

CLAIMS

1. An engineered murine T cell receptor (mTCR) V α chain polypeptide comprising at least 90% sequence identity to SEQ ID NO:2, 3, 4, 5, 6, 7, 8, 9, or 10, wherein the mTCR specifically binds hAFP158 (SEQ ID NO: 1).
2. An engineered murine T cell receptor (mTCR) V β chain polypeptide comprising at least 90% sequence identity to SEQ ID NO: 11, 12, 13, or 14, wherein the mTCR specifically binds hAFP158 (SEQ ID NO: 1).
3. An engineered murine T cell receptor (mTCR) full length α chain polypeptide comprising at least 90% sequence identity to SEQ ID NO: 15, 16, 17, 18, 19, 20, 21, 22, or 23, wherein the mTCR specifically binds hAFP158 (SEQ ID NO: 1).
4. An engineered murine T cell receptor (mTCR) full length β chain polypeptide comprising at least 90% sequence identity to SEQ ID NO:24, 25, 26, or 27, wherein the mTCR specifically binds hAFP158 (SEQ ID NO: 1).
5. An engineered murine T cell receptor (mTCR) α chain polypeptide comprising a CDR3 region with at least 90% sequence identity to SEQ ID NO:28, 29, 30, 31, 32, 33, 34, 35, or 36, wherein the mTCR specifically binds hAFP158 (SEQ ID NO: 1).
6. An engineered murine T cell receptor (mTCR) β chain polypeptide comprising a CDR3 region with at least 90% sequence identity to SEQ ID NO:37, 38, 39, or 40, wherein the mTCR specifically binds hAFP158 (SEQ ID NO: 1).
7. An engineered murine T cell receptor (mTCR) comprising:
 - a) a V α domain having at least 90% sequence identity to SEQ ID NO:2, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO:28; and
 - b) a V β domain having at least 90% sequence identity to SEQ ID NO: 11, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO:37.
8. An engineered murine T cell receptor (mTCR) comprising:
 - a) a V α domain having at least 90% sequence identity to SEQ ID NO:3, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO:29; and

b) a V β domain having at least 90% sequence identity to SEQ ID NO: 11, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO:37.

9. An engineered murine T cell receptor (mTCR) comprising:

a) a V α domain having at least 90% sequence identity to SEQ ID NO:4, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO: 30; and

b) a V β domain having at least 90% sequence identity to SEQ ID NO: 12, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO:38.

10. An engineered murine T cell receptor (mTCR) comprising:

a) a V α domain having at least 90% sequence identity to SEQ ID NO:5, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO: 31; and

b) a V β domain having at least 90% sequence identity to SEQ ID NO: 13, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO:39.

11. An engineered murine T cell receptor (mTCR) comprising:

a) a V α domain having at least 90% sequence identity to SEQ ID NO: 6, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO:32; and

b) a V β domain having at least 90% sequence identity to SEQ ID NO: 11, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO:37.

12. An engineered murine T cell receptor (mTCR) comprising:

a) a V α domain with at least 90% sequence identity to SEQ ID NO:7, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO:33; and

b) a V β domain having at least 90% sequence identity to SEQ ID NO: 14, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO:40.

13. An engineered murine T cell receptor (mTCR) comprising:

a) a V α domain having at least 90% sequence identity to SEQ ID NO: 8, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO:34; and

b) a V β domain having at least 90% sequence identity to SEQ ID NO: 11, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO:37.

14. An engineered murine T cell receptor (mTCR) comprising:

a) a V α domain having at least 90% sequence identity to SEQ ID NO: 9, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO:35; and

b) a V β domain having at least 90% sequence identity to SEQ ID NO: 11, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO:37.

15. An engineered murine T cell receptor (mTCR) comprising:

a) a V α domain having at least 90% sequence identity to SEQ ID NO: 10, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO: 36; and

b) a V β domain having at least 90% sequence identity to SEQ ID NO: 11, wherein the CDR3 region has at least 90% sequence identity to SEQ ID NO:37.

16. The engineered murine T cell receptor (mTCR) of any one of claims 7-15, wherein the mTCR is humanized.

17. A T cell engineered to express the mTCR of any one of claims 7-16.

18. The T cell of claim 17, wherein the T cell is human.

19. The T cell of claim 18, wherein the T cell is autologous.

20. A soluble mTCR α chain comprising Q21 to L242 of SEQ ID NO:2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 16, 17, 18, 19, 20, 21, 22, or 23.

21. The extracellular domain of an engineered mTCR β chain comprising SEQ ID NO:50, 51, 52, or 53, or E18 to Y276 of SEQ ID NO:24, 25, 26, or 27.

22. A fusion protein comprising at least 90% sequence identity to SEQ ID NO:54, 55, 56, 57, 58, 59, 60, 61, or 62.

23. A nucleic acid comprising at least 90% sequence identity to SEQ ID NO:63, 64, 65, 66, 67, 68, 69, 70, or 71.

24. A non-naturally occurring hAFP158 epitope-specific murine T cell receptor comprising:
- a) . an α chain variable domain ($V\alpha$) having at least 90% sequence identity to amino acid residues 21-132 of SEQ ID NO:2, 3, 4, 5, 6, 7, 8, 9, or 10; and
 - b) . a β chain variable domain ($V\beta$) having at least 90% sequence identity to amino acid residues 18-131 of SEQ ID NO: 11, 12, 13, or 14.
25. A fusion protein comprising a first polypeptide having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:2, 3, 4, 5, 6, 7, 8, 9, or 10, linked to a second polypeptide having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO: 11, 12, 13, or 14.
26. A fusion protein comprising a first polypeptide having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO: 15, 16, 17, 18, 19, 20, 21, 22, or 23 linked to a second polypeptide having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:24, 25, 26, or 27.
27. A T cell engineered to express the mTCR encoded by SEQ ID NO:63, 64, 65, 66, 67, 68, 69, 70, or 71.
28. The T cell of claim 27, wherein the T cell is human.
29. A hybridoma comprising a CD8⁺Tet158⁺ cell fused to a donor cell lacking TCR α and β chains.
30. The hybridoma of claim 29, wherein the hybridoma responds to hAFP⁺ tumor cells.
31. The hybridoma of claim 29, wherein the hybridoma secretes IL-2.
32. A fusion protein comprising a first polypeptide having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO:2, 3, 4, 5, 6, 7, 8, 9 or 10 linked to a second polypeptide having at least 90% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NO: 11, 12, 13, 14, 24, 25, 26, or 27, wherein the fusion protein is linked to a single chain anti-CD3 antibody.

33. Use of a composition in the manufacture of a medicament for treating tumors in a subject, wherein the composition comprises genetically engineering human T cells to express the mTCR of any one of claims 7-16.
34. The use of claim 33, wherein the tumors are hepatocellular carcinoma.
35. The use of claim 33, wherein the T cells are autologous T cells.
36. The polypeptide or protein according to any one of claims 1-15 and 24-26 further comprising a detectable label.
37. A method for detecting hepatocellular carcinoma comprising contacting the polypeptide or protein of claim 36 to a sample of cells, wherein specific binding of the polypeptide or protein to a cell is indicative of a hepatocellular carcinoma cell.
38. An antibody or antigen binding fragment thereof that specifically binds to the polypeptide or protein according to any one of claims 1-6 and 20-22.