CLAIMS:

1. An isolated or purified T-cell receptor (TCR) comprising an α chain complementarity determining region (CDR) 1 comprising the amino acid sequence of SEQ ID NO: 1, an α chain CDR2 comprising the amino acid sequence of SEQ ID NO: 2, an α chain CDR3 comprising the amino acid sequence of SEQ ID NO: 3, a β chain CDR1 comprising the amino acid sequence of SEQ ID NO: 4, a β chain CDR2 comprising the amino acid sequence of SEQ ID NO: 5, and a β chain CDR3 comprising the amino acid sequence of SEQ ID NO: 6, wherein the TCR has antigenic specificity for a mutated human RAS amino acid sequence with a substitution of glycine at position 12 with aspartic acid,

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 isolated or purified TCR according to claim 1, wherein the mutated human RAS amino acid sequence is presented by a human leukocyte antigen (HLA) Class I molecule and wherein the HLA Class I molecule is encoded by the HLA-A*11:01 allele.

3. The isolated or purified TCR according to claim 1 or 2, comprising:

(i) the amino acid sequence of SEQ ID NO: 7;

(ii) the amino acid sequence of SEQ ID NO: 8;

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

(iv) the amino acid sequence of SEQ ID NO: 52;

(v) the amino acid sequence of SEQ ID NO: 32;

(vi) the amino acid sequence of SEQ ID NO: 33;

(vii) the amino acid sequence of SEQ ID NO: 59;

(viii) the amino acid sequence of SEQ ID NO: 60; or

(ix) both (i) and (ii), both (i) and (iv), both (ii) and (iii), both (iii) and (iv), both (v) and (vi), both (v) and (viii), both (vi) and (vii), or both (vii) and (viii).

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

(a) an α chain constant region comprising the amino acid sequence of SEQ ID NO: 17, wherein:

(i) X at position 48 of SEQ ID NO: 17 is Thr or Cys;

(ii) X at position 112 of SEQ ID NO: 17 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 114 of SEQ ID NO: 17 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 115 of SEQ ID NO: 17 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: 18, wherein X at position 57 of SEQ ID NO: 18 is Ser or Cys; or

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

5. The isolated or purified TCR according to any one of claims 1-4, comprising:

(a) an α chain comprising the amino acid sequence of SEQ ID NO: 21, wherein:

(i) X at position 193 of SEQ ID NO: 21 is Thr or Cys;

(ii) X at position 257 of SEQ ID NO: 21 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 259 of SEQ ID NO: 21 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 260 of SEQ ID NO: 21 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) a β chain comprising the amino acid sequence of SEQ ID NO: 22, wherein X at position 191 of SEQ ID NO: 22 is Ser or Cys;

(c) an α chain comprising the amino acid sequence of SEQ ID NO: 53, wherein:

(i) X at position 193 of SEQ ID NO: 53is Thr or Cys;

(ii) X at position 257 of SEQ ID NO: 53is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 259 of SEQ ID NO: 53is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 260 of SEQ ID NO: 53is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(d) a β chain comprising the amino acid sequence of SEQ ID NO: 54, wherein X at position 191 of SEQ ID NO: 54 is Ser or Cys;

(e) both (a) and (b), both (a) and (d), both (b) and (c), or both (c) and (d);

(f) an α chain comprising the amino acid sequence of SEQ ID NO: 34, wherein:

(i) X at position 165 of SEQ ID NO: 34 is Thr or Cys;

(ii) X at position 229 of SEQ ID NO: 34 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 231 of SEQ ID NO: 34 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 232 of SEQ ID NO: 34 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(g) a β chain comprising the amino acid sequence of SEQ ID NO: 35, wherein X at position 172 of SEQ ID NO: 35 is Ser or Cys;

(h) an α chain comprising the amino acid sequence of SEQ ID NO: 61, wherein:

(i) X at position 172 of SEQ ID NO: 61 is Thr or Cys;

(ii) X at position 236 of SEQ ID NO: 61 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 238 of SEQ ID NO: 61 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 239 of SEQ ID NO: 61 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(i) a β chain comprising the amino acid sequence of SEQ ID NO: 62, wherein X at position 170 of SEQ ID NO: 62 is Ser or Cys;

(j) both (f) and (g), or both (h) and (i);

(k) an α chain comprising the amino acid sequence of SEQ ID NO: 36;

(l) a β chain comprising the amino acid sequence of SEQ ID NO: 37;

(m) an α chain comprising the amino acid sequence of SEQ ID NO: 63;

(n) a β chain comprising the amino acid sequence of SEQ ID NO: 64;

(o) an α chain comprising the amino acid sequence of SEQ ID NO: 42;

(p) a β chain comprising the amino acid sequence of SEQ ID NO: 43;

(q) an α chain comprising the amino acid sequence of SEQ ID NO: 65;

(r) a β chain comprising the amino acid sequence of SEQ ID NO: 66;

(s) both (k) and (l), both (m) and (n), both (o) and (p), or both (q) and (r);

(t) an α chain comprising the amino acid sequence of SEQ ID NO: 23;

(u) a β chain comprising the amino acid sequence of SEQ ID NO: 24;

(v) an α chain comprising the amino acid sequence of SEQ ID NO: 55;

(w) a β chain comprising the amino acid sequence of SEQ ID NO: 56;

(x) an α chain comprising the amino acid sequence of SEQ ID NO: 40;

(y) a β chain comprising the amino acid sequence of SEQ ID NO: 41;

(z) an α chain comprising the amino acid sequence of SEQ ID NO: 57;

(aa) a β chain comprising the amino acid sequence of SEQ ID NO: 58; or

(ab) both (t) and (u), both (t) and (w), both (u) and (v), both (v) and (w), both (x) and (y), both (x) and (aa), both (y) and (z), or both (z) and (aa).

6. An isolated or purified polypeptide comprising a functional portion of the TCR according to any one of claims 1-5, 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.

7. The isolated or purified polypeptide according to claim 6, 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: 51;

(iv) SEQ ID NO: 52;

(v) SEQ ID NO: 32;

(vi) SEQ ID NO: 33;

(vii) SEQ ID NO: 59;

(viii) SEQ ID NO: 60; or

(ix) both (i) and (ii), both (i) and (iv), both (ii) and (iii), both (iii) and (iv), both (v) and (vi), both (v) and (viii), both (vi) and (vii), or both (vii) and (viii).

8. The isolated or purified polypeptide according to claim 6 or 7, further comprising:

(a) the amino acid sequence of SEQ ID NO: 17, wherein:

(i) X at position 48 of SEQ ID NO: 17 is Thr or Cys;

(ii) X at position 112 of SEQ ID NO: 17 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 114 of SEQ ID NO: 17 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 115 of SEQ ID NO: 17 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) the amino acid sequence of SEQ ID NO: 18, wherein X at position 57 of SEQ ID NO: 18 is Ser or Cys; or

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

9. The isolated or purified polypeptide according to any one of claims 6-8, comprising:

(a) an α chain comprising the amino acid sequence of SEQ ID NO: 21, wherein:

(i) X at position 193 of SEQ ID NO: 21 is Thr or Cys;

(ii) X at position 257 of SEQ ID NO: 21 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 259 of SEQ ID NO: 21 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 260 of SEQ ID NO: 21 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(b) a β chain comprising the amino acid sequence of SEQ ID NO: 22, wherein X at position 191 of SEQ ID NO: 22 is Ser or Cys;

(c) an α chain comprising the amino acid sequence of SEQ ID NO: 53, wherein:

(i) X at position 193 of SEQ ID NO: 53 is Thr or Cys;

(ii) X at position 257 of SEQ ID NO: 53 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 259 of SEQ ID NO: 53 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 260 of SEQ ID NO: 53 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(d) a β chain comprising the amino acid sequence of SEQ ID NO: 54, wherein X at position 191 of SEQ ID NO: 54 is Ser or Cys;

(e) both (a) and (b), both (a) and (d), both (b) and (c), or both (c) and (d);

(f) an α chain comprising the amino acid sequence of SEQ ID NO: 34, wherein:

(i) X at position 165 of SEQ ID NO: 34 is Thr or Cys;

(ii) X at position 229 of SEQ ID NO: 34 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 231 of SEQ ID NO: 34 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 232 of SEQ ID NO: 34 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(g) a β chain comprising the amino acid sequence of SEQ ID NO: 35, wherein X at position 172 of SEQ ID NO: 35 is Ser or Cys;

(h) an α chain comprising the amino acid sequence of SEQ ID NO: 61, wherein:

(i) X at position 172 of SEQ ID NO: 61 is Thr or Cys;

(ii) X at position 236 of SEQ ID NO: 61 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 238 of SEQ ID NO: 61 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 239 of SEQ ID NO: 61 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(i) a β chain comprising the amino acid sequence of SEQ ID NO: 62, wherein X at position 170 of SEQ ID NO: 62 is Ser or Cys;

(j) both (f) and (g), or both (h) and (i);

(k) an α chain comprising the amino acid sequence of SEQ ID NO: 36;

(l) a β chain comprising the amino acid sequence of SEQ ID NO: 37;

(m) an α chain comprising the amino acid sequence of SEQ ID NO: 63;

(n) a β chain comprising the amino acid sequence of SEQ ID NO: 64;

(o) an α chain comprising the amino acid sequence of SEQ ID NO: 42;

(p) a β chain comprising the amino acid sequence of SEQ ID NO: 43;

(q) an α chain comprising the amino acid sequence of SEQ ID NO: 65;

(r) a β chain comprising the amino acid sequence of SEQ ID NO: 66;

(s) both (k) and (l), both (m) and (n), both (o) and (p), or both (q) and (r);

(t) an α chain comprising the amino acid sequence of SEQ ID NO: 23;

(u) a β chain comprising the amino acid sequence of SEQ ID NO: 24;

(v) an α chain comprising the amino acid sequence of SEQ ID NO: 55;

(w) a β chain comprising the amino acid sequence of SEQ ID NO: 56;

(x) an α chain comprising the amino acid sequence of SEQ ID NO: 40;

(y) a β chain comprising the amino acid sequence of SEQ ID NO: 41;

(z) an α chain comprising the amino acid sequence of SEQ ID NO: 57;

(aa) a β chain comprising the amino acid sequence of SEQ ID NO: 58; or

(ab) both (t) and (u), both (t) and (w), both (u) and (v), both (v) and (w), both (x) and (y), both (x) and (aa), both (y) and (z), and both (z) and (aa).

10. 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.

11. The isolated or purified protein according to claim 10, wherein:

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

(ii) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 8;

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

(iv) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 52;

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

(vi) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 33;

(vii) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 59;

(viii) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 60; or

(ix) both (i) and (ii), both (i) and (iv), both (ii) and (iii), both (iii) and (iv), both (v) and (vi), both (v) and (viii), both (vi) and (vii), or both (vii) and (viii).

12. The isolated or purified protein according to claim 10 or 11, wherein:

(a) the first polypeptide chain further comprises the amino acid sequence of SEQ ID NO: 17, wherein:

(i) X at position 48 of SEQ ID NO: 17 is Thr or Cys;

(ii) X at position 112 of SEQ ID NO: 17 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 114 of SEQ ID NO: 17 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 115 of SEQ ID NO: 17 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: 18, wherein X at position 57 of SEQ ID NO: 18 is Ser or Cys; or

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

13. The isolated or purified protein according to any one of claims 10-12, wherein:

(a) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 21, wherein:

(i) X at position 193 of SEQ ID NO: 21 is Thr or Cys;

(ii) X at position 257 of SEQ ID NO: 21 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 259 of SEQ ID NO: 21 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 260 of SEQ ID NO: 21 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: 22, wherein X at position 191 of SEQ ID NO: 22 is Ser or Cys;

(c) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 53, wherein:

(i) X at position 193 of SEQ ID NO: 53 is Thr or Cys;

(ii) X at position 257 of SEQ ID NO: 53 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 259 of SEQ ID NO: 53 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 260 of SEQ ID NO: 53 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(d) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 45, wherein X at position 191 of SEQ ID NO: 54 is Ser or Cys;

(e) both (a) and (b), both (a) and (d), both (b) and (c), or both (c) and (d);

(f) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 34, wherein:

(i) X at position 165 of SEQ ID NO: 34 is Thr or Cys;

(ii) X at position 229 of SEQ ID NO: 34 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 231 of SEQ ID NO: 34 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 232 of SEQ ID NO: 34 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(g) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 35, wherein X at position 172 of SEQ ID NO: 35 is Ser or Cys;

(h) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 61, wherein:

(i) X at position 172 of SEQ ID NO: 61 is Thr or Cys;

(ii) X at position 236 of SEQ ID NO: 61 is Ser, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(iii) X at position 238 of SEQ ID NO: 61 is Met, Ala, Val, Leu, Ile, Pro, Phe, or Trp; and

(iv) X at position 239 of SEQ ID NO: 61 is Gly, Ala, Val, Leu, Ile, Pro, Phe, Met, or Trp;

(i) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 62, wherein X at position 170 of SEQ ID NO: 62 is Ser or Cys;

(j) both (f) and (g), or both (h) and (i);

(k) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 36;

(l) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 37;

(m) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 63;

(n) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 64;

(o) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 42;

(p) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 43;

(q) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 65;

(r) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 66;

(s) both (k) and (l), both (m) and (n), both (o) and (p), or both (q) and (r);

(t) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 23;

(u) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 24;

(v) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 55;

(w) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 56;

(x) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 40;

(y) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 41;

(z) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO: 57;

(aa) the second polypeptide chain comprises the amino acid sequence of SEQ ID NO: 58; or

(ab) both (t) and (u), both (t) and (w), both (u) and (v), both (v) and (w), both (x) and (y), both (x) and (aa), both (y) and (z), or both (z) and (aa).

14. An isolated or purified nucleic acid comprising a nucleotide sequence encoding the TCR according to any one of claims 1-5, the polypeptide according to any one of claims 6-9, or the protein according to any one of claims 10-13.

15. 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; 51 and 8; 7 and 52; 51 and 52; 8 and 7; 8 and 51; 52 and 7; 52 and 51; 21 and 22; 53 and 22; 21 and 54; 53 and 54; 22 and 21; 22 and 53; 54 and 21; 54 and 53; 23 and 24; 55 and 24; 23 and 56; 55 and 56; 24 and 23; 24 and 55; 56 and 23; 56 and 55; 32 and 33; 33 and 32; 59 and 60; 60 and 59; 34 and 35; 35 and 34; 61 and 62; 62 and 61; 36 and 37; 37 and 36; 63 and 64; 64 and 63; 40 and 41; 57 and 41; 40 and 58; 57 and 58; 41 and 40; 41 and 57; 58 and 40; 58 and 57; 42 and 43; 43 and 42; 65 and 66; or 66 and 65.

16. A recombinant expression vector comprising the nucleic acid according to claim 14 or 15.

17. The recombinant expression vector according to claim 16, which is a transposon or a lentiviral vector.

18. An isolated or purified TCR, polypeptide, or protein encoded by the nucleic acid according to claim 14 or 15 or the vector according to claim 16 or 17.

19. An isolated or purified host cell comprising the nucleic acid according to claim 14 or 15 or the recombinant expression vector according to claim 16 or 17.

20. The host cell according to claim 19, wherein the cell is selected from a T cell, a natural killer T (NKT) cell, an invariant natural killer T (iNKT) cell, and a natural killer (NK) cell.

21. An isolated or purified population of cells comprising the host cell according to claim 19 or 20.

22. A pharmaceutical composition comprising (a) the host cell according to claim 20, or an isolated or purified population of cells comprising the host cell and (b) a pharmaceutically acceptable carrier.

23. Use of the TCR according to any one of claims 1-5 and 18, the polypeptide according to any one of claims 6-9 and 18, the protein according to any one of claims 10-13 and 18, the nucleic acid according to claim 14 or 15, the recombinant expression vector according to claim 16 or 17, the host cell according to claim 19 or 20, the population of cells according to claim 21, or the pharmaceutical composition of claim 22 in the manufacture of a medicament for the detection, treatment or prevention of cancer in a mammal,

wherein the cancer expresses a mutated human RAS amino acid sequence with a substitution of glycine at position 12 with aspartic acid,

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.

24. The use according to claim 23, wherein the cancer is pancreatic, colorectal, lung, endometrial, ovarian, or prostate cancer.