

CLAIMS

1. A T cell receptor (TCR) having the property of binding to GGYDGREHTV (SEQ ID No: 1) in complex with HLA-A*0201 with a dissociation constant of from 0.05 μ M to 20.0 μ M when measured with surface plasmon resonance at 25°C and at a pH between 7.1 and 7.5 using a soluble form of the TCR, and has at least a ten-fold selectivity of binding to SEQ ID No:1 in complex with HLA-A*0201 over binding to GGYDGEEHSV (SEQ ID No: 2) in complex with HLA-A*0201 in which the TCR comprises a TCR alpha chain variable domain and a TCR beta chain variable domain, and in which the TCR variable domains form contacts with at least residues V2, Y3 and D4 of GGYDGREHTV (SEQ ID No: 1), in which:
 - (A) in the alpha chain variable domain, the sequence of
 - (i) amino acid residues 1-27 thereof has (a) at least 90% identity to the sequence of amino acid residues 1-27 of SEQ ID No: 3 or (b) one, two or three amino acid insertions, deletions or substitutions relative to the sequence of (a);
 - (ii) amino acid residues 28-33 is VSPFSN;
 - (iii) amino acid residues 34-47 thereof has (a) at least 90% identity to the sequence of amino acid residues 34-47 of SEQ ID NO: 3 or (b) one, two or three amino acid insertions, deletions or substitutions relative to the sequence of (a);
 - (iv) amino acid residues 48-53 is LTIMTF or LTIVTF or LTILTF
 - (v) amino acid residues 54-90 thereof has (a) at least 90% identity to the sequence of amino acid residues 54-90 of SEQ ID No: 3 or (b) one, two or three amino acid insertions, deletions or substitutions relative to the sequence of (a); and
 - (vi) amino acids 91-105 is CVVSGGTDSWGKLQF; and
 - (B) in the beta chain variable domain, the sequence of
 - (i) amino acid residues 1-45 thereof has (a) at least 90% identity to the amino acid sequence of residues 1-45 of SEQ ID No: 4; or (b) one, two or three amino acid insertions, deletions or substitutions relative to the sequence of (a);
 - (ii) amino acid residues 46-50 is KGHDR;

(iii) amino acid residues 51-67 thereof has (a) at least 90% identity to the sequence of amino acid residues 51-67 of SEQ ID NO: 4 or (b) one, two or three amino acid insertions, deletions or substitutions relative to the sequence of (a);

(iv) amino acid residues 68-72 is SFDVK;

5 (v) amino acid residues 73-109 thereof has (a) at least 90% identity to the sequence of amino acid residues 73-109 of SEQ ID NO: 4 or (b) one, two or three amino acid insertions, deletions or substitutions relative to the sequence of (a); and

(vi) amino acids 110-123 are CATSGQGAYEEQFF.

10 2. A TCR according to Claim 1, which is an alpha-beta heterodimer, having an alpha chain TRAV10 + TRAC constant domain sequence and a beta chain TRBV24-1 + TRBC-2 constant domain sequence.

3. A TCR according to Claim 1, which is in single chain format of the type $V\alpha$ -L- $V\beta$, $V\beta$ -L- $V\alpha$, $V\alpha$ -C α -L- $V\beta$, or $V\alpha$ -L- $V\beta$ -C β , in which $V\alpha$ 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
15 sequence.

4. A TCR according to Claim 1, 2 or 3, which is associated with a detectable label, a therapeutic agent or a pharmacokinetics (PK) modifying moiety.

20 5. A TCR according to any preceding claim, in which the alpha chain variable domain is the alpha chain variable domain sequence set forth in SEQ ID No. 3 and the beta chain variable domain is the beta chain variable domain sequence set forth in SEQ ID No. 9; or the alpha chain variable domain is the alpha chain variable domain sequence set forth in SEQ ID No. 7 and the beta chain variable domain is the beta chain variable domain sequence set forth in SEQ ID No. 9; or the alpha chain variable domain is the alpha chain variable domain
25 sequence set forth in SEQ ID No. 8 and the beta chain variable domain is the beta chain variable domain sequence set forth in SEQ ID No. 9.

6. A TCR according to any preceding claim, in which the alpha chain variable domain comprises the amino acid sequence of SEQ ID No: 3 or 7 or 8.

30 7. A TCR according to any preceding claim, in which the alpha chain variable domain comprises the amino acid sequence of amino acid residues 1-105 of SEQ ID No: 7 or 8.

8. A TCR according to any preceding claim, in which the beta chain variable domain comprises the amino acid sequence of SEQ ID No: 9.
9. A nucleic acid encoding a TCR according to any preceding claim.
10. An isolated or non-naturally occurring cell presenting a TCR according to any preceding
5 claim.
11. An isolated or non-naturally occurring cell according to Claim 10, in which the cell is a T-cell.
12. A cell harbouring:
 - (a) a TCR expression vector which comprises a nucleic acid as claimed in Claim 9 in
10 a single open reading frame, or two distinct open reading frames encoding the alpha chain and the beta chain respectively; or
 - (b) a first expression vector which comprises nucleic acid encoding the alpha chain of a TCR as claimed in any of Claims 1 to 8, and a second expression vector which
15 comprises nucleic acid encoding the beta chain of a TCR as claimed in any of Claims 1 to 8.
13. A pharmaceutical composition comprising a TCR according to any of Claims 1 to 8, a nucleic acid according to Claim 9 or a cell according to Claims 10, 11 or 12, together with one or more pharmaceutically acceptable carriers or excipients.
14. A cell according to Claim 11 for use in medicine.
- 20 15. A cell for use according to Claim 15, for use in a method of treating cancer.