CLAIM(S):

1. An isolated or purified T-cell receptor (TCR) comprising the amino acid sequences of:

(a) all of SEQ ID NOs: 1-3,

(b) all of SEQ ID NOs: 4-6, or

(c) all of SEQ ID NOs: 1-6,

wherein the TCR has antigenic specificity for a mutated human RAS amino acid sequence with a substitution of glycine at position 12 with valine,

wherein the mutated human RAS amino acid sequence is a mutated human Kirsten rat sarcoma viral oncogene homolog (KRAS), a mutated human Harvey rat sarcoma viral oncogene homolog (HRAS), or a mutated human Neuroblastoma rat sarcoma viral oncogene homolog (NRAS) amino acid sequence, and

wherein position 12 is defined by reference to the wild-type human KRAS, wild-type human HRAS, or wild-type human NRAS protein, respectively.

2. The TCR according to claim 1, wherein the mutated human RAS amino acid sequence is MTEYKLVVVGA**V**GVGKSALTIQLI (SEQ ID NO: 34).

3. The TCR according to claim 1 or 2, wherein the TCR does not have antigenic specificity for the wild-type human RAS amino acid sequence of MTEYKLVVVGAG**G**VGKSALTIQLI (SEQ ID NO: 35).

4. The TCR according to any one of claims 1-3, wherein the mutated human RAS amino acid sequence is presented by a human leukocyte antigen (HLA) Class II molecule.

5. The TCR according to claim 4, wherein the HLA Class II molecule is an HLA-DR heterodimer.

6. The TCR according to claim 4, wherein the HLA Class II molecule comprises a HLA-DR α chain in combination with a HLA-DR β chain encoded by the HLA-DRB1 gene.

7. The TCR according to claim 4, wherein the HLA Class II molecule is an HLA-DRB1*01:HLA-DRA*01 heterodimer.

8. The TCR according to any one of claims 1-7, comprising the amino acid sequences of:

(i) SEQ ID NO: 7,

(ii) SEQ ID NO: 8,

(iii) SEQ ID NO: 9,

(iv) SEQ ID NO: 10,

(v) both of SEQ ID NOs: 7 and 8, or

(vi) both of SEQ ID NOs: 9 and 10.

9. The TCR of any one of claims 1-8, further comprising:

(a) an α chain constant region comprising the amino acid sequence of SEQ ID NO: 19, wherein:

(i) X at position 48 of SEQ ID NO: 19 is Thr or Cys;

(ii) X at position 112 of SEQ ID NO: 19 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 114 of SEQ ID NO: 19 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 115 of SEQ ID NO: 19 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: 20, wherein X at position 57 of SEQ ID NO: 20 is Ser or Cys; or

(c) both (a) and (b).

10. The isolated or purified TCR of any one of claims 1-9, comprising:

(a) an α chain comprising the amino acid sequence of SEQ ID NO: 25, wherein:

(i) X at position 175 of SEQ ID NO: 25 is Thr or Cys;

(ii) X at position 239 of SEQ ID NO: 25 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 241 of SEQ ID NO: 25 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 242 of SEQ ID NO: 25 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) a β chain comprising the amino acid sequence of SEQ ID NO: 26, wherein X at position 186 of SEQ ID NO: 26 is Ser or Cys;

(c) both (a) and (b);

(d) an α chain comprising the amino acid sequence of SEQ ID NO: 27, wherein:

(i) X at position 156 of SEQ ID NO: 27 is Thr or Cys;

(ii) X at position 220 of SEQ ID NO: 27 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 222 of SEQ ID NO: 27 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 223 of SEQ ID NO: 27 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(e) a β chain comprising the amino acid sequence of SEQ ID NO: 28, wherein X at position 171 of SEQ ID NO: 28 is Ser or Cys;

(f) both (d) and (e);

(g) SEQ ID NO: 29;

(h) SEQ ID NO: 30;

(i) SEQ ID NO: 31;

(j) SEQ ID NO: 32;

(k) both (g) and (h); or

(l) both (i) and (j).

11. An isolated or purified polypeptide comprising a functional portion of the TCR of any one of claims 1-10, wherein the functional portion comprises the amino acid sequences of:

(a) all of SEQ ID NOs: 1-3,

(b) all of SEQ ID NOs: 4-6, or

(c) all of SEQ ID NOs: 1-6.

12. The isolated or purified polypeptide according to claim 11, wherein the functional portion comprises the amino acid sequence(s) of:

(i) SEQ ID NO: 7,

(ii) SEQ ID NO: 8,

(iii) SEQ ID NO: 9,

(iv) SEQ ID NO: 10,

(v) both of SEQ ID NOs: 7 and 8, or

(vi) both of SEQ ID NOs: 9 and 10.

13. The isolated or purified polypeptide of claim 11 or 12, further comprising:

(a) the amino acid sequence of SEQ ID NO: 19, wherein:

(i) X at position 48 of SEQ ID NO: 19 is Thr or Cys;

(ii) X at position 112 of SEQ ID NO: 19 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 114 of SEQ ID NO: 19 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 115 of SEQ ID NO: 19 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) the amino acid sequence of SEQ ID NO: 20, wherein X at position 57 of SEQ ID NO: 20 is Ser or Cys; or

(c) both (a) and (b).

14. The isolated or purified polypeptide of any one of claims 11-13, comprising:

(a) an α chain comprising the amino acid sequence of SEQ ID NO: 25, wherein:

(i) X at position 175 of SEQ ID NO: 25 is Thr or Cys;

(ii) X at position 239 of SEQ ID NO: 25 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 241 of SEQ ID NO: 25 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 242 of SEQ ID NO: 25 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) a β chain comprising the amino acid sequence of SEQ ID NO: 26, wherein X at position 186 of SEQ ID NO: 26 is Ser or Cys;

(c) both (a) and (b);

(d) an α chain comprising the amino acid sequence of SEQ ID NO: 27, wherein:

(i) X at position 156 of SEQ ID NO: 27 is Thr or Cys;

(ii) X at position 220 of SEQ ID NO: 27 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 222 of SEQ ID NO: 27 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 223 of SEQ ID NO: 27 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(e) a β chain comprising the amino acid sequence of SEQ ID NO: 28, wherein X at position 171 of SEQ ID NO: 28 is Ser or Cys;

(f) both (d) and (e);

(g) SEQ ID NO: 29;

(h) SEQ ID NO: 30;

(i) SEQ ID NO: 31;

(j) SEQ ID NO: 32;

(k) both (g) and (h); or

(l) both (i) and (j).

15. An isolated or purified protein comprising a first polypeptide chain comprising the amino acid sequences of SEQ ID NOs: 1-3 and a second polypeptide chain comprising the amino acid sequences of SEQ ID NOs: 4-6.

16. The isolated or purified protein according to claim 15, wherein:

(i) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 7 and the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 8; or

(ii) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 9 and the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 10.

17. The isolated or purified protein of claim 15 or 16, wherein:

(a) the first polypeptide chain further comprises the amino acid sequence of SEQ ID NO: 19, wherein:

(i) X at position 48 of SEQ ID NO: 19 is Thr or Cys;

(ii) X at position 112 of SEQ ID NO: 19 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 114 of SEQ ID NO: 19 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 115 of SEQ ID NO: 19 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: 20, wherein X at position 57 of SEQ ID NO: 20 is Ser or Cys; or

(c) both (a) and (b).

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

(a) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 25, wherein:

(i) X at position 175 of SEQ ID NO: 25 is Thr or Cys;

(ii) X at position 239 of SEQ ID NO: 25 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 241 of SEQ ID NO: 25 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 242 of SEQ ID NO: 25 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 26, wherein X at position 186 of SEQ ID NO: 26 is Ser or Cys;

(c) both (a) and (b);

(d) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 27, wherein:

(i) X at position 156 of SEQ ID NO: 27 is Thr or Cys;

(ii) X at position 220 of SEQ ID NO: 27 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 222 of SEQ ID NO: 27 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 223 of SEQ ID NO: 27 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(e) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 28, wherein X at position 171 of SEQ ID NO: 28 is Ser or Cys;

(f) both (d) and (e);

(g) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 29;

(h) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 30;

(i) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 31;

(j) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 32;

(k) both (g) and (h); or

(l) both (i) and (j).

19. An isolated or purified nucleic acid comprising a nucleotide sequence encoding the TCR according to any one of claims 1-10, the polypeptide according to any one of claims 11-14, or the protein according to any one of claims 15-18.

20. An isolated or purified nucleic acid comprising, from 5’ to 3’, a first nucleic acid sequence and a second nucleotide sequence, wherein the first and second nucleotide sequence, respectively, encode the amino sequences of SEQ ID NOs: 7 and 8; 8 and 7; 9 and 10; 10 and 9; 25 and 26; 26 and 25; 27 and 28; 28 and 27; 29 and 30; 30 and 29; 31 and 32; or 32 and 31.

21. The isolated or purified nucleic acid according to claim 20, further comprising a third nucleotide sequence interposed between the first and second nucleotide sequence, wherein the third nucleotide sequence encodes a cleavable linker peptide.

22. The isolated or purified nucleic acid according to claim 21, wherein the cleavable linker peptide comprises the amino acid sequence of RAKRSGSGATNFSLLKQAGDVEENPGP (SEQ ID NO: 33).

23. A recombinant expression vector comprising the nucleic acid according to any one of claims 19-22.

24. The recombinant expression vector according to claim 23, which is a transposon or a lentiviral vector.

25. An isolated or purified TCR, polypeptide, or protein encoded by the nucleic acid according to any one of claims 19-22 or the vector according to claim 23 or 24.

26. An isolated or purified TCR, polypeptide, or protein that results from expression of the nucleic acid according to any one of claims 19-22 or the vector according to claim 23 or 24 in a cell.

27. A method of producing a host cell expressing a TCR that has antigenic specificity for the peptide of MTEYKLVVVGA**V**GVGKSALTIQLI (SEQ ID NO: 34), the method comprising contacting an isolated or purified host cell with the vector according to claim 23 or 24 under conditions that allow introduction of the vector into the cell.

28. An isolated or purified host cell comprising the nucleic acid according to any one of claims 19-22 or the recombinant expression vector according to claim 23 or 24.

29. The host cell according to claim 28, wherein the cell is a human lymphocyte.

30. The host cell according to claim 28 or 29, 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.

31. An isolated or purified population of cells comprising the host cell according to any one of claims 28-30.

32. A method of producing the TCR according to any one of claims 1-10, 25, or 26, the polypeptide according to any one of claims 11-14, 25, or 26, or the protein according to any one of claims 15-18, 25, or 26, the method comprising culturing the host cell according to any one of claims 28-30, or the population of host cells according to claim 31, so that the TCR, polypeptide, or protein is produced.

33. A pharmaceutical composition comprising (a) the TCR according to any one of claims 1-10, 25, or 26, the polypeptide according to any one of claims 11-14, 25, or 26, the protein according to any one of claims 15-18, 25, or 26, the nucleic acid according to any one of claims 19-22, the recombinant expression vector according to claim 23 or 24, the host cell according to any one of claims 28-30, or the population of cells according to claim 31 and (b) a pharmaceutically acceptable carrier.

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

(a) contacting a sample comprising cells of the cancer with the TCR according to any one of claims 1-10, 25, or 26, the polypeptide according to any one of claims 11-14, 25, or 26, the protein according to any one of claims 15-18, 25, or 26, the nucleic acid according to any one of claims 19-22, the recombinant expression vector according to claim 23 or 24, the host cell according to any one of claims 28-30, the population of cells according to claim 31, or the pharmaceutical composition of claim 33, thereby forming a complex; and

(b) detecting the complex,

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

35. Use of the TCR according to any one of claims 1-10, 25, or 26, the polypeptide according to any one of claims 11-14, 25, or 26, the protein according to any one of claims 15-18, 25, or 26, the nucleic acid according to any one of claims 19-22, the recombinant expression vector according to claim 23 or 24, the host cell according to any one of claims 28-30, the population of cells according to claim 31, or the pharmaceutical composition according to claim

33, in the manufacture of a medicament for the inducement of an immune response against cancer in a mammal.

36. Use of the TCR according to any one of claims 1-10, 25, or 26, the polypeptide according to any one of claims 11-14, 25, or 26, the protein according to any one of claims 15-18, 25, or 26, the nucleic acid according to any one of claims 19-22, the recombinant expression vector according to claim 23 or 24, the host cell according to any one of claims 28-30, the population of cells according to claim 31, or the pharmaceutical composition of claim 33, in the manufacture of a medicament for the treatment or prevention of cancer in a mammal.

37. The method of claim 34, or the use of claim 35 or 36, wherein the cancer expresses a mutated human RAS amino acid sequence with a substitution of glycine at position 12 with valine,

wherein the mutated human RAS amino acid sequence is a mutated human Kirsten rat sarcoma viral oncogene homolog (KRAS), a mutated human Harvey rat sarcoma viral oncogene homolog (HRAS), or a mutated human Neuroblastoma rat sarcoma viral oncogene homolog (NRAS) amino acid sequence, and

wherein position 12 is defined by reference to the wild-type human KRAS, wild-type human HRAS, or wild-type human NRAS protein, respectively.

38. The method of claim 37, or the use of claim 37, wherein the mutated human RAS amino acid sequence is a mutated human Kirsten rat sarcoma viral oncogene homolog (KRAS) amino acid sequence.

39. The method of claim 37, or the use of claim 37, wherein the mutated human RAS amino acid sequence is a mutated human neuroblastoma rat sarcoma viral oncogene homolog (NRAS) amino acid sequence.

40. The method of claim 37, or the use of claim 37, wherein the mutated human RAS amino acid sequence is a mutated human Harvey rat sarcoma viral oncogene homolog (HRAS) amino acid sequence.

41. The method according to any one of claims 34 and 37-40, or the use of any one of claims 35-40, wherein the cancer is pancreatic, colorectal, lung, endometrial, ovarian, or prostate cancer.