

CLAIM(S):

1. An isolated or purified T cell receptor (TCR) having antigenic specificity for human p53^{R175H} amino acid sequence, wherein the TCR comprises the amino acid sequences of all of SEQ ID NOs: 3-8.
2. The TCR of claim 1, wherein the TCR comprises the amino acid sequences of:
 - (1) both of SEQ ID NOs: 9 and 10;
 - (2) both of SEQ ID NOs: 142 and 143;
 - (3) both of SEQ ID NOs: 178 and 10; or
 - (4) both of SEQ ID NOs: 9 and 205.
3. The TCR of claim 1 or 2, wherein the TCR comprises the amino acid sequences of:
 - (1) both of SEQ ID NOs: 11 and 12;
 - (2) both of SEQ ID NOs: 160 and 161;
 - (3) both of SEQ ID NOs: 179 and 12; or
 - (4) both of SEQ ID NOs: 11 and 206.
4. The TCR of any one of claims 1-3, wherein the human p53^{R175H} amino acid sequence is SEQ ID NO: 2 or SEQ ID NO: 96.
5. The TCR of any one of claims 1-4, wherein the TCR does not have antigenic specificity for the wild-type human p53 amino acid sequence of SEQ ID NO: 95.
6. An isolated or purified polypeptide comprising a functional portion of the TCR of any one of claims 1-3, wherein the functional portion has antigenic specificity for human p53^{R175H} and comprises an alpha chain complementarity determining region (CDR)1 comprising the amino acid sequence of SEQ ID NO: 3, an alpha chain CDR2 comprising the amino acid sequence of SEQ ID NO: 4, an alpha chain CDR3 comprising the amino acid sequence of SEQ ID NO: 5, a beta chain CDR1 comprising the amino acid sequence of SEQ ID NO: 6, a beta chain CDR2 comprising the amino acid sequence of SEQ ID NO: 7, and a beta chain CDR3 comprising the amino acid sequence of SEQ ID NO: 8.

7. The polypeptide of claim 6, wherein the polypeptide comprises the amino acid sequences of:

- (1) both of SEQ ID NOs: 9 and 10;
- (2) both of SEQ ID NOs: 142 and 143;
- (3) both of SEQ ID NOs: 178 and 10; or
- (4) both of SEQ ID NOs: 9 and 205.

8. The polypeptide of claim 6 or 7, wherein the polypeptide comprises the amino acid sequences of:

- (1) both of SEQ ID NOs: 11 and 12;
- (2) both of SEQ ID NOs: 160 and 161;
- (3) both of SEQ ID NOs: 179 and 12; or
- (4) both of SEQ ID NOs: 11 and 206.

9. An isolated or purified protein having antigenic specificity for human p53^{R175H} and comprising a first polypeptide chain comprising an alpha chain complementarity determining region (CDR)1 comprising the amino acid sequence of SEQ ID NO: 3, an alpha chain CDR2 comprising the amino acid sequence of SEQ ID NO: 4, an alpha chain CDR3 comprising the amino acid sequence of SEQ ID NO: 5, and a second polypeptide chain comprising a beta chain CDR1 comprising the amino acid sequence of SEQ ID NO: 6, a beta chain CDR2 comprising the amino acid sequence of SEQ ID NO: 7, and a beta chain CDR3 comprising the amino acid sequence of SEQ ID NO: 8.

10. The protein of claim 9, wherein the protein comprises:

- (1) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 9 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 10;
- (2) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 142 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 143;
- (3) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 178 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 10;

(4) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 9 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 205.

11. The protein of claim 9 or 10, wherein the protein comprises:

(1) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 11 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 12;

(2) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 160 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 161;

(3) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 179 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 12; or

(4) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 11 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 206.

12. An isolated or purified nucleic acid comprising a nucleotide sequence encoding the TCR of any one of claims 1-5, the polypeptide of any one of claims 6-8, or the protein of any one of claims 9-11.

13. An isolated or purified nucleic acid comprising, from 5' to 3', a first nucleotide sequence and a second nucleotide sequence, wherein the first and second nucleotide sequence, respectively, encode the amino sequences of SEQ ID NOs: 9 and 10; 10 and 9; 142 and 143; 143 and 142; 178 and 10; 10 and 178; 9 and 205; or 205 and 9.

14. The isolated or purified nucleic acid of claim 13, further comprising a third nucleotide sequence interposed between the first and second nucleotide sequence, wherein the third nucleotide sequence encodes a cleavable linker peptide.

15. The isolated or purified nucleic acid of claim 14, wherein the cleavable linker peptide comprises the amino acid sequence of SEQ ID NO: 94.

16. The isolated or purified nucleic acid of claim 15, which encodes the amino acid sequence of SEQ ID NO: 13 or 180.

17. A recombinant expression vector comprising the nucleic acid of any one of claims 12-16.
18. The recombinant expression vector of claim 17, which is a transposon or a lentiviral vector.
19. An isolated or purified TCR, polypeptide, or protein encoded by the nucleic acid of any one of claims 12-16 or the vector of claim 17 or 18.
20. An isolated or purified TCR, polypeptide, or protein that is expressed by the nucleic acid of any one of claims 12-16 or the vector of claim 17 or 18 in a cell.
21. A method of producing a host cell expressing a TCR that has antigenic specificity for the peptide of SEQ ID NO: 2 or SEQ ID NO: 96, the method comprising contacting a cell with the vector of claim 17 or 18 under conditions that allow introduction of the vector into the cell.
22. An isolated or purified host cell comprising the nucleic acid of any one of claims 12-16 or the recombinant expression vector of claim 17 or 18.
23. The host cell of claim 22, wherein the cell is a human lymphocyte.
24. The host cell of claim 22, wherein the cell is selected from the group consisting of a T cell, a natural killer T (NKT) cell, an invariant natural killer T (iNKT) cell, and a natural killer (NK) cell.
25. An isolated or purified population of cells comprising the host cell of any one of claims 22-24.
26. A method of producing the TCR of any one of claims 1-5, 19, or 20, the polypeptide of any one of claims 6-8, 19, or 20, or the protein of any one of claims 9-11, 19, or 20, the

method comprising culturing the host cell of any one of claims 22-24, or the population of host cells of claim 25, so that the TCR, polypeptide, or protein is produced.

27. A pharmaceutical composition comprising (a) the TCR of any one of claims 1-5, 19, or 20, the polypeptide of any one of claims 6-8, 19, or 20, the protein of any one of claims 9-11, 19, or 20, the nucleic acid of any one of claims 12-16, the recombinant expression vector of claim 17 or 18, the host cell of any one of claims 22-24, or the population of cells of claim 25 and (b) a pharmaceutically acceptable carrier.

28. A method of detecting the presence of cancer in mammal, the method comprising:
(a) contacting a sample comprising cells of the cancer with a T cell expressing the TCR of any one of claims 1-5, 19, or 20, the polypeptide of any one of claims 6-8, 19, or 20, or the protein of any one of claims 9-11, 19, or 20; a population of T cells comprising the T cell; or a pharmaceutical composition comprising the T cell or population of T cells, thereby forming a complex; and

(b) detecting the complex,

wherein detection of the complex is indicative of the presence of cancer in the mammal, wherein the cancer is known to comprise an R175H mutation in human p53.

29. A T cell expressing the TCR of any one of claims 1-5, 19, or 20, the polypeptide of any one of claims 6-8, 19, or 20, or the protein of any one of claims 9-11, 19, or 20; a population of T cells comprising the T cell; or a pharmaceutical composition comprising the T cell or population of T cells, for use in inducing an immune response against a cancer in a mammal, wherein the cancer is known to comprise an R175H mutation in human p53.

30. A T cell expressing the TCR of any one of claims 1-5, 19, or 20, the polypeptide of any one of claims 6-8, 19, or 20, or the protein of any one of claims 9-11, 19, or 20; a population of T cells comprising the T cell; or a pharmaceutical composition comprising the T cell or population of T cells, for use in treating or preventing cancer in a mammal, wherein the cancer is known to comprise an R175H mutation in human p53.

31. The T cell, population of T cells, or pharmaceutical composition for the use of claim 29 or 30, wherein the T cell or population of cells is autologous to the mammal.

32. The T cell, population of T cells, or pharmaceutical composition for the use of claim 29 or 30, wherein the T cell or population of cells is allogeneic to the mammal.

33. The method of claim 28, or the T cell, population of T cells, or pharmaceutical composition for the use of any one of claims 29-32, wherein the cancer is an epithelial cancer.

34. The method of claim 28, or the T cell, population of T cells, or pharmaceutical composition for the use of any one of claims 29-32, wherein the cancer is cholangiocarcinoma, melanoma, colon cancer, rectal cancer, ovarian cancer, endometrial cancer, non-small cell lung cancer (NSCLC), glioblastoma, uterine cervical cancer, head and neck cancer, breast cancer, pancreatic cancer, or bladder cancer.