

CLAIMS

1. A TCR comprising an alpha chain and a beta chain, wherein the alpha chain comprises a TCR alpha variable domain comprising the complementarity determining regions CDR1, CDR2 and CDR3 of SEQ ID NO:2 or CDR1, CDR2 and CDR3 having one, ~~two or three~~ conservative amino acid substitutions relative to the corresponding CDR sequences of SEQ ID NO: 2; and the beta chain comprises a TCR beta variable domain comprising the complementarity determining regions CDR1, CDR2 and CDR3 of SEQ ID NO:10 or CDR1, CDR2 and CDR3 having one, ~~two or three~~ conservative amino acid substitutions relative to the corresponding CDR sequences of SEQ ID NO: 10, and wherein the TCR specifically binds to a IGF2BP3-001 peptide-MHC molecule complex, wherein the IGF2BP3-001 peptide consists of SEQ ID NO:1, and wherein the TCR binds to the positions 1 and 3 to 7 of said IGF2BP3-001 peptide.
2. A TCR of claim 1, wherein the alpha chain comprises a TCR alpha variable domain at least 90% identical to the TCR alpha variable domain of SEQ ID NO:2 and wherein the TCR alpha chain comprises the CDR1, CDR2 and CDR3 of SEQ ID NO:2; and the beta chain comprises a TCR beta variable domain at least 90% identical to the TCR beta variable domain of SEQ ID NO:10 and wherein the TCR beta chain comprises the CDR1, CDR2 and CDR3 of SEQ ID NO: 10.
3. The TCR of claim 1 or 2, further comprising a TCR alpha constant domain and a TCR beta constant domain, wherein the TCR alpha constant domain is at least ~~70~~90% identical to the TCR alpha constant domain of SEQ ID NO:2, and the beta constant domain is at least ~~70~~90% identical to the TCR beta constant domain of SEQ ID NO:10.
4. The TCR of any of claims 1 to 3, wherein the alpha constant domain comprises the alpha transmembrane domain VIGFRILLKLVAGFNLLMTL (SEQ ID NO:18) and the beta constant domain comprises the beta transmembrane domain TILYEILLGKATLYAVLVSAVLV (SEQ ID NO:19).
5. The TCR of any of claims 1 to 4, wherein
 - a. the alpha chain and beta chain are fused to form a single chain TCR;
 - b. the alpha and/or beta chain comprises a detectable label; and/or

c. the alpha and/or beta chain is conjugated to a therapeutically active agent.

6. A TCR comprising a gamma chain and a delta chain, wherein the gamma chain comprises the complementarity determining regions CDR1, CDR2 and CDR3 of SEQ ID NO:2; and ~~the~~ the TCR delta chain comprises the complementarity determining regions CDR1, CDR2 and CDR3 of SEQ ID NO:10, and wherein the TCR specifically binds to a IGF2BP3-001 peptide-MHC molecule complex, wherein the IGF2BP3-001 peptide consists of SEQ ID NO:1, and wherein the TCR binds to the positions 1 and 3 to 7 of said IGF2BP3-001 peptide.

7. An expression vector comprising a nucleic acid or nucleic acids encoding the alpha chain and ~~the~~ beta chain of the TCR of any of claims 1 to 5, or the gamma chain and ~~the~~ delta chain of the TCR of claim 6 operably linked to at least one promoter sequence.

8. A host cell transformed with the expression vector of claim 7.

9. The host cell of claim 8, which is a T cell or T cell progenitor.

10. A pharmaceutical composition comprising the TCR of any of claims 1 to 6, an expression vector of claim 7, and/or a host cell of claim 8 or 9; and a pharmaceutically acceptable carrier, and optionally, pharmaceutically acceptable excipients and/or stabilizers.

11. A method for producing a TCR that specifically binds to the peptide of SEQ ID NO:1 when presented by an MHC molecule, said method comprising culturing the host cell of claim 8 or 9 under conditions suitable to promote expression of the TCR.

12. A TCR of any one of claims 1 to 6, an expression vector of claim 7, a host cell of claim 8 or 9, and/or a pharmaceutical composition of claim 10 for use as a medicament.

13. A TCR of any one of claims 1 to 6, an expression vector of claim 7, a host cell of claim 8 or 9, and/or a pharmaceutical composition of claim 10 for use in a method of treatment of a cancer expressing IGF2BP3-001.

14. Use of a TCR of any of claims 1 to 6, an expression vector of claim 7, and/or a host cell of claim 8 or 9, and/or a pharmaceutical composition of claim 10 in the manufacture of a medicament for the treatment of a cancer expressing IGF2BP3-001.
- 5 15. Use of a TCR of any one of claims 1 to 6, an expression vector of claim 7, a host cell of claim 8 or 9, and/or a pharmaceutical composition of claim 10 in the manufacture of a medicament for the treatment of a cancer expressing IGF2BP3-001, wherein the cancer is non-small cell lung cancer, small cell lung cancer, renal cell cancer, brain cancer, gastric cancer, colorectal cancer, hepatocellular cancer, head and neck cancer, pancreatic cancer, 10 prostate cancer, leukemia, breast cancer, Merkel cell carcinoma, melanoma, ovarian cancer, urinary bladder cancer, uterine cancer, gallbladder and bile duct cancer, esophageal cancer, or a combination thereof.
- 15 16. A method of detecting cancers expressing IGF2BP3-001 in a biological sample comprising:
a) contacting the biological sample with the TCR of any of claims 1 to 6, and
b) detecting binding of the TCR to the biological sample.
- 20 17. Use of a TCR of any one of claims 1 to 6, an expression vector of claim 7, a host cell of claim 8 or 9, and/or a pharmaceutical composition of claim 10 in the manufacture of a medicament for killing target-cells in a patient which target-cells aberrantly express IGF2BP3.
- 25 18. The TCR of any of claims 1 to 6 which is a soluble TCR.