

Claims

1. A tumour specific T-cell receptor (TCR) having a γ chain and a δ chain, or a fragment thereof, characterised by having a complementarity-determining region (CDR) comprising or consisting of the amino acid sequence: CATWDRRDYKKLF (SEQ ID NO: 1) or a sequence that shares at least 88% identity therewith as CDR3 γ and/or a CDR comprising or consisting of the amino acid sequence: CALGVLPTVTGGGLIF (SEQ ID No: 2) or a sequence that shares at least 88% identity therewith as CDR3 δ .

2. The tumour specific T-cell receptor (TCR) according to claim 1 wherein said TCR comprises both of the said CDRs.

3. The tumour specific T-cell receptor (TCR) according to claim 1 or claim 2 wherein said TCR comprises one or more, including any combination, of the following complementarity-determining regions:

VTNTFY (SEQ ID NO:3) as CDR1 γ ,

YDVSTARD (SEQ ID NO:4) as CDR2 γ ,

TSWWSYY (SEQ ID NO:5) as CDR1 δ or

QGS (SEQ ID NO:6) as CDR2 δ .

4. A tumour specific T-cell receptor (TCR), or a fragment thereof, according to claim 1 characterised by having complementarity-determining regions (CDRs) comprising or consisting of the amino acid sequences: CATWDRRDYKKLF (SEQ ID NO: 1) or a sequence that shares at least 88% identity therewith as CDR3 γ ; CALGVLPTVTGGGLIF (SEQ ID No: 2) or a sequence that shares at least 88% identity therewith as CDR3 δ , VTNTFY (SEQ ID NO:3) as CDR1 γ , YDVSTARD (SEQ ID NO: 4) as CDR2 γ , TSWWSYY (SEQ ID NO: 5) as CDR1 δ and QGS (SEQ ID NO: 6) as CDR2 δ .

5. A tumour specific T-cell receptor (TCR), or a fragment thereof, according to claim 4 characterised by having complementarity-determining regions (CDRs) comprising or consisting of the amino acid sequences: CATWDRRDYKKLF (SEQ ID NO: 1) as CDR3 γ ; CALGVLPTVTGGGLIF (SEQ ID No: 2) as CDR3 δ , VTNTFY

(SEQ ID NO:3) as CDR1 γ , YDVSTARD (SEQ ID NO: 4) as CDR2 γ , TSWWSYY (SEQ ID NO: 5) as CDR1 δ and QGS (SEQ ID NO: 6) as CDR2 δ .

6. The tumour specific T-cell receptor (TCR) according to any one of claims 1-5 wherein said TCR has a gamma chain comprising or consisting of the amino acid sequence:

SSNLEGRTKSVTRQTGSSAEITCDLTVTNTFYIHWYHQQEGKAPQRLLYYDV
STARDVLESGLSPGKYTHTPRRWSWILRLQNLIENDSGVYYCATWDRRDY
KKLFGSGTTLVVTDKQLDADVSPKPTIFLPSIAETKLQKAGTYLCLLEKFFPD
VIKIHWEKKSNTILGSQEGNTMKTNDTYMKFSWLTVPEKSLDKEHRCIVRH
ENNKNQVDQEIIFFPIKT (SEQ ID NO:7) or an amino acid sequence that
shares at least 88% identity therewith.

7. The tumour specific T-cell receptor (TCR) according to any one of claims 1-6 wherein said TCR has a delta chain comprising or consisting of the amino acid sequence:

AQKVTQAQSSVSMPVRKAVTLNCLYETSWWSYYIFWYKQLPSKEMIFLIRQGSDE
QNAKSGRYSVNFKKAASVALTISALQLEDSAKYFCALGVLPTVTGGGLIFGKGTRV
TVEPNSQPHTKPSVFVMKNGTNVACLVKEFYPKDIRINLVSSKKITEFDPAIVISPSG
KYNVAVKLGKYEDSNSVTCSVQHDKTVHSTDFEVKTDST (SEQ ID NO:8) or an
amino acid sequence that shares at least 88% identity therewith.

8. The tumour specific T-cell receptor (TCR) according to any one of claims 1-7 wherein said TCR is in a soluble form.

9. The tumour specific T-cell receptor (TCR) according to any one of claims 1-7 wherein said TCR is in a membrane compatible form and has a transmembrane region and an intracellular region.

10. The tumour specific T-cell receptor (TCR) according to any one of claims 1-7 in a single chain form.

11. The tumour specific T-cell receptor (TCR), or a fragment thereof, according to any one of claims 1-10 which binds to a tumour specific ligand in the context of SCNN1A gene expression.

12. A T-cell or T cell clone expressing said TCR according to any one of claims 1-11.
13. The T-cell clone according to claim 12 wherein said clone is a SW.3G1 clone.
14. A vector encoding the TCR, or a fragment thereof, according to anyone of claims 1-11.
15. A bispecific comprising a TCR, or a fragment thereof, according to any one of claims 1-11 and an immune cell activating component or ligand that binds and so activates an immune cell, such as a Killer T-cell.
16. A pharmaceutical composition comprising said TCR, or a fragment thereof, according to any one of claims 1-11 or said cell or clone according to claims 12 or 13 or said vector according to claim 14.
17. Use of a TCR according to any one of claims 1-11 or cell or clone according to claims 12 or 13 or vector according to claim 14 or bispecific according to claim 15 or the pharmaceutical composition according to claim 16 in the manufacture of a medicament for the treatment of cancer.
18. The TCR, the cell, the clone, the vector, the bispecific or the pharmaceutical composition according to claim 17 wherein said cancer is selected from the group consisting of colorectal cancer, lung, kidney, prostate, bladder, cervical, melanoma (skin), bone, breast, blood, brain, pancreas, testicle, ovary, head/neck, liver, bladder, thyroid, and uterine cancers.
19. A combination therapeutic for the treatment of cancer comprising:
 - a) the said TCR according to claims 1-11 or the said cell or clone according to claims 12 or 13 or the said vector according to claim 14 or the said bispecific according to claim 15 or the said pharmaceutical composition according to claim 16 in combination with;
 - b) a further cancer therapeutic agent.
20. A TCR or polypeptide or bispecific or antibody, or a fragment of said antibody, that binds to at least one of the SCNNA1 gene product isoforms shown in Figure 9,

optionally wherein the TCR or polypeptide or bispecific or antibody, or a fragment of said antibody binds to the extracellular domain of said isoform.