 of the α chain; Q81 of the α chain; A83 of the α chain; K90 of the α chain; S92 of the α chain; D93 of the α chain; and M101 of the α chain.

23. The cell of claim 22 for use in the treatment and/or prevention of a disease.