

Claims

1. A T cell receptor (TCR) having the property of binding to GVDYDGREHTV (SEQ ID NO: 1) HLA-A*02 complex and comprising a TCR alpha chain variable domain and a TCR beta chain variable domain, wherein:

(a) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:17; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:28;

(b) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:25;

(c) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:28;

(d) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:20; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:28;

(e) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(f) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:27;

(g) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:24; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:29;

(h) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:23; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:29;

(i) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:46; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:29;

(j) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:47; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:29;

(k) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:48; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:29;

(l) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:49; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:29;

(m) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:50; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:29;

(n) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:51; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:29;

(o) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:20; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:65;

(p) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:24; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:66;

(q) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:24; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:67;

(r) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:24; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:68;

(s) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:24; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:69;

(t) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:24; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:70;

(u) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:52; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(v) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:53; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(w) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:54; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(x) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:55; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(y) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:56; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(z) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:57; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(aa) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:58; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(bb) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:59; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(cc) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:60; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(dd) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:71;

(ee) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:72;

(ff) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:73;

(gg) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:74;

(hh) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:75;

(ii) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:76;

(jj) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:77;

(kk) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:78; or

(ll) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:79;

~~(mm) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:62; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:5;~~

~~(nn) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:63; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:5;~~

~~(oo) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:64; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:5;~~

~~(pp) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:61; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:80; or~~

~~(qq) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:61; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:81.~~

2. A TCR that binds to a GGYDGREHTV (SEQ ID NO: 1) HLA-A*02 complex with an affinity greater than 200 μ M, wherein the alpha chain variable domain comprises:

(a) a CDR1 comprising the amino acid sequence of VSPFSN, a CDR2 comprising the amino acid sequence of MTFSENT, and a CDR3 comprising the amino acid sequence of VVNSANGLYIPTF;

(b) a CDR1 comprising the amino acid sequence of VSPFSN, a CDR2 comprising the amino acid sequence of MTFSENT, and a CDR3 comprising the amino acid sequence of VVNRADGLYIPTF;

(c) a CDR1 comprising the amino acid sequence of VSPFSN, a CDR2 comprising the amino acid sequence of LDYAIN, and a CDR3 comprising the amino acid sequence of VVNHSNGSYIPTF;

(d) a CDR1 comprising the amino acid sequence of VSPFSN, a CDR2 comprising the amino acid sequence of LDYAIN, and a CDR3 comprising the amino acid sequence of VVNRADGLYIPTF;

(e) a CDR1 comprising the amino acid sequence of VSPFSN, a CDR2 comprising the amino acid sequence of LTFSENT, and a CDR3 comprising the amino acid sequence of VVNSASGLYIPTF; or

(f) a CDR1 comprising the amino acid sequence of VSPFSN, a CDR2 comprising the amino acid sequence of LTFSENT, and a CDR3 comprising the amino acid sequence of VVNSAQGLYIPTF;

and wherein the beta chain variable domain comprises:

(g) a CDR1 comprising the amino acid sequence of MDHEN, a CDR2 comprising the amino acid sequence of SRFATG, and a CDR3 comprising the amino acid sequence of ASSSDQNSGDPYEYF;

(h) a CDR1 comprising the amino acid sequence of MDHEN, a CDR2 comprising the amino acid sequence of SYDVKM, and a CDR3 comprising the amino acid sequence of ASSSDQNSGDPYEYF;

(i) a CDR1 comprising the amino acid sequence of LDHEN, a CDR2 comprising the amino acid sequence of SRFATG, and a CDR3 comprising the amino acid sequence of ASSSDQNSGDPYEYF;

(j) a CDR1 comprising the amino acid sequence of APLSK, a CDR2 comprising the amino acid sequence of SYDVKM, and a CDR3 comprising the amino acid sequence of ASSSDQNSGDPYEYF; or

(k) a CDR1 comprising the amino acid sequence of APLSK, a CDR2 comprising the amino acid sequence of SYDVKL, and a CDR3 comprising the amino acid sequence of ASSSDQNSGDPYEYF.

3. A TCR as claimed in claim 2, wherein the alpha chain variable domain comprises the following set of CDR1, CDR2, and CDR3 sequences; and the beta chain variable domain comprises the following set of CDR1, CDR2, and CDR3 sequences:

(a) alpha chain variable domain CDR1: VSPFSN, CDR2: LDY AINT, and CDR3: VVNRADGLYIPTF, and beta chain variable domain CDR1: APLSK, CDR2: SYDVKM, and CDR3: ASSSDQNSGDPYEYF;

- (b) alpha chain variable domain CDR1: VSPFSN, CDR2: LDYAIN, and CDR3: VVNRADGLYIP, and beta chain variable domain CDR1: APLSK, CDR2: SYDVKL, and CDR3: ASSSDQNSGDPYEQYF;
- (c) alpha chain variable domain CDR1: VSPFSN, CDR2: MTFSENT, and CDR3: VVNSANGLYIP, and beta chain variable domain CDR1: MDHEN, CDR2: SRFATG, and CDR3: ASSSDQNSGDPYEQYF;
- (d) alpha chain variable domain CDR1: VSPFSN, CDR2: LTFSENT, and CDR3: VVNSAQGLYIP, and beta chain variable domain CDR1: LDHEN, CDR2: SRFATG, and CDR3: ASSSDQNSGDPYEQYF; or
- (e) alpha chain variable domain CDR1: VSPFSN, CDR2: LTFSENT, and CDR3: VVNSASGLYIP, and beta chain variable domain CDR1: LDHEN, CDR2: SRFATG, and CDR3: ASSSDQNSGDPYEQYF.

4. A TCR claimed in any one of claims 2-3, comprising:

- (a) an alpha chain variable domain sequence corresponding to SEQ ID NO:22, and a beta chain variable domain sequence corresponding to SEQ ID NO:26;
- (b) an alpha chain variable domain sequence corresponding to SEQ ID NO:22, and a beta chain variable domain sequence corresponding to SEQ ID NO:27;
- (c) an alpha chain variable domain sequence corresponding to SEQ ID NO:20, and a beta chain variable domain sequence corresponding to SEQ ID NO:28;
- (d) an alpha chain variable domain sequence corresponding to SEQ ID NO:24, and a beta chain variable domain sequence corresponding to SEQ ID NO:29; or
- (e) an alpha chain variable domain sequence corresponding to SEQ ID NO:23, and a beta chain variable domain sequence corresponding to SEQ ID NO:29.

5. A TCR as claimed in any preceding claim, which is an alpha-beta heterodimer, having an alpha chain TRAC constant domain sequence and a beta chain TRBC1 or TRBC2 constant domain sequence.

6. A TCR as claimed in claim 5, wherein the alpha and beta chain constant domain sequences are modified by truncation or substitution to delete a native disulphide bond between Cys4 of exon 2 of TRAC and Cys2 of exon 2 of TRBC1 or TRBC2.
7. A TCR as claimed in claim 5 or claim 6, wherein the alpha and/or beta chain constant domain sequence(s) are modified by substitution of cysteine residues for Thr 48 of TRAC and Ser 57 of TRBC1 or TRBC2, the said cysteines forming a non-native disulphide bond between the alpha and beta constant domains of the TCR.
8. A TCR as claimed in any preceding claim, which is in single chain format of the type $V\alpha$ -L- $V\beta$, $V\beta$ -L- $V\alpha$, $V\alpha$ -C α -L- $V\beta$, $V\alpha$ -L- $V\beta$ -C β , wherein $V\alpha$ and $V\beta$ are TCR α and β variable regions respectively, C α and C β are TCR α and β constant regions respectively, and L is a linker sequence.
9. A TCR as claimed in any preceding claim, wherein the TCR is associated with a detectable label, a therapeutic agent or a pharmacokinetics (PK) modifying moiety.
10. A TCR as claimed in claim 9, wherein an anti-CD3 antibody is covalently linked to the C- or N-terminus of the alpha or beta chain of the TCR.
11. A TCR as claimed in claim 10, wherein the anti-CD3 antibody is covalently linked to the C- or N-terminus of the beta chain of the TCR via a linker sequence.
12. A TCR as claimed in claim 11, wherein the linker sequence is selected from the group consisting of GGGGS (SEQ ID NO: 30), GGGSG (SEQ ID NO: 31), GGSGG (SEQ ID NO: 32), GSGGG (SEQ ID NO: 33), GSGGGP (SEQ ID NO: 34), GGEPS (SEQ ID NO: 35), GGEGGGP (SEQ ID NO: 36), and GGEGGGSEGGGS (SEQ ID NO: 37).
13. A TCR-anti-CD3 fusion molecule comprising a TCR that binds to a GGYDGREHTV (SEQ ID NO: 1) HLA-A*02 complex;
wherein the alpha chain variable domain comprises:

(a) a CDR1 comprising the amino acid sequence of VSPFSN, a CDR2 comprising the amino acid sequence of MTFSENT, and a CDR3 comprising the amino acid sequence of VVNSANGLYIPTF;

(b) a CDR1 comprising the amino acid sequence of VSPFSN, a CDR2 comprising the amino acid sequence of MTFSENT, and a CDR3 comprising the amino acid sequence of VVNRADGLYIPTF;

(c) a CDR1 comprising the amino acid sequence of VSPFSN, a CDR2 comprising the amino acid sequence of LDYAIN, and a CDR3 comprising the amino acid sequence of VVNHSGGSYIPTF;

(d) a CDR1 comprising the amino acid sequence of VSPFSN, a CDR2 comprising the amino acid sequence of LDYAIN, and a CDR3 comprising the amino acid sequence of VVNRADGLYIPTF;

(e) a CDR1 comprising the amino acid sequence of VSPFSN, a CDR2 comprising the amino acid sequence of LTFSENT, and a CDR3 comprising the amino acid sequence of VVNSASGLYIPTF; or

(f) a CDR1 comprising the amino acid sequence of VSPFSN, a CDR2 comprising the amino acid sequence of LTFSENT, and a CDR3 comprising the amino acid sequence of VVNSAQGLYIPTF;

and wherein the beta chain variable domain comprises:

(g) a CDR1 comprising the amino acid sequence of MDHEN, a CDR2 comprising the amino acid sequence of SRFATG, and a CDR3 comprising the amino acid sequence of ASSSDQNSGDPYEQYF;

(h) a CDR1 comprising the amino acid sequence of MDHEN, a CDR2 comprising the amino acid sequence of SYDVKM, and a CDR3 comprising the amino acid sequence of ASSSDQNSGDPYEQYF;

(i) a CDR1 comprising the amino acid sequence of LDHEN, a CDR2 comprising the amino acid sequence of SRFATG, and a CDR3 comprising the amino acid sequence of ASSSDQNSGDPYEQYF;

(j) a CDR1 comprising the amino acid sequence of APLSK, a CDR2 comprising the amino acid sequence of SYDVKM, and a CDR3 comprising the amino acid sequence of ASSSDQNSGDPYEQYF; or

(k) a CDR1 comprising the amino acid sequence of APLSK, a CDR2 comprising the amino acid sequence of SYDVKL, and a CDR3 comprising the amino acid sequence of ASSSDQNSGDPYEQYF, and wherein the anti-CD3 antibody is covalently linked to the N-terminus or C-terminus of the TCR beta chain via a linker sequence selected from SEQ ID NOs: 30-37.

14. A TCR-anti-CD3 fusion molecule as claimed in claim 13, wherein:

(a) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:17; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:28;

(b) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:25;

(c) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:28;

(d) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:20; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:28;

(e) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(f) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:27;

(g) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:24; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:29;

(h) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:23; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:29;

(i) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:46; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:29;

(j) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:47; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:29;

(k) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:48; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:29;

(l) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:49; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:29;

(m) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:50; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:29;

(n) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:51; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:29;

(o) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:20; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:65;

(p) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:24; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:66;

(q) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:24; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:67;

(r) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:24; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:68;

(s) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:24; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:69;

(t) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:24; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:70;

(u) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:52; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(v) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:53; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(w) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:54; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(x) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:55; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(y) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:56; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(z) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:57; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(aa) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:58; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(bb) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:59; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(cc) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:60; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:26;

(dd) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:71;

(ee) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:72;

(ff) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:73;

(gg) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:74;

(hh) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:75;

(ii) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:76;

(jj) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:77;

(kk) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:78; or

(ll) the TCR alpha chain variable domain comprises the amino acid sequence of SEQ ID NO:22; and the TCR beta chain variable domain comprises the amino acid sequence of SEQ ID NO:79.

15. A TCR-anti CD3 fusion molecule as claimed in claim 14, comprising
- (a) an alpha chain amino acid sequence corresponding to SEQ ID NO: 38 and beta chain amino acid sequence corresponding to SEQ ID NO: 42;
 - (b) an alpha chain amino acid sequence corresponding to SEQ ID NO: 38 and beta chain amino acid sequence corresponding to SEQ ID NO: 43;
 - (c) an alpha chain amino acid sequence corresponding to SEQ ID NO: 39 and beta chain amino acid sequence corresponding to SEQ ID NO: 44;
 - (d) an alpha chain amino acid sequence corresponding to SEQ ID NO: 40 and beta chain amino acid sequence corresponding to SEQ ID NO: 45; or
 - (e) an alpha chain amino acid sequence corresponding to SEQ ID NO: 41 and beta chain amino acid sequence corresponding to SEQ ID NO: 45.
16. A TCR-anti CD3 fusion molecule as claimed in claim 15, comprising the alpha chain amino acid sequence of SEQ ID NO: 40 and the beta chain amino acid sequence of SEQ ID NO: 45.
17. A TCR-anti CD3 fusion molecule as claimed in claim 15, comprising the alpha chain amino acid sequence of SEQ ID NO: 38 and the beta chain amino acid sequence of SEQ ID NO: 42.
18. A nucleic acid encoding a TCR alpha chain and/or a TCR beta chain as claimed in any one of the preceding claims.
19. An expression vector comprising the nucleic acid of claim 18.
20. A cell harbouring
- (a) an expression vector as claimed in claim 19 encoding TCR alpha and beta chains as claimed in any one of claims 1-17, in a single open reading frame, or two distinct open reading frames; or
 - (b) a first expression vector which comprises nucleic acid encoding the alpha chain of a TCR as claimed in any one of claims 1-17, and a second expression vector which

comprises nucleic acid encoding the beta chain of a TCR as claimed in any one of claims 1-17.

21. A non-naturally occurring and/or purified and/or engineered cell, especially a T-cell, presenting a TCR as claimed in any one of claims 1-12.

22. A pharmaceutical composition comprising a TCR as claimed in any one of claims 1-12, a TCR-anti CD3 fusion molecule as claimed in any one of claims 13-17, a nucleic acid as claimed in claim 18, and/or a cell as claimed in claim 20 or 21, together with one or more pharmaceutically acceptable carriers or excipients.

23. The TCR of any one of claims 1-12, TCR-anti-CD3 fusion molecule of any one of claims 13-17, nucleic acid of claim 18, pharmaceutical composition of claim 22 and/or cell of claim 20 or 21, for use in medicine, preferably in a human subject.

24. The TCR of any one of claims 1-12, TCR-anti-CD3 fusion molecule of any one of claims 13-17, nucleic acid of claim 18, pharmaceutical composition of claim 22 and/or cell of claim 20 or 21, for use in a method of treating cancer or a tumour, preferably in a human subject.

25. The TCR, TCR anti-CD3 fusion molecule, nucleic acid, pharmaceutical composition and/or cell for use according to claim 24, wherein the human subject has a tumour that expresses MAGE A4.

26. The TCR, TCR anti-CD3 fusion molecule, nucleic acid, pharmaceutical composition and/or cell for use according to claim 24 or 25, wherein the tumour is a solid tumour.

27. The TCR, TCR anti-CD3 fusion molecule, nucleic acid, pharmaceutical composition and/or cell for use according to any one of claims 24-26, wherein the human subject is of HLA-A*02 subtype.

28. The TCR, TCR-anti-CD3 fusion molecule, nucleic acid, pharmaceutical composition and/or cell for use according to any one of claims 24-27, which is to be administered by injection, such as intravenous or direct intratumoral injection.

29. An injectable formulation suitable for administering to a human subject comprising a TCR according to any one of claims 1-12 or a TCR-anti-CD3 fusion molecule of any one of claims 13-17.

30. A method of producing a TCR according to any one of claims 1-12, or a TCR-anti-CD3 fusion molecule according to any one of claims 13-17, comprising a) maintaining a cell according to claim 20 under optimal conditions for expression of the TCR chains acid and b) isolating the TCR chains.