

T CELL RECEPTORS RECOGNIZING MUTATED P53

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This patent application claims the benefit of U.S. Provisional Patent Application No. 62/565,383, filed September 29, 2017, which is incorporated by reference in its entirety herein.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

[0002] This invention was made with Government support under project number BC010985 by the National Institutes of Health, National Cancer Institute. The Government has certain rights in the invention.

INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ELECTRONICALLY

[0003] Incorporated by reference in its entirety herein is a computer-readable nucleotide/amino acid sequence listing submitted concurrently herewith and identified as follows: One 687,555 Byte ASCII (Text) file named "739980_ST25.txt," dated September 7, 2018.

BACKGROUND OF THE INVENTION

[0004] Some cancers may have very limited treatment options, particularly when the cancer becomes metastatic and unresectable. Despite advances in treatments such as, for example, surgery, chemotherapy, and radiation therapy, the prognosis for many cancers, such as, for example, pancreatic, colorectal, lung, endometrial, ovarian, and prostate cancers, may be poor. Accordingly, there exists an unmet need for additional treatments for cancer.

BRIEF SUMMARY ~~OF THE INVENTION~~

[0005] In one aspect, the present disclosure provides an isolated or purified T cell receptor (TCR) having antigenic specificity for mutated human p53 with the R175H mutation, wherein the TCR comprises:

(1) the alpha chain complementarity determining region (CDR) 1 amino acid sequence of SEQ ID NO: 67, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 68, the alpha chain CDR3 amino acid sequence of SEQ ID NO: 69, the beta chain CDR1 amino acid sequence of SEQ ID NO: 70, the beta chain CDR2 amino acid sequence of SEQ ID NO: 71, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 72;

2) the alpha chain CDR1 amino acid sequence of SEQ ID NO: 77, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 78, the alpha chain CDR3 amino acid sequence of SEQ ID NO: 79, the beta chain CDR1 amino acid sequence of SEQ ID NO: 80, the beta chain CDR2 amino acid sequence of SEQ ID NO: 81, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 82;

(3) the alpha chain CDR1 amino acid sequence of SEQ ID NO: 87, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 88, the alpha chain CDR3 amino acid sequence of SEQ ID NO: 89, the beta chain CDR1 amino acid sequence of SEQ ID NO: 90, the beta chain CDR2 amino acid sequence of SEQ ID NO: 91, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 92;

(4) the alpha chain CDR1 amino acid sequence of SEQ ID NO: 487, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 488, the alpha chain CDR3 amino acid sequence of SEQ ID NO: 489, the beta chain CDR1 amino acid sequence of SEQ ID NO: 490, the beta chain CDR2 amino acid sequence of SEQ ID NO: 491, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 492. An ~~embodiment~~example of the ~~invention~~disclosure provides an isolated or purified T cell receptor (TCR) having antigenic specificity for mutated human p53.

[0005a] In another aspect, the present disclosure provides an isolated or purified polypeptide comprising a functional portion of the TCR as described herein, wherein the functional portion comprises:

(1) the alpha chain CDR1 amino acid sequence of SEQ ID NO: 67, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 68, the alpha chain CDR3 amino acid sequence of SEQ ID NO: 69, the beta chain CDR1 amino acid sequence of SEQ ID NO: 70, the beta chain CDR2 amino acid sequence of SEQ ID NO: 71, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 72;

(2) the alpha chain CDR1 amino acid sequence of SEQ ID NO: 77, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 78, the alpha chain CDR3 amino acid sequence of SEQ ID NO: 79, the beta chain CDR1 amino acid sequence of SEQ ID NO: 80, the beta chain CDR2 amino acid sequence of SEQ ID NO: 81, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 82;

(3) the alpha chain CDR1 amino acid sequence of SEQ ID NO: 87, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 88, the alpha chain CDR3 amino acid sequence of SEQ ID NO: 89, the beta chain CDR1 amino acid sequence of SEQ ID NO: 90, the beta chain CDR2 amino acid sequence of SEQ ID NO: 91, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 92; or

(4) the alpha chain CDR1 amino acid sequence of SEQ ID NO: 487, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 488, the alpha chain CDR3 amino acid sequence of SEQ ID NO: 489, the beta chain CDR1 amino acid sequence of SEQ ID NO: 490, the beta chain CDR2 amino acid sequence of SEQ ID NO: 491, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 492.

[0005b] In yet another aspect, the present disclosure provides an isolated or purified protein comprising a functional portion of a TCR having antigenic specificity for human p53 with the R175H mutation, wherein the functional portion comprises:

(1) a first polypeptide chain comprising the alpha chain CDR1 amino acid sequence of SEQ ID NO: 67, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 68, and the alpha chain CDR3 amino acid sequence of SEQ ID NO: 69 and a second polypeptide chain comprising the beta chain CDR1 amino acid sequence of SEQ ID NO: 70, the beta chain CDR2 amino acid sequence of SEQ ID NO: 71, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 72;

(2) a first polypeptide chain comprising the alpha chain CDR1 amino acid sequence of SEQ ID NO: 77, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 78, and the alpha chain CDR3 amino acid sequence of SEQ ID NO: 79 and a second polypeptide chain comprising the beta chain CDR1 amino acid sequence of SEQ ID NO: 80, the beta chain CDR2 amino acid sequence of SEQ ID NO: 81, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 82;

(3) a first polypeptide chain comprising the alpha chain CDR1 amino acid sequence of SEQ ID NO: 87, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 88, and the alpha chain CDR3 amino acid sequence of SEQ ID NO: 89 and a second polypeptide chain comprising the beta chain CDR1 amino acid sequence of SEQ ID NO: 90, the beta chain CDR2 amino acid sequence of SEQ ID NO: 91, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 92; or

(4) a first polypeptide chain comprising the alpha chain CDR1 amino acid sequence of SEQ ID NO: 487, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 488, and the alpha chain CDR3 amino acid sequence of SEQ ID NO: 489 and a second polypeptide chain comprising the beta chain CDR1 amino acid sequence of SEQ ID NO: 490, the beta chain CDR2 amino acid sequence of SEQ ID NO: 491, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 492.

[0005c] In yet another aspect, the present disclosure provides an isolated or purified nucleic acid comprising a nucleotide sequence encoding the TCR as described herein, the polypeptide as described herein, or the protein as described herein. In yet another aspect, the present disclosure provides a recombinant expression vector comprising the nucleic acid as described herein. In a further aspect, the present disclosure provides an isolated or purified host cell comprising the recombinant expression vector as described herein. In a further aspect, the present disclosure provides an isolated or purified population of cells comprising the host cell as described herein.

[0005d] In yet another aspect, the present disclosure provides a pharmaceutical composition comprising (a) the TCR as described herein, the polypeptide as described herein, the protein as described herein, the nucleic acid as described herein, the recombinant expression vector as described herein, the host cell as described herein, or the population of cells as described herein and (b) a pharmaceutically acceptable carrier.

[0005e] In yet another aspect, the present disclosure provides 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 as described herein, the polypeptide as described herein, the protein as described herein, the nucleic acid as described herein, the recombinant expression vector as described herein, the host cell as described herein, the population of cells as described herein, or the pharmaceutical composition as described herein, thereby forming a

complex; and (b) detecting the complex, wherein detection of the complex is indicative of the presence of cancer in the mammal.

[0005f] In yet another aspect, the present disclosure provides a use of a pharmaceutical composition in the manufacture of a medicament for treating or preventing cancer in a mammal, which comprises the TCR as described herein, the polypeptide as described herein, the protein as described herein, the nucleic acid as described herein, the recombinant expression vector as described herein, the host cell as described herein, or the population of cells as described herein.

[0006] Further ~~embodiment~~examples of the ~~invention~~disclosure provide related polypeptides and proteins, as well as related nucleic acids, recombinant expression vectors, host cells, populations of cells, and pharmaceutical compositions relating to the TCRs of the ~~invention~~disclosure.

[0007] Still further embodiment examples of the invention disclosure provide methods of detecting the presence of cancer in a mammal and methods of treating or preventing cancer in a mammal.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

[0008] Figure 1 is a graph showing the concentration of IFN- γ (pg/mL) measured following co-culture of autologous PBL transduced with one of the indicated TCRs from patient 4127 following co-culture with autologous dendritic cells (DCs) pulsed with either WT p53-G245 peptide (wt) (unshaded bars) or mutated p53-G245S peptide (mut) (shaded bars) at the indicated decreasing peptide concentrations (μ g/mL).

[0009] Figure 2 is a graph showing the percentage of 4-1BB positive cells (% of CD4+ mTCR β +) detected following co-culture of autologous PBL transduced with one of the indicated TCRs from patient 4127 with autologous DCs pulsed with either WT p53-G245 peptide (wt) (unshaded bars) or mutated p53-G245S peptide (mut) (shaded bars) at the indicated decreasing peptide concentrations (μ g/mL).

[0010] Figure 3 is a graph showing the percentage of 4-1BB positive cells (% of CD4+ mTCR β +) detected following co-culture of autologous PBL transduced with one of the indicated TCRs from patient 4127 with autologous DCs pulsed with one of the peptides shown in Table A.

[0011] Figure 4 is a graph showing the concentration of IFN- γ (pg/mL) measured following co-culture of TIL from patient 4127 or T cells transduced with one of the indicated TCRs with COS7 cells which were transduced with one of the indicated HLA alleles and pulsed with DMSO or one of the indicated peptides.

[0012] Figure 5 is a graph showing the percentage of 4-1BB positive cells (% of CD4+ mTCR β +) detected following co-culture of TIL from patient 4127 or T cells which were transduced with one of the indicated TCRs with COS7 cells which were transduced with one of the indicated HLA alleles and pulsed with DMSO or one of the indicated peptides.

[0013] Figure 6 is a graph showing the number of spots per 2×10^4 effector cells measured following co-culture of TIL from patient 4127 with allogeneic (DRB3*01:01:01 or DRB3*02:02:01) APCs which were (1) electroporated with TMG composed of irrelevant (IRR; left hatched open bars), WT p53 (p53-WT; left hatched gray bars) or mutated p53 (p53-MUT; gray bars) sequence or (2) pulsed with peptide vehicle (DMSO; right hatched open bars) or purified (>95% by HPLC) 25-amino acid peptides composed of WT p53-G245

CLAIMS

1. An isolated or purified T cell receptor (TCR) having antigenic specificity for mutated human p53 with the R175H mutation, wherein the TCR comprises:

(1) the alpha chain complementarity determining region (CDR) 1 amino acid sequence of SEQ ID NO: 67, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 68, the alpha chain CDR3 amino acid sequence of SEQ ID NO: 69, the beta chain CDR1 amino acid sequence of SEQ ID NO: 70, the beta chain CDR2 amino acid sequence of SEQ ID NO: 71, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 72;

(2) the alpha chain CDR1 amino acid sequence of SEQ ID NO: 77, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 78, the alpha chain CDR3 amino acid sequence of SEQ ID NO: 79, the beta chain CDR1 amino acid sequence of SEQ ID NO: 80, the beta chain CDR2 amino acid sequence of SEQ ID NO: 81, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 82;

(3) the alpha chain CDR1 amino acid sequence of SEQ ID NO: 87, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 88, the alpha chain CDR3 amino acid sequence of SEQ ID NO: 89, the beta chain CDR1 amino acid sequence of SEQ ID NO: 90, the beta chain CDR2 amino acid sequence of SEQ ID NO: 91, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 92; or

(4) the alpha chain CDR1 amino acid sequence of SEQ ID NO: 487, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 488, the alpha chain CDR3 amino acid sequence of SEQ ID NO: 489, the beta chain CDR1 amino acid sequence of SEQ ID NO: 490, the beta chain CDR2 amino acid sequence of SEQ ID NO: 491, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 492.

2. The TCR of claim 1, wherein the TCR ~~has antigenic specificity for human p53 with a mutation at position 175, 220, 245, or 248 of SEQ ID NO: 1~~ comprises:

(1) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 73, and an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 74;

(2) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 83, and an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 84;

(3) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 93, and an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 94; or

(4) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 493, and an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 494;

(5) an amino acid sequence at least 95% identical to amino acids 21-131 of SEQ ID NO: 73, and an amino acid sequence at least 95% identical to amino acids 22-134 of SEQ ID NO: 74;

(6) an amino acid sequence at least 95% identical to amino acids 22-137 of SEQ ID NO: 83, and an amino acid sequence at least 95% identical to amino acids 22-133 of SEQ ID NO: 84;

(7) an amino acid sequence at least 95% identical to amino acids 22-131 of SEQ ID NO: 93, and an amino acid sequence at least 95% identical to amino acids 22-134 of SEQ ID NO: 94;
or

(8) an amino acid sequence at least 95% identical to amino acids 23-134 of SEQ ID NO: 493, and an amino acid sequence at least 95% identical to amino acids 22-132 of SEQ ID NO: 494.

3. The TCR of claim 1 or 2, wherein the TCR ~~has antigenic specificity for human p53 with one of the following human p53 mutations: R175H, Y220C, G245S, R248Q, or R248W~~ comprises the amino acid sequences of:

(1) both of SEQ ID NOs: 73-74;

(2) both of SEQ ID NOs: 83-84;

(3) both of SEQ ID NOs: 93-94;

(4) both of SEQ ID NOs: 493-494;

(5) both of amino acids 21-131 of SEQ ID NO: 73 and amino acids 22-134 of SEQ ID NO: 74;

(6) both of amino acids 22-137 of SEQ ID NO: 83 and amino acids 22-133 of SEQ ID NO: 84;

(7) both of amino acids 22-131 of SEQ ID NO: 93 and amino acids 22-134 of SEQ ID NO: 94; or

(8) both of amino acids 23-134 of SEQ ID NO: 493 and amino acids 22-132 of SEQ ID NO: 494.

4. The TCR of any one of claims 1-3, wherein the TCR comprises: ~~the amino acid sequences of:~~

- ~~(1) all of SEQ ID NOs: 27-32;~~
- ~~(2) all of SEQ ID NOs: 37-42;~~
- ~~(3) all of SEQ ID NOs: 47-52;~~
- ~~(4) all of SEQ ID NOs: 57-62;~~
- ~~(5) all of SEQ ID NOs: 67-72;~~
- ~~(6) all of SEQ ID NOs: 77-82;~~
- ~~(7) all of SEQ ID NOs: 87-92;~~
- ~~(8) all of SEQ ID NOs: 97-102;~~
- ~~(9) all of SEQ ID NOs: 107-112;~~
- ~~(10) all of SEQ ID NOs: 117-122;~~
- ~~(11) all of SEQ ID NOs: 127-132;~~
- ~~(12) all of SEQ ID NOs: 137-142;~~
- ~~(13) all of SEQ ID NOs: 147-152;~~
- ~~(14) all of SEQ ID NOs: 157-162;~~
- ~~(15) all of SEQ ID NOs: 167-172;~~
- ~~(16) all of SEQ ID NOs: 177-182;~~
- ~~(17) all of SEQ ID NOs: 187-192;~~
- ~~(18) all of SEQ ID NOs: 197-202;~~
- ~~(19) all of SEQ ID NOs: 207-212;~~
- ~~(20) all of SEQ ID NOs: 217-222;~~
- ~~(21) all of SEQ ID NOs: 227-232;~~
- ~~(22) all of SEQ ID NOs: 237-242;~~
- ~~(23) all of SEQ ID NOs: 247-252;~~
- ~~(24) all of SEQ ID NOs: 257-262;~~

~~(25) all of SEQ ID NOs: 267-272;~~
~~(26) all of SEQ ID NOs: 277-282;~~
~~(27) all of SEQ ID NOs: 287-292;~~
~~(28) all of SEQ ID NOs: 297-302;~~
~~(29) all of SEQ ID NOs: 307-312;~~
~~(30) all of SEQ ID NOs: 317-322;~~
~~(31) all of SEQ ID NOs: 327-332;~~
~~(32) all of SEQ ID NOs: 337-342;~~
~~(33) all of SEQ ID NOs: 347-352;~~
~~(34) all of SEQ ID NOs: 357-362;~~
~~(35) all of SEQ ID NOs: 367-372;~~
~~(36) all of SEQ ID NOs: 377-382;~~
~~(37) all of SEQ ID NOs: 387-392;~~
~~(38) all of SEQ ID NOs: 397-402;~~
~~(39) all of SEQ ID NOs: 407-412;~~
~~(40) all of SEQ ID NOs: 417-422;~~
~~(41) all of SEQ ID NOs: 427-432;~~
~~(42) all of SEQ ID NOs: 437-442;~~
~~(43) all of SEQ ID NOs: 447-452;~~
~~(44) all of SEQ ID NOs: 457-462;~~
~~(45) all of SEQ ID NOs: 467-472;~~
~~(46) all of SEQ ID NOs: 477-482; or~~
~~(47) all of SEQ ID NOs: 487-492~~

(1) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 75, and an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 76;

(2) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 85, and an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 86;

(3) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 95, and an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 96;

(4) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 495, and an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 496;

(5) an amino acid sequence at least 95% identical to amino acids 21-268 of SEQ ID NO: 75, and an amino acid sequence at least 95% identical to amino acids 22-307 of SEQ ID NO: 76;

(6) an amino acid sequence at least 95% identical to amino acids 22-274 of SEQ ID NO: 85, and an amino acid sequence at least 95% identical to amino acids 22-306 of SEQ ID NO: 86;

(7) an amino acid sequence at least 95% identical to amino acids 22-268 of SEQ ID NO: 95, and an amino acid sequence at least 95% identical to amino acids 22-307 of SEQ ID NO: 96;

or

(8) an amino acid sequence at least 95% identical to amino acids 23-271 of SEQ ID NO: 495, and an amino acid sequence at least 95% identical to amino acids 22-305 of SEQ ID NO: 496.

5. The TCR of any one of claims 1-~~43~~, wherein the TCR comprises the amino acid sequences of:

(1) both of SEQ ID NOs: ~~33-34~~ 75-76;

(2) both of SEQ ID NOs: ~~43-44~~ 85-86;

(3) both of SEQ ID NOs: ~~53-54~~ 95-96;

(4) both of SEQ ID NOs: ~~63-64~~ 495-496;

~~(5) both of SEQ ID NOs: 73-74;~~

~~(6) both of SEQ ID NOs: 83-84;~~

~~(7) both of SEQ ID NOs: 93-94;~~

~~(8) both of SEQ ID NOs: 103-104;~~

~~(9) both of SEQ ID NOs: 113-114;~~

~~(10) both of SEQ ID NOs: 123-124;~~

~~(11) both of SEQ ID NOs: 133-134;~~

~~(12) both of SEQ ID NOs: 143-144;~~

~~(13) both of SEQ ID NOs: 153-154;~~
~~(14) both of SEQ ID NOs: 163-164;~~
~~(15) both of SEQ ID NOs: 173-174;~~
~~(16) both of SEQ ID NOs: 183-184;~~
~~(17) both of SEQ ID NOs: 193-194;~~
~~(18) both of SEQ ID NOs: 203-204;~~
~~(19) both of SEQ ID NOs: 213-214;~~
~~(20) both of SEQ ID NOs: 223-224;~~
~~(21) both of SEQ ID NOs: 233-234;~~
~~(22) both of SEQ ID NOs: 243-244;~~
~~(23) both of SEQ ID NOs: 253-254;~~
~~(24) both of SEQ ID NOs: 263-264;~~
~~(25) both of SEQ ID NOs: 273-274;~~
~~(26) both of SEQ ID NOs: 283-284;~~
~~(27) both of SEQ ID NOs: 293-294;~~
~~(28) both of SEQ ID NOs: 303-304;~~
~~(29) both of SEQ ID NOs: 313-314;~~
~~(30) both of SEQ ID NOs: 323-324;~~
~~(31) both of SEQ ID NOs: 333-334;~~
~~(32) both of SEQ ID NOs: 343-344;~~
~~(33) both of SEQ ID NOs: 353-354;~~
~~(34) both of SEQ ID NOs: 363-364;~~
~~(35) both of SEQ ID NOs: 373-374;~~
~~(36) both of SEQ ID NOs: 383-384;~~
~~(37) both of SEQ ID NOs: 393-394;~~
~~(38) both of SEQ ID NOs: 403-404;~~
~~(39) both of SEQ ID NOs: 413-414;~~
~~(40) both of SEQ ID NOs: 423-424;~~
~~(41) both of SEQ ID NOs: 433-434;~~
~~(42) both of SEQ ID NOs: 443-444;~~
~~(43) both of SEQ ID NOs: 453-454;~~

~~(44) both of SEQ ID NOs: 463-464;~~

~~(45) both of SEQ ID NOs: 473-474;~~

~~(46) both of SEQ ID NOs: 483-484; or~~

~~(47) both of SEQ ID NOs: 493-494~~

(5) both of amino acids 21-268 of SEQ ID NO: 75 and amino acids 22-307 of SEQ ID NO: 76;

(6) both of amino acids 22-274 of SEQ ID NO: 85 and amino acids 22-306 of SEQ ID NO: 86;

(7) both of amino acids 22-268 of SEQ ID NO: 95 and amino acids 22-307 of SEQ ID NO: 96; or

(8) both of amino acids 23-271 of SEQ ID NO: 495 and amino acids 22-305 of SEQ ID NO: 496.

6. The An isolated or purified polypeptide comprising a functional portion of the TCR of any one of claims 1-5, wherein the ~~TCR comprises the amino acid sequences of~~ functional portion comprises:

~~(1) both of SEQ ID NOs: 35-36;~~

~~(2) both of SEQ ID NOs: 45-46;~~

~~(3) both of SEQ ID NOs: 55-56;~~

~~(4) both of SEQ ID NOs: 65-66;~~

~~(5) both of SEQ ID NOs: 75-76;~~

~~(6) both of SEQ ID NOs: 85-86;~~

~~(7) both of SEQ ID NOs: 95-96;~~

~~(8) both of SEQ ID NOs: 105-106;~~

~~(9) both of SEQ ID NOs: 115-116;~~

~~(10) both of SEQ ID NOs: 125-126;~~

~~(11) both of SEQ ID NOs: 135-136;~~

~~(12) both of SEQ ID NOs: 145-146;~~

~~(13) both of SEQ ID NOs: 155-156;~~

~~(14) both of SEQ ID NOs: 165-166;~~

~~(15) both of SEQ ID NOs: 175-176;~~

~~(16) both of SEQ ID NOs: 185-186;~~
~~(17) both of SEQ ID NOs: 195-196;~~
~~(18) both of SEQ ID NOs: 205-206;~~
~~(19) both of SEQ ID NOs: 215-216;~~
~~(20) both of SEQ ID NOs: 225-226;~~
~~(21) both of SEQ ID NOs: 235-236;~~
~~(22) both of SEQ ID NOs: 245-246;~~
~~(23) both of SEQ ID NOs: 255-256;~~
~~(24) both of SEQ ID NOs: 265-266;~~
~~(25) both of SEQ ID NOs: 275-276;~~
~~(26) both of SEQ ID NOs: 285-286;~~
~~(27) both of SEQ ID NOs: 295-296;~~
~~(28) both of SEQ ID NOs: 305-306;~~
~~(29) both of SEQ ID NOs: 315-316;~~
~~(30) both of SEQ ID NOs: 325-326;~~
~~(31) both of SEQ ID NOs: 335-336;~~
~~(32) both of SEQ ID NOs: 345-346;~~
~~(33) both of SEQ ID NOs: 355-356;~~
~~(34) both of SEQ ID NOs: 365-366;~~
~~(35) both of SEQ ID NOs: 375-376;~~
~~(36) both of SEQ ID NOs: 385-386;~~
~~(37) both of SEQ ID NOs: 395-396;~~
~~(38) both of SEQ ID NOs: 405-406;~~
~~(39) both of SEQ ID NOs: 415-416;~~
~~(40) both of SEQ ID NOs: 425-426;~~
~~(41) both of SEQ ID NOs: 435-436;~~
~~(42) both of SEQ ID NOs: 445-446;~~
~~(43) both of SEQ ID NOs: 455-456;~~
~~(44) both of SEQ ID NOs: 465-466;~~
~~(45) both of SEQ ID NOs: 475-476;~~
~~(46) both of SEQ ID NOs: 485-486; or~~

~~(47) both of SEQ ID NOs: 495-496~~

(1) the alpha chain CDR1 amino acid sequence of SEQ ID NO: 67, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 68, the alpha chain CDR3 amino acid sequence of SEQ ID NO: 69, the beta chain CDR1 amino acid sequence of SEQ ID NO: 70, the beta chain CDR2 amino acid sequence of SEQ ID NO: 71, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 72;

(2) the alpha chain CDR1 amino acid sequence of SEQ ID NO: 77, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 78, the alpha chain CDR3 amino acid sequence of SEQ ID NO: 79, the beta chain CDR1 amino acid sequence of SEQ ID NO: 80, the beta chain CDR2 amino acid sequence of SEQ ID NO: 81, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 82;

(3) the alpha chain CDR1 amino acid sequence of SEQ ID NO: 87, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 88, the alpha chain CDR3 amino acid sequence of SEQ ID NO: 89, the beta chain CDR1 amino acid sequence of SEQ ID NO: 90, the beta chain CDR2 amino acid sequence of SEQ ID NO: 91, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 92; or

(4) the alpha chain CDR1 amino acid sequence of SEQ ID NO: 487, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 488, the alpha chain CDR3 amino acid sequence of SEQ ID NO: 489, the beta chain CDR1 amino acid sequence of SEQ ID NO: 490, the beta chain CDR2 amino acid sequence of SEQ ID NO: 491, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 492.

~~7. An isolated or purified polypeptide comprising a functional portion of the TCR of any one of claims 1-6, wherein the polypeptide comprises the amino acid sequences of The polypeptide of claim 6, wherein the polypeptide comprises:~~

~~(1) all of SEQ ID NOs: 27-32;~~

~~(2) all of SEQ ID NOs: 37-42;~~

~~(3) all of SEQ ID NOs: 47-52;~~

~~(4) all of SEQ ID NOs: 57-62;~~

~~(5) all of SEQ ID NOs: 67-72;~~

~~(6) all of SEQ ID NOs: 77-82;~~

~~(7) all of SEQ ID NOs: 87-92;~~
~~(8) all of SEQ ID NOs: 97-102;~~
~~(9) all of SEQ ID NOs: 107-112;~~
~~(10) all of SEQ ID NOs: 117-122;~~
~~(11) all of SEQ ID NOs: 127-132;~~
~~(12) all of SEQ ID NOs: 137-142;~~
~~(13) all of SEQ ID NOs: 147-152;~~
~~(14) all of SEQ ID NOs: 157-162;~~
~~(15) all of SEQ ID NOs: 167-172;~~
~~(16) all of SEQ ID NOs: 177-182;~~
~~(17) all of SEQ ID NOs: 187-192;~~
~~(18) all of SEQ ID NOs: 197-202;~~
~~(19) all of SEQ ID NOs: 207-212;~~
~~(20) all of SEQ ID NOs: 217-222;~~
~~(21) all of SEQ ID NOs: 227-232;~~
~~(22) all of SEQ ID NOs: 237-242;~~
~~(23) all of SEQ ID NOs: 247-252;~~
~~(24) all of SEQ ID NOs: 257-262;~~
~~(25) all of SEQ ID NOs: 267-272;~~
~~(26) all of SEQ ID NOs: 277-282;~~
~~(27) all of SEQ ID NOs: 287-292;~~
~~(28) all of SEQ ID NOs: 297-302;~~
~~(29) all of SEQ ID NOs: 307-312;~~
~~(30) all of SEQ ID NOs: 317-322;~~
~~(31) all of SEQ ID NOs: 327-332;~~
~~(32) all of SEQ ID NOs: 337-342;~~
~~(33) all of SEQ ID NOs: 347-352;~~
~~(34) all of SEQ ID NOs: 357-362;~~
~~(35) all of SEQ ID NOs: 367-372;~~
~~(36) all of SEQ ID NOs: 377-382;~~
~~(37) all of SEQ ID NOs: 387-392;~~

~~(38) all of SEQ ID NOs: 397-402;~~

~~(39) all of SEQ ID NOs: 407-412;~~

~~(40) all of SEQ ID NOs: 417-422;~~

~~(41) all of SEQ ID NOs: 427-432;~~

~~(42) all of SEQ ID NOs: 437-442;~~

~~(43) all of SEQ ID NOs: 447-452;~~

~~(44) all of SEQ ID NOs: 457-462;~~

~~(45) all of SEQ ID NOs: 467-472;~~

~~(46) all of SEQ ID NOs: 477-482; or~~

~~(47) all of SEQ ID NOs: 487-492~~

(1) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 73, and an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 74;

(2) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 83, and an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 84;

(3) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 93, and an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 94;

(4) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 493, and an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 494;

(5) an amino acid sequence at least 95% identical to amino acids 21-131 of SEQ ID NO: 73, and an amino acid sequence at least 95% identical to amino acids 22-134 of SEQ ID NO: 74;

(6) an amino acid sequence at least 95% identical to amino acids 22-137 of SEQ ID NO: 83, and an amino acid sequence at least 95% identical to amino acids 22-133 of SEQ ID NO: 84;

(7) an amino acid sequence at least 95% identical to amino acids 22-131 of SEQ ID NO: 93, and an amino acid sequence at least 95% identical to amino acids 22-134 of SEQ ID NO: 94;

or

(8) an amino acid sequence at least 95% identical to amino acids 23-134 of SEQ ID NO: 493, and an amino acid sequence at least 95% identical to amino acids 22-132 of SEQ ID NO: 494.

8. The polypeptide of claim 76, wherein the polypeptide comprises the amino acid sequences of:

- ~~(1) both of SEQ ID NOs: 33-34;~~
- ~~(2) both of SEQ ID NOs: 43-44;~~
- ~~(3) both of SEQ ID NOs: 53-54;~~
- ~~(4) both of SEQ ID NOs: 63-64;~~
- (5) both of SEQ ID NOs: 73-74;
- (6) both of SEQ ID NOs: 83-84;
- (7) both of SEQ ID NOs: 93-94;
- ~~(8) both of SEQ ID NOs: 103-104;~~
- ~~(9) both of SEQ ID NOs: 113-114;~~
- ~~(10) both of SEQ ID NOs: 123-124;~~
- ~~(11) both of SEQ ID NOs: 133-134;~~
- ~~(12) both of SEQ ID NOs: 143-144;~~
- ~~(13) both of SEQ ID NOs: 153-154;~~
- ~~(14) both of SEQ ID NOs: 163-164;~~
- ~~(15) both of SEQ ID NOs: 173-174;~~
- ~~(16) both of SEQ ID NOs: 183-184;~~
- ~~(17) both of SEQ ID NOs: 193-194;~~
- ~~(18) both of SEQ ID NOs: 203-204;~~
- ~~(19) both of SEQ ID NOs: 213-214;~~
- ~~(20) both of SEQ ID NOs: 223-224;~~
- ~~(21) both of SEQ ID NOs: 233-234;~~
- ~~(22) both of SEQ ID NOs: 243-244;~~
- ~~(23) both of SEQ ID NOs: 253-254;~~
- ~~(24) both of SEQ ID NOs: 263-264;~~
- ~~(25) both of SEQ ID NOs: 273-274;~~

~~(26) both of SEQ ID NOs: 283-284;~~
~~(27) both of SEQ ID NOs: 293-294;~~
~~(28) both of SEQ ID NOs: 303-304;~~
~~(29) both of SEQ ID NOs: 313-314;~~
~~(30) both of SEQ ID NOs: 323-324;~~
~~(31) both of SEQ ID NOs: 333-334;~~
~~(32) both of SEQ ID NOs: 343-344;~~
~~(33) both of SEQ ID NOs: 353-354;~~
~~(34) both of SEQ ID NOs: 363-364;~~
~~(35) both of SEQ ID NOs: 373-374;~~
~~(36) both of SEQ ID NOs: 383-384;~~
~~(37) both of SEQ ID NOs: 393-394;~~
~~(38) both of SEQ ID NOs: 403-404;~~
~~(39) both of SEQ ID NOs: 413-414;~~
~~(40) both of SEQ ID NOs: 423-424;~~
~~(41) both of SEQ ID NOs: 433-434;~~
~~(42) both of SEQ ID NOs: 443-444;~~
~~(43) both of SEQ ID NOs: 453-454;~~
~~(44) both of SEQ ID NOs: 463-464;~~
~~(45) both of SEQ ID NOs: 473-474;~~
~~(46) both of SEQ ID NOs: 483-484; or~~
 (47) both of SEQ ID NOs: 493-494;

(5) both of amino acids 21-131 of SEQ ID NO: 73 and amino acids 22-134 of SEQ ID NO: 74;

(6) both of amino acids 22-137 of SEQ ID NO: 83 and amino acids 22-133 of SEQ ID NO: 84;

(7) both of amino acids 22-131 of SEQ ID NO: 93 and amino acids 22-134 of SEQ ID NO: 94; or

(8) both of amino acids 23-134 of SEQ ID NO: 493 and amino acids 22-132 of SEQ ID NO: 494.

9. The polypeptide of any one of claims 6-8-7-or-8, wherein the polypeptide comprises the amino acid sequences of:

- (1) both of SEQ ID NOs: 35-36;
- (2) both of SEQ ID NOs: 45-46;
- (3) both of SEQ ID NOs: 55-56;
- (4) both of SEQ ID NOs: 65-66;
- (5) both of SEQ ID NOs: 75-76;
- (6) both of SEQ ID NOs: 85-86;
- (7) both of SEQ ID NOs: 95-96;
- (8) both of SEQ ID NOs: 105-106;
- (9) both of SEQ ID NOs: 115-116;
- (10) both of SEQ ID NOs: 125-126;
- (11) both of SEQ ID NOs: 135-136;
- (12) both of SEQ ID NOs: 145-146;
- (13) both of SEQ ID NOs: 155-156;
- (14) both of SEQ ID NOs: 165-166;
- (15) both of SEQ ID NOs: 175-176;
- (16) both of SEQ ID NOs: 185-186;
- (17) both of SEQ ID NOs: 195-196;
- (18) both of SEQ ID NOs: 205-206;
- (19) both of SEQ ID NOs: 215-216;
- (20) both of SEQ ID NOs: 225-226;
- (21) both of SEQ ID NOs: 235-236;
- (22) both of SEQ ID NOs: 245-246;
- (23) both of SEQ ID NOs: 255-256;
- (24) both of SEQ ID NOs: 265-266;
- (25) both of SEQ ID NOs: 275-276;
- (26) both of SEQ ID NOs: 285-286;
- (27) both of SEQ ID NOs: 295-296;
- (28) both of SEQ ID NOs: 305-306;
- (29) both of SEQ ID NOs: 315-316;

~~(30) both of SEQ ID NOs: 325-326;~~
~~(31) both of SEQ ID NOs: 335-336;~~
~~(32) both of SEQ ID NOs: 345-346;~~
~~(33) both of SEQ ID NOs: 355-356;~~
~~(34) both of SEQ ID NOs: 365-366;~~
~~(35) both of SEQ ID NOs: 375-376;~~
~~(36) both of SEQ ID NOs: 385-386;~~
~~(37) both of SEQ ID NOs: 395-396;~~
~~(38) both of SEQ ID NOs: 405-406;~~
~~(39) both of SEQ ID NOs: 415-416;~~
~~(40) both of SEQ ID NOs: 425-426;~~
~~(41) both of SEQ ID NOs: 435-436;~~
~~(42) both of SEQ ID NOs: 445-446;~~
~~(43) both of SEQ ID NOs: 455-456;~~
~~(44) both of SEQ ID NOs: 465-466;~~
~~(45) both of SEQ ID NOs: 475-476;~~
~~(46) both of SEQ ID NOs: 485-486; or~~
~~(47) both of SEQ ID NOs: 495-496;~~

(1) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 75, and an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 76;

(2) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 85, and an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 86;

(3) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 95, and an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 96;

(4) an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 495, and an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 496;

(5) an amino acid sequence at least 95% identical to amino acids 21-268 of SEQ ID NO: 75, and an amino acid sequence at least 95% identical to amino acids 22-307 of SEQ ID NO: 76;

(6) an amino acid sequence at least 95% identical to amino acids 22-274 of SEQ ID NO: 85, and an amino acid sequence at least 95% identical to amino acids 22-306 of SEQ ID NO: 86;

(7) an amino acid sequence at least 95% identical to amino acids 22-268 of SEQ ID NO: 95, and an amino acid sequence at least 95% identical to amino acids 22-307 of SEQ ID NO: 96;

or

(8) an amino acid sequence at least 95% identical to amino acids 23-271 of SEQ ID NO: 495, and an amino acid sequence at least 95% identical to amino acids 22-305 of SEQ ID NO: 496.

10. An isolated or purified protein comprisingThe polypeptide of any one of claims 6-8, wherein the polypeptide comprises the amino acid sequences of:

(1) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 27-29 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 30-32;

(2) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 37-39 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 40-42;

(3) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 47-49 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 50-52;

(4) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 57-59 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 60-62;

(5) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 67-69 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 70-72;

(6) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 77-79 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 80-82;

~~(7) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 87-89 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 90-92;~~

~~(8) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 97-99 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 100-102;~~

~~(9) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 107-109 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 110-112;~~

~~(10) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 117-119 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 120-122;~~

~~(11) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 127-129 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 130-132;~~

~~(12) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 137-139 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 140-142;~~

~~(13) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 147-149 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 150-152;~~

~~(14) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 157-159 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 160-162;~~

~~(15) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 167-169 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 170-172;~~

~~(16) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 177-179 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 180-182;~~

~~(17) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 187-189 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 190-192;~~

~~(18) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 197-199 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 200-202;~~

~~(19) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 207-209 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 210-212;~~

~~(20) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 217-219 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 220-222;~~

~~(21) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 227-229 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 230-232;~~

~~(22) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 237-239 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 240-242;~~

~~(23) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 247-249 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 250-252;~~

~~(24) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 257-259 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 260-262;~~

~~(25) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 267-269 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 270-272;~~

~~(26) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 277-279 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 280-282;~~

~~(27) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 287-289 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 290-292;~~

~~(28) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 297-299 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 300-302;~~

~~(29) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 307-309 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 310-312;~~

~~(30) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 317-319 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 320-322;~~

~~(31) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 327-329 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 330-332;~~

~~(32) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 337-339 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 340-342;~~

~~(33) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 347-349 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 350-352;~~

~~(34) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 357-359 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 360-362;~~

~~(35) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 367-369 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 370-372;~~

~~(36) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 377-379 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 380-382;~~

~~(37) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 387-389 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 390-392;~~

~~(38) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 397-399 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 400-402;~~

~~(39) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 407-409 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 410-412;~~

~~(40) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 417-419 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 420-422;~~

~~(41) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 427-429 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 430-432;~~

~~(42) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 437-439 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 440-442;~~

~~(43) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 447-449 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 450-452;~~

~~(44) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 457-459 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 460-462;~~

~~(45) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 467-469 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 470-472;~~

~~(46) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 477-479 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 480-482; or~~

~~(47) a first polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 487-489 and a second polypeptide chain comprising the amino acid sequences of all of SEQ ID NOs: 490-492~~

(1) both of SEQ ID NOs: 75-76;

(2) both of SEQ ID NOs: 85-86;

(3) both of SEQ ID NOs: 95-96;

(4) both of SEQ ID NOs: 495-496;

(5) both of amino acids 21-268 of SEQ ID NO: 75 and amino acids 22-307 of SEQ ID NO: 76;

(6) both of amino acids 22-274 of SEQ ID NO: 85 and amino acids 22-306 of SEQ ID NO: 86;

(7) both of amino acids 22-268 of SEQ ID NO: 95 and amino acids 22-307 of SEQ ID NO: 96; or

(8) both of amino acids 23-271 of SEQ ID NO: 495 and amino acids 22-305 of SEQ ID NO: 496.

11. ~~The protein of claim 10, wherein the protein comprises~~ An isolated or purified protein comprising a functional portion of a TCR having antigenic specificity for human p53 with the R175H mutation, wherein the functional portion comprises:

~~(1) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 33 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 34~~ alpha chain CDR1 amino acid sequence of SEQ ID NO: 67, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 68, and the alpha chain CDR3 amino acid sequence of SEQ ID NO: 69 and a second polypeptide chain comprising the beta chain CDR1 amino acid sequence of SEQ ID NO: 70, the beta chain CDR2 amino acid sequence of SEQ ID NO: 71, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 72;

~~(2) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 43 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 44~~ alpha chain CDR1 amino acid sequence of SEQ ID NO: 77, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 78, and the alpha chain CDR3 amino acid sequence of SEQ ID NO: 79 and a second polypeptide chain comprising the beta chain CDR1 amino acid sequence of SEQ ID NO:

80, the beta chain CDR2 amino acid sequence of SEQ ID NO: 81, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 82;

(3) a first polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 53~~ and a second polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 54~~ alpha chain CDR1 amino acid sequence of SEQ ID NO: 87, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 88, and the alpha chain CDR3 amino acid sequence of SEQ ID NO: 89 and a second polypeptide chain comprising the beta chain CDR1 amino acid sequence of SEQ ID NO: 90, the beta chain CDR2 amino acid sequence of SEQ ID NO: 91, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 92; or

(4) a first polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 63~~ and a second polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 64~~ alpha chain CDR1 amino acid sequence of SEQ ID NO: 487, the alpha chain CDR2 amino acid sequence of SEQ ID NO: 488, and the alpha chain CDR3 amino acid sequence of SEQ ID NO: 489 and a second polypeptide chain comprising the beta chain CDR1 amino acid sequence of SEQ ID NO: 490, the beta chain CDR2 amino acid sequence of SEQ ID NO: 491, and the beta chain CDR3 amino acid sequence of SEQ ID NO: 492;

(5) a first polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 73~~ and a second polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 74;~~

(6) a first polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 83~~ and a second polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 84;~~

(7) a first polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 93~~ and a second polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 94;~~

(8) a first polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 103~~ and a second polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 104;~~

(9) a first polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 113~~ and a second polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 114;~~

(10) a first polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 123~~ and a second polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 124;~~

(11) a first polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 133~~ and a second polypeptide chain comprising the ~~amino acid sequence of SEQ ID NO: 134;~~

(12) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 143 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 144;

(13) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 153 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 154;

(14) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 163 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 164;

(15) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 173 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 174;

(16) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 183 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 184;

(17) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 193 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 194;

(18) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 203 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 204;

(19) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 213 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 214;

(20) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 223 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 224;

(21) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 233 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 234;

(22) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 243 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 244;

(23) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 253 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 254;

(24) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 263 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 264;

(25) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 273 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 274;

(26) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 283 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 284;

(27) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 293 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 294;

(28) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 303 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 304;

(29) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 313 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 314;

(30) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 323 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 324;

(31) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 333 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 334;

(32) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 343 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 344;

(33) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 353 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 354;

(34) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 363 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 364;

(35) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 373 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 374;

(36) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 383 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 384;

(37) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 393 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 394;

(38) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 403 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 404;

(39) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 413 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 414;

(40) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 423 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 424;

(41) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 433 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 434;

~~(42) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 443 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 444;~~

~~(43) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 453 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 454;~~

~~(44) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 463 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 464;~~

~~(45) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 473 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 474;~~

~~(46) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 483 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 484; or~~

~~(47) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 493 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 494.~~

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

(1) a first polypeptide chain comprising ~~the amino acid sequence of SEQ ID NO: 35 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 36~~ an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 73 and a second polypeptide chain comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 74;

(2) a first polypeptide chain comprising ~~the amino acid sequence of SEQ ID NO: 45 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 46~~ an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 83 and a second polypeptide chain comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 84;

(3) a first polypeptide chain comprising ~~the amino acid sequence of SEQ ID NO: 55 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 56~~ an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 93 and a second polypeptide chain comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 94;

(4) a first polypeptide chain comprising ~~the amino acid sequence of SEQ ID NO: 65 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 66~~ an amino

acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 493 and a second polypeptide chain comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 494;

~~(5) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 75 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 76~~ an amino acid sequence at least 95% identical to amino acids 21-131 of SEQ ID NO: 73 and a second polypeptide chain comprising an amino acid sequence at least 95% identical to amino acids 22-134 of SEQ ID NO: 74;

~~(6) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 85 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 86~~ an amino acid sequence at least 95% identical to amino acids 22-137 of SEQ ID NO: 83 and a second polypeptide chain comprising an amino acid sequence at least 95% identical to amino acids 22-133 of SEQ ID NO: 84;

~~(7) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 95 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 96;~~ an amino acid sequence at least 95% identical to amino acids 22-131 of SEQ ID NO: 93 and a second polypeptide chain comprising an amino acid sequence at least 95% identical to amino acids 22-134 of SEQ ID NO: 94; or

~~(8) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 105 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 106;~~ an amino acid sequence at least 95% identical to amino acids 23-134 of SEQ ID NO: 493 and a second polypeptide chain comprising an amino acid sequence at least 95% identical to amino acids 22-132 of SEQ ID NO: 494.

~~(9) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 115 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 116;~~

~~(10) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 125 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 126;~~

~~(11) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 135 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 136;~~

~~(12) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 145 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 146;~~

(13) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 155 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 156;

(14) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 165 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 166;

(15) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 175 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 176;

(16) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 185 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 186;

(17) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 195 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 196;

(18) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 205 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 206;

(19) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 215 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 216;

(20) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 225 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 226;

(21) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 235 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 236;

(22) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 245 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 246;

(23) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 255 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 256;

(24) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 265 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 266;

(25) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 275 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 276;

(26) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 285 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 286;

(27) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 295 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 296;

~~(43) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 455 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 456;~~

~~(44) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 465 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 466;~~

~~(45) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 475 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 476;~~

~~(46) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 485 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 486; or~~

~~(47) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 495 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 496.~~

13. ~~An isolated or purified nucleic acid comprising a nucleotide sequence encoding the TCR according to any one of claims 1-6, the polypeptide according to any one of claims 7-9, or the protein according to any one of claims 10-12~~ The protein of claim 11, wherein the protein comprises:

(1) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 73 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 74;

(2) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 83 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 84;

(3) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 93 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 94;

(4) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 493 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 494;

(5) a first polypeptide chain comprising amino acids 21-131 of SEQ ID NO: 73 and a second polypeptide chain comprising amino acids 22-134 of SEQ ID NO: 74;

(6) a first polypeptide chain comprising amino acids 22-137 of SEQ ID NO: 83 and a second polypeptide chain comprising amino acids 22-133 of SEQ ID NO: 84;

(7) a first polypeptide chain comprising of amino acids 22-131 of SEQ ID NO: 93 and a second polypeptide chain comprising amino acids 22-134 of SEQ ID NO: 94; or

(8) a first polypeptide chain comprising amino acids 23-134 of SEQ ID NO: 493 and a second polypeptide chain comprising amino acids 22-132 of SEQ ID NO: 494.

14. ~~A recombinant expression vector comprising the nucleic acid according to claim 13~~
The protein of any one of claims 11-13, wherein the protein comprises:

(1) a first polypeptide chain comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 75 and a second polypeptide chain comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 76;

(2) a first polypeptide chain comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 85 and a second polypeptide chain comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 86;

(3) a first polypeptide chain comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 95 and a second polypeptide chain comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 96;

(4) a first polypeptide chain comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 495 and a second polypeptide chain comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 496;

(5) a first polypeptide chain comprising an amino acid sequence at least 95% identical to amino acids 21-268 of SEQ ID NO: 75 and a second polypeptide chain comprising an amino acid sequence at least 95% identical to amino acids 22-307 of SEQ ID NO: 76;

(6) a first polypeptide chain comprising an amino acid sequence at least 95% identical to amino acids 22-274 of SEQ ID NO: 85 and a second polypeptide chain comprising an amino acid sequence at least 95% identical to amino acids 22-306 of SEQ ID NO: 86;

(7) a first polypeptide chain comprising an amino acid sequence at least 95% identical to amino acids 22-268 of SEQ ID NO: 95 and a second polypeptide chain comprising an amino acid sequence at least 95% identical to amino acids 22-307 of SEQ ID NO: 96; or

(8) a first polypeptide chain comprising an amino acid sequence at least 95% identical to amino acids 23-271 of SEQ ID NO: 495 and a second polypeptide chain comprising an amino acid sequence at least 95% identical to amino acids 22-305 of SEQ ID NO: 496.

15. ~~An isolated or purified host cell comprising the recombinant expression vector according to claim 14~~
The protein of any one of claims 11-13, wherein the protein comprises:

(1) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 75 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 76;

(2) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 85 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 86;

(3) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 95 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 96;

(4) a first polypeptide chain comprising the amino acid sequence of SEQ ID NO: 495 and a second polypeptide chain comprising the amino acid sequence of SEQ ID NO: 496;

(5) a first polypeptide chain comprising amino acids 21-268 of SEQ ID NO: 75 and a second polypeptide chain comprising amino acids 22-307 of SEQ ID NO: 76;

(6) a first polypeptide chain comprising amino acids 22-274 of SEQ ID NO: 85 and a second polypeptide chain comprising amino acids 22-306 of SEQ ID NO: 86;

(7) a first polypeptide chain comprising amino acids 22-268 of SEQ ID NO: 95 and a second polypeptide chain comprising amino acids 22-307 of SEQ ID NO: 96; or

(8) a first polypeptide chain comprising amino acids 23-271 of SEQ ID NO: 495 and a second polypeptide chain comprising amino acids 22-305 of SEQ ID NO: 496.

16. ~~An isolated or purified population of cells comprising the host cell according to claim 15~~ 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 6-10, or the protein according to any one of claims 11-15.

17. ~~A pharmaceutical composition comprising (a) the TCR according to any one of claims 1-6, the polypeptide according to any one of claims 7-9, the protein according to any one of claims 10-12, the nucleic acid according to claim 13, the recombinant expression vector according to claim 14, the host cell according to claim 15, or the population of cells according to claim 16 and (b) a pharmaceutically acceptable carrier~~ A recombinant expression vector comprising the nucleic acid according to claim 16.

18. ~~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 1-6, the polypeptide according to any one of claims 7-9, the protein according to any one of claims 10-12, the nucleic acid according to claim 13, the recombinant expression vector according to claim 14, the host cell according to claim 15, the population of cells according to claim 16, or the pharmaceutical composition of claim 17, thereby forming a complex; and~~
~~(b) detecting the complex,~~
 wherein detection of the complex is indicative of the presence of cancer in the mammal An isolated or purified host cell comprising the recombinant expression vector according to claim 17.

19. ~~The TCR according to any one of claims 1-6, the polypeptide according to any one of claims 7-9, the protein according to any one of claims 10-12, the nucleic acid according to claim 13, the recombinant expression vector according to claim 14, the host cell according to claim 15, the population of cells according to claim 16, or the pharmaceutical composition of claim 17, for use in the treatment or prevention of cancer in a mammal~~ An isolated or purified population of cells comprising the host cell according to claim 18.

20. ~~The population of cells for the use according to claim 19, wherein the population of cells is autologous to the mammal~~ A pharmaceutical composition comprising (a) the TCR according to any one of claims 1-5, the polypeptide according to any one of claims 6-10, the protein according to any one of claims 11-15, the nucleic acid according to claim 16, the recombinant expression vector according to claim 17, the host cell according to claim 18, or the population of cells according to claim 19 and (b) a pharmaceutically acceptable carrier.

21. ~~The population of cells for the use according to claim 19, wherein the population of cells is allogeneic to the mammal~~ 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 1-5, the polypeptide according to any one of claims 6-10, the protein according to any one of claims 11-15, the nucleic acid according to claim 16, the recombinant expression vector

according to claim 17, the host cell according to claim 18, the population of cells according to claim 19, or the pharmaceutical composition of claim 20, thereby forming a complex; and

(b) detecting the complex,

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

22. The method according to claim 18, or the TCR, polypeptide, protein, nucleic acid, recombinant expression vector, host cell, population of cells, or pharmaceutical composition for the use according to any one of claims 19-21, wherein the cancer is an epithelial cancer. Use of a pharmaceutical composition in the manufacture of a medicament for treating or preventing cancer in a mammal, which comprises the TCR according to any one of claims 1-5, the polypeptide according to any one of claims 6-10, the protein according to any one of claims 11-15, the nucleic acid according to claim 16, the recombinant expression vector according to claim 17, the host cell according to claim 18, or the population of cells according to claim 19.

23. The method according to claim 18, or the TCR, polypeptide, protein, nucleic acid, recombinant expression vector, host cell, population of cells, or pharmaceutical composition for the use according to any one of claims 19-21, 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. The use according to claim 22, wherein the population of cells is autologous to the mammal.

24. The use according to claim 22, wherein the population of cells is allogeneic to the mammal.

25. The method according to claim 21, wherein the cancer is an epithelial cancer.

26. The method according to claim 21, 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.

27. The use according to any one of claims 22-24, wherein the cancer is an epithelial cancer.

28. The use according to any one of claims 22-24, 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.