NOs: 25-27 and a second polypeptide chain comprising the amino acid sequences of SEQ ID NOs: 28-30; or (d) a first polypeptide chain comprising the amino acid sequences of SEQ ID NOs: 33-35 and a second polypeptide chain comprising the amino acid sequences of SEQ ID NOs: 36-38.

[0006a] In one aspect, the present disclosure provides an isolated or purified TCR comprising the amino acid sequences of all of SEQ ID NOs: 9-14.

[0006b] In another aspect, the present disclosure provides an isolated or purified polypeptide comprising the amino acid sequences of all of SEQ ID NOs: 9-14.

[0006c] In yet another aspect, the present disclosure provides an isolated or purified protein comprising: (a) a first polypeptide chain comprising the amino acid sequences of SEQ ID NOs: 9-11; and (b) a second polypeptide chain comprising the amino acid sequences of SEQ ID NOs: 12-14.

[0006d] In a further aspect, the present disclosure provides an isolated or purified nucleic acid comprising a nucleotide sequence encoding the TCR, the polypeptide, or the protein as disclosed herein.

[0007] The present disclosure further provides related nucleic acids, recombinant expression vectors, host cells, populations of cells, and pharmaceutical compositions relating to the TCRs, polypeptides, and proteins of the invention.

[0007a] In one aspect, the present disclosure provides a recombinant expression vector comprising the nucleic acid as disclosed herein.

[0007b] In another aspect, the present disclosure provides an isolated or purified host cell comprising the recombinant expression vector as disclosed herein.

[0007c] In another aspect, the present disclosure provides a population of cells comprising at least one isolated or purified host cell as disclosed herein.

[0007d] In another aspect, the present disclosure provides a pharmaceutical composition comprising the TCR, the polypeptide, the protein, the nucleic acid, the recombinant expression vector, the host cell, or the population of host cells as disclosed herein, and a pharmaceutically acceptable carrier.

[0008] Methods of detecting the presence of cancer in a mammal and methods of treating or preventing cancer in a mammal are further provided by the present disclosure.

[0008a] In one aspect, the present disclosure provides a method of detecting the presence of cancer in a mammal, the method comprising: (a) contacting a sample comprising cells of the cancer with the TCR, the polypeptide, the protein, the host cell, the population of

host cells, or the pharmaceutical composition comprising the TCR, polypeptide, protein, host cell, or population of host cells as disclosed herein and a pharmaceutically acceptable carrier, thereby forming a complex; and (b) detecting the complex, wherein detection of the complex is indicative of the presence of cancer in the mammal.

[0008b] In another aspect, the present disclosure provides the use of the TCR, the polypeptide, the protein, the nucleic acid, the recombinant expression vector, the host cell, the population of host cells, or the pharmaceutical composition, in the manufacture of a medicament for the treatment or prevention of cancer in a mammal.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S)

[0009] Figure 1A is a graph showing IFN-γ production (spots/2e4 cells) as determined by ELISPOT assay of 24 individual TIL cultures after co-culture with autologous dendritic cells transfected with an irrelevant tandem minigene (TMG) RNA (closed circles), or the indicated TMG construct encoding the 61 mutations identified by whole-exomic and transcriptome sequencing (TMG-1 (stars), TMG-2 (△), TMG-3 (▽), TMG-4 (open diamond), TMG-5 (closed diamond)).

[0010] Figure 1B is a graph showing IFN-γ production (spots/2e4 cells) as determined by ELISPOT assay (left axis; unshaded bars), and flow cytometric analysis of 4-1BB expression on CD8+ T cells (%) (right axis; shaded bars) of TIL culture #6 after co-culture with dendritic cells (DCs) transfected with an irrelevant TMG RNA or TMG-1, or incubated overnight with the mutated long peptides encoded by TMG-1.

[0011] Figure 1C is a graph showing IFN-γ production as determined by ELISPOT assay (left axis; unshaded bars), and flow cytometric analysis of 4-1BB expression on CD8+ T cells (%) (right axis; shaded bars) of the infusion product (TIL culture #6 after undergoing clinical scale rapid expansion) after co-culture with DCs transfected with the indicated TMG RNA, or incubated overnight with the 24-AA long KRAS-wild type (WT) or $KRAS^{G12D}$ peptides.

[0012] Figures 2A-2D are graphs showing the results of a TCR-Vβ deep sequencing analysis quantitating the frequency of each of the four identified $KRAS^{G12D}$-reactive T-cell clones in the infusion product (Rx1, filled bar), three metastatic lung samples prior to cell transfer (Tu-1, diamond; Tu-2A, square; and Tu-2B, triangle), the one progressing lesion after cell transfer (Tu-Pro, inverted triangle), and the peripheral blood of the patient before and at various times after cell infusion (circles). Numbers in parentheses indicate the rank of

CLAIM(S):

1. An isolated or purified TCR comprising the amino acid sequences of all of SEQ ID NOs: 9-14.

2. The isolated or purified TCR of claim 1, comprising:

(i) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 15;

(ii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 16;

(iii) an amino acid sequence at least 99% identical to amino acids 20-129 of SEQ ID NO: 15;

(iv) an amino acid sequence at least 99% identical to amino acids 22-133 of SEQ ID NO: 16; or

(v) both (i) and (ii); both (i) and (iv); both (ii) and (iii); or both (iii) and (iv).

3. The isolated or purified TCR of claim 1, comprising:

(i) the amino acid sequence of SEQ ID NO: 15;

(ii) the amino acid sequence of SEQ ID NO: 16;

(iii) amino acids 20-129 of SEQ ID NO: 15;

(iv) amino acids 22-133 of SEQ ID NO: 16; or

(v) both (i) and (ii); both (i) and (iv); both (ii) and (iii); or both (iii) and (iv).

4. The isolated or purified TCR of any one of claims 1-3, further comprising:

(A) an α chain constant region comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 46, wherein:

(i) X at position 48 of SEQ ID NO: 46 is Thr or Cys;

(ii) X at position 112 of SEQ ID NO: 46 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 114 of SEQ ID NO: 46 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp;

and

(iv) X at position 115 of SEQ ID NO: 46 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(B) a β chain constant region comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 47, wherein X at position 57 of SEQ ID NO: 47 is Ser or Cys; or

(C) both (A) and (B).

5. The isolated or purified TCR of any one of claims 1-3, further comprising:

(A) an α chain constant region comprising the amino acid sequence of SEQ ID NO: 46, wherein:

(i) X at position 48 of SEQ ID NO: 46 is Thr or Cys;

(ii) X at position 112 of SEQ ID NO: 46 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 114 of SEQ ID NO: 46 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp;

and

(iv) X at position 115 of SEQ ID NO: 46 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(B) a β chain constant region comprising the amino acid sequence of SEQ ID NO: 47, wherein X at position 57 of SEQ ID NO: 47 is Ser or Cys; or

(C) both (A) and (B).

6. The isolated or purified TCR of any one of claims 1-5, comprising:

(1) an α chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 50;

(2) a β chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 51;

(3) an α chain comprising an amino acid sequence at least 99% identical to amino acids 20-266 of SEQ ID NO: 50;

(4) a β chain comprising an amino acid sequence at least 99% identical to amino acids 22-306 of SEQ ID NO: 51; or

(5) both (1) and (2); both (1) and (4); both (2) and (3); or both (3) and (4).

7. The isolated or purified TCR of any one of claims 1-5, comprising:

(1) an α chain comprising the amino acid sequence of SEQ ID NO: 50;

(2) a β chain comprising the amino acid sequence of SEQ ID NO: 51;

(3) an α chain comprising amino acids 20-266 of SEQ ID NO: 50;

(4) a β chain comprising amino acids 22-306 of SEQ ID NO: 51; or

(5) both (1) and (2); both (1) and (4); both (2) and (3); or both (3) and (4).

8. An isolated or purified polypeptide comprising the amino acid sequences of all of SEQ ID NOs: 9-14.

9. The isolated or purified polypeptide of claim 8, comprising:

(i) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 15;

(ii) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 16;

(iii) an amino acid sequence at least 99% identical to amino acids 20-129 of SEQ ID NO: 15;

(iv) an amino acid sequence at least 99% identical to amino acids 22-133 of SEQ ID NO: 16; or

(v) both (i) and (ii); both (i) and (iv); both (ii) and (iii); or both (iii) and (iv).

10. The isolated or purified polypeptide of claim 8, comprising:

(i) the amino acid sequence of SEQ ID NO: 15;

(ii) the amino acid sequence of SEQ ID NO: 16;

(iii) amino acids 20-129 of SEQ ID NO: 15;

(iv) amino acids 22-133 of SEQ ID NO: 16; or

(v) both (i) and (ii); both (i) and (iv); both (ii) and (iii); or both (iii) and (iv).

11. The isolated or purified polypeptide of any one of claims 8-10, further comprising:

(A) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 46, wherein:

(i) X at position 48 of SEQ ID NO: 46 is Thr or Cys;

(ii) X at position 112 of SEQ ID NO: 46 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 114 of SEQ ID NO: 46 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp;

and

(iv) X at position 115 of SEQ ID NO: 46 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(B) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 47, wherein X at position 57 of SEQ ID NO: 47 is Ser or Cys; or

(C) both (A) and (B).

12. The isolated or purified polypeptide of any one of claims 8-10, further comprising:

(A) the amino acid sequence of SEQ ID NO: 46, wherein:

(i) X at position 48 of SEQ ID NO: 46 is Thr or Cys;

(ii) X at position 112 of SEQ ID NO: 46 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 114 of SEQ ID NO: 46 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp;

and

(iv) X at position 115 of SEQ ID NO: 46 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(B) the amino acid sequence of SEQ ID NO: 47, wherein X at position 57 of SEQ ID NO: 47 is Ser or Cys; or

(C) both (A) and (B).

13. The isolated or purified polypeptide of any one of claims 8-12, comprising:

(1) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 50;

(2) an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 51;

(3) an amino acid sequence at least 99% identical to amino acids 20-266 of SEQ ID NO: 50;

(4) an amino acid sequence at least 99% identical to amino acids 22-306 of SEQ ID NO: 51; or

(5) both (1) and (2); both (1) and (4); both (2) and (3); or both (3) and (4).

14. The isolated or purified polypeptide of any one of claims 8-12, comprising:

(1) the amino acid sequence of SEQ ID NO: 50;

(2) the amino acid sequence of SEQ ID NO: 51;

(3) amino acids 20-266 of SEQ ID NO: 50;

(4) amino acids 22-306 of SEQ ID NO: 51; or

(5) both (1) and (2); both (1) and (4); both (2) and (3); or both (3) and (4).

15. An isolated or purified protein comprising:

(a) a first polypeptide chain comprising the amino acid sequences of SEQ ID NOs: 9-11; and

(b) a second polypeptide chain comprising the amino acid sequences of SEQ ID NOs: 12-14.

16. The isolated or purified protein of claim 15 comprising:

(i) a first polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 15;

(ii) a second polypeptide chain comprising an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 16;

(iii) a first polypeptide chain comprising an amino acid sequence at least 99% identical to amino acids 20-129 of SEQ ID NO: 15;

(iv) a second polypeptide chain comprising an amino acid sequence at least 99% identical to amino acids 22-133 of SEQ ID NO: 16; or

(v) both (i) and (ii); both (i) and (iv); both (ii) and (iii); or both (iii) and (iv).

17. The isolated or purified protein of claim 15 comprising:

(i) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 15;

(ii) a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 16;

(iii) a first polypeptide chain comprising amino acids 20-129 of SEQ ID NO: 15;

(iv) a second polypeptide chain comprising amino acids 22-133 of SEQ ID NO: 16; or

(v) both (i) and (ii); both (i) and (iv); both (ii) and (iii); or both (iii) and (iv).

18. The isolated or purified protein of any one of claims 15-17, wherein:

(A) the first polypeptide chain further comprises an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 46, wherein:

(i) X at position 48 of SEQ ID NO: 46 is Thr or Cys;

(ii) X at position 112 of SEQ ID NO: 46 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 114 of SEQ ID NO: 46 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp;

and

(iv) X at position 115 of SEQ ID NO: 46 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(B) the second polypeptide chain further comprises an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 47, wherein X at position 57 of SEQ ID NO: 47 is Ser or Cys; or

(C) both (A) and (B).

19. The isolated or purified protein of any one of claims 15-17, wherein:

(A) the first polypeptide chain further comprises the amino acid sequence of SEQ ID NO: 46, wherein:

(i) X at position 48 of SEQ ID NO: 46 is Thr or Cys;

(ii) X at position 112 of SEQ ID NO: 46 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 114 of SEQ ID NO: 46 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp;

and

(iv) X at position 115 of SEQ ID NO: 46 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(B) the second polypeptide chain further comprises the amino acid sequence of SEQ ID NO: 47, wherein X at position 57 of SEQ ID NO: 47 is Ser or Cys; or

(C) both (A) and (B).

20. The isolated or purified protein of any one of claims 15-19, wherein:

(1) the first polypeptide chain comprises an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 50;

(2) the second polypeptide chain comprises an amino acid sequence at least 99% identical to the amino acid sequence of SEQ ID NO: 51;

(3) the first polypeptide chain comprises an amino acid sequence at least 99% identical to amino acids 20-266 of SEQ ID NOs: 50;

(4) the second polypeptide chain comprises an amino acid sequence at least 99% identical to amino acids 22-306 of SEQ ID NO: 51; or

(5) both (1) and (2); both (1) and (4); both (2) and (3); or both (3) and (4).

21. The isolated or purified protein of any one of claims 15-19, wherein:

(1) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 50;

(2) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 51;

(3) the first polypeptide chain comprises amino acids 20-266 of SEQ ID NOs: 50;

(4) the second polypeptide chain comprises amino acids 22-306 of SEQ ID NO: 51; or

(5) both (1) and (2); both (1) and (4); both (2) and (3); or both (3) and (4).

22. An isolated or purified nucleic acid comprising a nucleotide sequence encoding the TCR of any one of claims 1-7, the polypeptide of any one of claims 8-14, or the protein of any one of claims 15-21.

23. A recombinant expression vector comprising the nucleic acid of claim 22.

24. An isolated or purified host cell comprising the recombinant expression vector of claim 23.

25. A population of cells comprising at least one isolated or purified host cell of claim 24.

26. A pharmaceutical composition comprising the TCR of any one of claims 1-7, the polypeptide of any one of claims 8-14, the protein of any one of claims 15-21, the nucleic

acid of claim 22, the recombinant expression vector of claim 23, the host cell of claim 24, or the population of host cells of claim 25, and a pharmaceutically acceptable carrier.

27. A method of detecting the presence of cancer in a mammal, the method comprising:

(a) contacting a sample comprising cells of the cancer with the TCR of any one of claims 1-7, the polypeptide of any one of claims 8-14, the protein of any one of claims 15-21, the host cell of claim 24, the population of host cells of claim 25, or a pharmaceutical composition comprising (i) the TCR, polypeptide, protein, host cell, or population of host cells and (ii) a pharmaceutically acceptable carrier, thereby forming a complex; and

(b) detecting the complex,

wherein detection of the complex is indicative of the presence of cancer in the mammal.

28. The method of claim 27, wherein the cancer is pancreatic, colorectal, lung, endometrial, ovarian, or prostate cancer.

29. Use of the TCR of any one of claims 1-7, the polypeptide of any one of claims 8-14, the protein of any one of claims 15-21, the nucleic acid of claim 22, the recombinant expression vector of claim 23, the host cell of claim 24, the population of host cells of claim 25, or the pharmaceutical composition of claim 26, in the manufacture of a medicament for the treatment or prevention of cancer in a mammal.

30. The use of claim 29, wherein the cancer is pancreatic, colorectal, lung, endometrial, ovarian, or prostate cancer.