

T CELL RECEPTOR CONSTRUCTS AND USES THEREOF

CROSS REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application No. 62/764,817, filed on August 16, 2018, and U.S. Provisional Application No. 62/810,112, filed on February 25, 2019, both of which are hereby incorporated by reference in their entirety.

BACKGROUND

[0002] T cell receptors (TCRs) are members of the immunoglobulin superfamily and usually consist of two subunits, namely the α - and β -subunits. These possess one N-terminal immunoglobulin (Ig)-variable (V) domain, one Ig-constant (C) domain, a transmembrane/cell membrane-spanning region, and a short cytoplasmic tail at the C-terminal end. The variable domains of both the TCR α -chain and β -chain have three hypervariable or complementarity determining regions (CDRs), whereas the variable region of the β -chain has an additional area of hypervariability (HV4) that does not normally contact antigen and therefore is not considered a CDR.

[0003] CDR3 is the principle CDR responsible for recognizing processed antigen, although CDR1 of the alpha chain has also been shown to interact with the N-terminal part of the antigenic peptide, whereas CDR1 of the β -chain interacts with the C-terminal part of the peptide. CDR2 is thought to recognize the MHC. The constant domain of the TCR domain consists of short connecting sequences in which a cysteine residue forms disulfide bonds, which forms a link between the two chains. The affinity of TCR's for a specific antigen makes them valuable for several therapeutic approaches. For example, cancer patients, such as melanoma patients, can be effectively treated by using adoptive immunotherapy as TCRs are exquisitely sensitive for their antigen and can direct immune responses at tumor cells expressing their cognate antigen. Accordingly, there is a need for TCRs against peptide-MHC complexes for development of new and effective therapeutics.

SUMMARY

[0004] The instant application is based on development of TCRs against peptide-MHC complexes and effective therapeutics comprising the TCRs. Provided herein, isolated nucleic acid molecules encoding TCRs against peptide-MHC complexes, T cells expressing TCRs against peptide-MHC complexes, and pharmaceutical compositions for use in the treatment of diseases.

[0005] Provided herein is a recombinant nucleic acid encoding a T cell receptor (TCR) comprising a TCR beta chain construct comprising a complementarity determining region 3 (CDR3) having an amino acid sequence set forth in SEQ ID NO: 52. In some embodiments, the T cell receptor (TCR) construct further comprises a complementarity determining region 1 (CDR1) and a complementarity determining region 2 (CDR2), wherein the CDR1 has an amino acid sequence set forth in SEQ ID NO: 50; and the CDR2 has an amino acid sequence set forth in SEQ ID NO: 51. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80% sequence identity to an amino acid sequence set forth in SEQ ID NO: 58. In some embodiments, the TCR beta chain construct comprises a variable region having at least

90% sequence identity to an amino acid sequence set forth in SEQ ID NO: 58. In some embodiments, the TCR beta chain construct comprises a variable region having at least 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 58. In some embodiments, the TCR beta chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 58. In some embodiments, the recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the preceding embodiments, further comprises a TCR alpha chain construct having a CDR1, a CDR2, and a CDR3, wherein, the CDR1 has an amino acid sequence set forth in SEQ ID NO: 47; the CDR2 has an amino acid sequence set forth in SEQ ID NO: 48; and, the CDR has an amino acid sequence set forth in SEQ ID NO: 49. In some embodiments, the recombinant nucleic acid of any one of the preceding embodiments, comprises: (a) a sequence having at least 80% sequence identity with SEQ ID NOs: 56 or 57, further comprising a sequence encoding at least SEQ ID NO: 52; and (b) a sequence having at least 80% sequence identity with SEQ ID NOs: 53 or 54, further comprising a sequence encoding at least SEQ ID NO: 49. In some embodiments, the recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the preceding embodiments comprises the TCR alpha chain construct which comprises a variable region having at least 80% sequence identity to an amino acid sequence set forth in SEQ ID NO: 55. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 90% sequence identity to an amino acid sequence set forth in SEQ ID NO: 55. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 55. In some embodiments, the TCR alpha chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 55. In some embodiments, the recombinant nucleic acid encoding a TCR described above comprises: (a) a beta chain having an amino acid sequence set forth in SEQ ID NO: 60, or an amino acid sequence that is at least 80% identical to SEQ ID NO: 60; and (b) an alpha chain having an amino acid sequence set forth in SEQ ID NO: 59, or an amino acid sequence that is at least 80% identical to SEQ ID NO: 59. In some embodiments, the recombinant nucleic acid encoding a TCR of any one of the preceding embodiments, binds to an epitope from human RAS comprising a mutation G12V.

[0006] Provided herein is a recombinant nucleic acid encoding a TCR comprising a TCR beta chain construct and a TCR alpha chain construct, the TCR beta chain construct comprising a complementarity determining region 3 (CDR3) having an amino acid sequence selected from SEQ ID NO: 537 and 563. In some embodiments, the TCR beta chain construct comprises a CDR3 having an amino acid sequence of SEQ ID NO: 537. In some embodiments, the TCR beta chain construct comprising a CDR3 having an amino acid sequence of SEQ ID NO: 537, comprises a variable region having at least 80%, 90%, 95%, 96%, 97%, 98%, 99% or 100% sequence identity to an amino acid sequence set forth in SEQ ID NO: 541. In some embodiments, the TCR beta chain construct has an amino acid sequence identity set forth in SEQ ID NO: 541. In some embodiments, the TCR comprising a TCR beta chain CDR3 having an amino acid sequence of SEQ ID NO: 537, further comprises a TCR alpha chain construct that comprises a variable region having at least 80%, 90%, 95%, 96%, 97%, 98%, 99% or 100% sequence identity to an amino acid sequence set forth in SEQ ID NO: 539 or SEQ ID NO: 552.

In some embodiments, the TCR alpha chain construct has an amino acid sequence identity set forth in SEQ ID NO: 539. In some embodiments, the TCR alpha chain construct has an amino acid sequence identity set forth in SEQ ID NO: 552. In some embodiments, the recombinant nucleic acid described above encodes a TCR comprising a beta chain having an amino acid sequence set forth in SEQ ID NO: 543, or a sequence that has at least 80% sequence identity to SEQ ID NO: 543; and an alpha chain having an amino acid sequence set forth in SEQ ID NO: 542, or a sequence that has at least 80% sequence identity to SEQ ID NO: 542. In some embodiments, the recombinant nucleic acid described above encodes a TCR comprising a beta chain having an amino acid sequence set forth in SEQ ID NO: 543, or a sequence that has at least 80% sequence identity to SEQ ID NO: 543; and an alpha chain having an amino acid sequence set forth in SEQ ID NO: 555, or a sequence that has at least 80% sequence identity to SEQ ID NO: 555. In some embodiments, the recombinant nucleic acid described above encodes a TCR comprising a beta chain variable domain having an amino acid sequence set forth in SEQ ID NO: 541, or a sequence that has at least 80% sequence identity to SEQ ID NO: 541; and an alpha chain variable domain having an amino acid sequence set forth in SEQ ID NO: 539, or a sequence that has at least 80% sequence identity to SEQ ID NO: 539. In some embodiments, the recombinant nucleic acid described above encodes a TCR comprising a beta chain variable domain having an amino acid sequence set forth in SEQ ID NO: 541, or a sequence that has at least 80% sequence identity to SEQ ID NO: 541; and an alpha chain variable domain having an amino acid sequence set forth in SEQ ID NO: 552, or a sequence that has at least 80% sequence identity to SEQ ID NO: 552.

[0007] In some embodiments, the recombinant nucleic acid encoding a TCR comprising a TCR beta chain construct and a TCR alpha chain construct, the TCR beta chain construct comprises a CDR3 having an amino acid sequence of SEQ ID NO: 563. In some embodiments the TCR beta chain construct comprises a variable region having at least 80%, 90%, 95%, 96%, 97%, 98%, 99% or 100% sequence identity to an amino acid sequence set forth in SEQ ID NO: 567. In some embodiments the TCR alpha chain construct comprises a variable region having at least 80%, 90%, 95%, 96%, 97%, 98%, 99% or 100% sequence identity to an amino acid sequence set forth in SEQ ID NO: 565. In some embodiments, the recombinant nucleic acid described above encodes a TCR comprising a beta chain having an amino acid sequence set forth in SEQ ID NO: 569, or a sequence that has at least 80% sequence identity to SEQ ID NO: 569; and an alpha chain variable domain having an amino acid sequence set forth in SEQ ID NO: 568, or a sequence that has at least 80% sequence identity to SEQ ID NO: 568. Disclosed herein is a vector comprising the recombinant nucleic acid of any one of the embodiments described above. Also disclosed herein is a cell comprising the recombinant nucleic acid of any one of the embodiments described above or the vector of as described above.

[0008] Provided herein is a recombinant nucleic acid encoding a TCR construct comprising: (a) a TCR beta chain construct, and (b) a TCR alpha chain construct; wherein the TCR recognizes and binds to an epitope from human RAS comprising a point mutation G12V or G12C, the epitope being in a human MHC-protein complex, wherein the human MHC-protein is an HLA antigen encoded by the HLA A03:01 allele. In some embodiments, the TCR beta chain construct comprises a CDR3 having an amino acid sequence set forth in SEQ ID NO: 68.

In some embodiments, the TCR beta chain construct further comprises a complementarity determining region 1 (CDR1) and a complementarity determining region 2 (CDR2), wherein the CDR1 has an amino acid sequence set forth in SEQ ID NO: 66; and the CDR2 has an amino acid sequence set forth in SEQ ID NO: 67. In some embodiments, the recombinant nucleic acid encoding a T cell receptor (TCR) described in this paragraph, further comprising a TCR alpha chain construct having a CDR1, a CDR2, and a CDR3, wherein, the CDR1 has an amino acid sequence set forth in SEQ ID NO: 63; the CDR2 has an amino acid sequence set forth in SEQ ID NO: 64; and, the CDR has an amino acid sequence set forth in SEQ ID NO: 65. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80%, or at least 90%, 95%, 96%, 97%, 98%, or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 74. In some embodiments, the TCR beta chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 74. In some embodiments, T cell receptor (TCR) comprises a TCR alpha chain construct, wherein the TCR alpha chain construct comprises a variable region having at least 80%, or at least 90%, 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 71. In some embodiments, the TCR alpha chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 71. In some embodiment, the TCR comprises a beta chain construct having an amino acid sequence set forth in SEQ ID NO: 76, or a sequence having at least 80% sequence identity to SEQ ID NO: 76; and an alpha chain construct having an amino acid sequence set forth in SEQ ID NO: 75, or a sequence having at least 80% sequence identity to SEQ ID NO: 75. Provided herein is a vector comprising a recombinant nucleic acid of any one of the embodiments described in this paragraph. Also provided herein is a cell comprising any one of the recombinant nucleic acid of any one of the embodiments described in this paragraph or the vector described in this paragraph.

[0009] In some embodiments, the TCR that recognizes and binds to an epitope from human RAS comprising a point mutation G12V in complex with an HLA antigen encoded by the HLA A03:01 allele, comprises a TCR beta chain construct comprises a CDR3 having an amino acid sequence set forth in SEQ ID NO: 84. In some embodiments, the TCR beta chain construct further comprises a complementarity determining region 1 (CDR1) and a complementarity determining region 2 (CDR2), wherein the CDR1 has an amino acid sequence set forth in SEQ ID NO: 82; and the CDR2 has an amino acid sequence set forth in SEQ ID NO: 83. In some embodiments, the TCR further comprises a TCR alpha construct having a CDR1, a CDR2, and a CDR3, wherein, the CDR1 has an amino acid sequence set forth in SEQ ID NO: 79; the CDR2 has an amino acid sequence set forth in SEQ ID NO: 80; and, the CDR3 has an amino acid sequence set forth in SEQ ID NO: 81. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80%, or at least 90%, 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 90. In some embodiments, the TCR beta chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 90. In some embodiments, the TCR described above further comprises a TCR alpha chain construct that comprises a variable region having at least 80%, or at least 90%, 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 87. In some embodiments, the TCR

alpha chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 71. In some embodiments, the TCR comprises a beta chain construct having an amino acid sequence of SEQ ID NO: 92, or a sequence that has at least 80% sequence identity to SEQ ID NO: 92; and an alpha chain construct having an amino acid sequence of SEQ ID NO: 91, or a sequence that has at least 80% sequence identity to SEQ ID NO: 91. Provided herein is a vector comprising the recombinant nucleic acid of any one of the embodiments described in this paragraph and a cell comprising any one of the recombinant nucleic acid of any one of the embodiments described herein.

[0010] In some embodiments, the recombinant nucleic acid of embodiment described in the preceding paragraph, the TCR that recognizes and binds to an epitope from human RAS comprising a point mutation G12V or G12C in complex with an HLA antigen encoded by the HLA A03:01 allele, comprises a TCR beta chain construct comprises a CDR3 having an amino acid sequence set forth in SEQ ID NO: 388. In some embodiments, the TCR beta chain construct further comprises a complementarity determining region 1 (CDR1) and a complementarity determining region 2 (CDR2), wherein the CDR1 has an amino acid sequence set forth in SEQ ID NO: 386; and the CDR2 has an amino acid sequence set forth in SEQ ID NO: 387. In some embodiments, the TCR further comprises a TCR alpha construct having a CDR1, a CDR2, and a CDR3, wherein, the CDR1 has an amino acid sequence set forth in SEQ ID NO: 383; the CDR2 has an amino acid sequence set forth in SEQ ID NO: 384; and, the CDR3 has an amino acid sequence set forth in SEQ ID NO: 385. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80%, or at least 90%, 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 394. In some embodiments, the TCR beta chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 394. In some embodiments, the TCR described above further comprises a TCR alpha chain construct that comprises a variable region having at least 80%, or at least 90%, 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 391. In some embodiments, the TCR alpha chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 391. In some embodiments, the TCR comprises a beta chain construct having an amino acid sequence of SEQ ID NO: 396, or a sequence that has at least 80% sequence identity to SEQ ID NO: 396; and an alpha chain construct having an amino acid sequence of SEQ ID NO: 395, or a sequence that has at least 80% sequence identity to SEQ ID NO: 395. Provided herein is a vector comprising the recombinant nucleic acid of any one of the embodiments described in this paragraph and a cell comprising any one of the recombinant nucleic acid of any one of the embodiments described herein.

[0011] In some embodiments, the recombinant nucleic acid of embodiment described in the preceding paragraph, the TCR that recognizes and binds to an epitope from human RAS comprising a point mutation G12C in complex with an HLA antigen encoded by the HLA A03:01 allele, comprises a TCR beta chain construct comprises a CDR3 having an amino acid sequence set forth in SEQ ID NO: 100. In some embodiments, the TCR beta chain construct further comprises a complementarity determining region 1 (CDR1) and a complementarity determining region 2 (CDR2), wherein the CDR1 has an amino acid sequence set forth

in SEQ ID NO: 98; and the CDR2 has an amino acid sequence set forth in SEQ ID NO: 99. In some embodiments, the TCR further comprises a TCR alpha construct having a CDR1, a CDR2, and a CDR3, wherein, the CDR1 has an amino acid sequence set forth in SEQ ID NO: 95; the CDR2 has an amino acid sequence set forth in SEQ ID NO: 96; and, the CDR3 has an amino acid sequence set forth in SEQ ID NO: 97. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80%, or at least 90%, 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 106. In some embodiments, the TCR beta chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 106. In some embodiments, the TCR described above further comprises a TCR alpha chain construct that comprises a variable region having at least 80%, or at least 90%, 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 103. In some embodiments, the TCR alpha chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 103. In some embodiments, the TCR comprises a beta chain construct having an amino acid sequence of SEQ ID NO: 108, or a sequence that has at least 80% sequence identity to SEQ ID NO: 108; and an alpha chain construct having an amino acid sequence of SEQ ID NO: 107, or a sequence that has at least 80% sequence identity to SEQ ID NO: 107. Provided herein is a vector comprising the recombinant nucleic acid of any one of the embodiments described in this paragraph and a cell comprising any one of the recombinant nucleic acid of any one of the embodiments described herein.

[0012] In some embodiments, the epitope has a length of from 8-25 amino acids. In some embodiments the epitope comprises a mutation that differs from the wild type epitope by at least one amino acid. In some embodiments, the epitope binds to the human MHC with a greater affinity than a corresponding wild-type epitope. In some embodiments, the epitope binds to the human MHC with a K_D or an IC_{50} less than 500 nM, 250 nM, 150 nM, 100 nM, 50 nM, 25 nM or 10 nM. In some embodiments, the mutation is not present in non-cancer cells of a subject. In some embodiments, the TCR binds to an MHC-peptide complex with a K_D or an IC_{50} of less than 500 nM, 250 nM, 150 nM, 100 nM, 50 nM, 25 nM or 10 nM. In some embodiments, the nucleic acid is operably linked to a promoter. In some embodiments, the cell is a $CD4^+$ T cell. In some embodiments, the cell is a $CD8^+$ T cell. In some embodiments, the cell is isolated from a subject having a RAS mutation.

[0013] Provided herein is a pharmaceutical composition comprising: (a) the nucleic acid of any one of embodiments described above; or, the vector of any one of embodiments described above; or, the cell of any one of embodiments above; and, (b) a pharmaceutically acceptable excipient or diluent. In some embodiments, the pharmaceutical composition further comprising an immunomodulatory agent or an adjuvant. In some embodiments, the adjuvant is poly I:C. In some embodiments, the pharmaceutical composition of any one of embodiments described above is for use in treating an immune disease or cancer.

[0014] Provided herein is method of treating a subject having a disease or condition, comprising administering to the subject the pharmaceutical composition of any one of embodiments described above. In some embodiments, the method of treating a subject with cancer comprises administering to the subject the pharmaceutical composition of any one of embodiments described above.

[0015] Also provided herein is a method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising determining the subject as a subject that expresses a protein encoded by an HLA-A03:01 allele or an HLA-A11:01 allele, wherein the therapeutic is the pharmaceutical composition selected from any one of embodiments described above.

[0016] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from RAS in complex with a human MHC, wherein the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 84% sequence identity to an amino acid sequence selected from SEQ ID NOs: 3, 18, 33, 49, 65, 81, 97, 113, 241, 257, 273, 289, 305, 321, 337, 353, 369, 385, 401, 417, and 433 and/or wherein the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 84% sequence identity to an amino acid sequence selected from SEQ ID NOs: 6, 21, 36, 52, 68, 84, 100, 116, 244, 260, 276, 292, 308, 324, 340, 356, 372, 388, 404, 420, and 436.

[0017] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from RAS in complex with a human MHC, wherein the epitope from RAS comprises a region having at least 70% sequence identity to an amino acid sequence selected from SEQ ID NOs: 15, 30, 45, 46, 61, 62, 77, 78, 93, 94, 109, 110, 125, 126, 219-222, 253, 254, 269, 270, 285, 286, 301, 302, 317, 318, 333, 334, 349, 350, 365, 366, 381, 382, 397, 398, 413, 414, 429, 430, 445 and 446.

[0018] Provided herein is an isolated nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct; wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A03:01 allele. In some embodiments, the alpha chain construct comprises a variable region having at least 80% sequence identity to an amino acid sequence selected from SEQ ID NOs: 71, 87, 103, 295, 311, 327, 343, 359 and 391, wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A03:01 allele. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80% sequence identity to an amino acid sequence selected from SEQ ID NOs: 74, 90, 106, 298, 314, 330, 346, 362 and 394, wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A03:01 allele.

[0019] In some embodiments, the TCR alpha chain construct as described above comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 63, 79, 95, 287, 303, 319, 335, 351 and 383. In some embodiments, the TCR beta chain construct as described above comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 66, 82, 98, 290, 306, 322, 338, 354 and 386. In some embodiments, the TCR alpha chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 64, 80, 96, 288, 304, 320, 336, 352 and 384. In some embodiments, the TCR beta chain construct comprises a complementarity

determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 67, 83, 99, 291, 307, 323, 339, 355 and 387. In some embodiments, the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 65, 81, 97, 289, 305, 321, 337, 353 and 385. In some embodiments, the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 68, 84, 100, 292, 308, 324, 340, 356 and 388.

[0020] Provided herein is an isolated nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct; wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A02:01 allele. In some embodiments, the alpha chain construct comprises a variable region having at least 80% sequence identity to an amino acid sequence selected from SEQ ID NOs: 9 and 24 wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A02:01 allele. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80% sequence identity to an amino acid sequence selected from SEQ ID NOs: 12 and 27, wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A02:01 allele.

[0021] In some embodiments, the TCR alpha chain construct as described above comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 1 and 16. In some embodiments, the TCR beta chain construct as described above comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 4 and 19. In some embodiments, the TCR alpha chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 2 and 17. In some embodiments TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 5 and 20. In some embodiments, the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 3 and 18. In some embodiments, the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 6 and 21.

[0022] Provided herein is an isolated nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct; wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A11:01 allele. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to an amino acid sequence selected from SEQ ID NOs: 39, 55, 122, 247, 263, 279, 375, 407, and 423, wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A11:01 allele. In some embodiments, the TCR beta chain

construct comprises a variable region having at least 80% sequence identity to an amino acid sequence selected from SEQ ID NOs: 42, 58, 125, 250, 266, 282, 378, 413, and 426, wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A11:01 allele.

[0023] In some embodiments, the TCR alpha chain construct as described above comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 31, 47, 111, 239, 255, 271, 367, 399, and 415. In some embodiments, the TCR beta chain construct as described above comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 34, 50, 114, 242, 258, 274, 370, 402, and 418. In some embodiments, the TCR alpha chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 32, 48, 112, 240, 256, 272, 368, 400, and 416. In some embodiments, the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 35, 51, 115, 243, 259, 275, 371, 403, and 419. In some embodiments, the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 33, 49, 113, 241, 257, 273, 369, 401, 417, and 433. In some embodiments, the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 36, 52, 116, 244, 260, 276, 372, 404, and 420. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 9; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 12. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 1, a CDR2 of SEQ ID NO: 2, and a CDR3 of SEQ ID NO: 3; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 4, a CDR2 of SEQ ID NO: 5, and a CDR3 of SEQ ID NO: 6. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 13, or a sequence that has at least 80% identity to SEQ ID NO: 13. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 14 or a sequence that has at least 80% identity to SEQ ID NO: 14. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 24; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 27. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 16, a CDR2 of SEQ ID NO: 17, and a CDR3 of SEQ ID NO: 18; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 19, a CDR2 of SEQ ID NO: 20, and a CDR3 of SEQ ID NO: 21. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 28, or a sequence that has at least 80% identity to SEQ ID NO: 28. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 29 or a sequence that has at least 80% identity to SEQ ID NO: 29. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 39; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 42. In some embodiments, the TCR alpha chain construct

comprises a CDR1 of SEQ ID NO: 31, a CDR2 of SEQ ID NO: 32, and a CDR3 of SEQ ID NO: 33; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 34, a CDR2 of SEQ ID NO: 35, and a CDR3 of SEQ ID NO: 36. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 43, or a sequence that has at least 80% identity to SEQ ID NO: 43. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 44 or a sequence that has at least 80% identity to SEQ ID NO: 44. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 55; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 58. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 47, a CDR2 of SEQ ID NO: 48, and a CDR3 of SEQ ID NO: 49; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 50, a CDR2 of SEQ ID NO: 51, and a CDR3 of SEQ ID NO: 52. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 71; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 74. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 63, a CDR2 of SEQ ID NO: 64, and a CDR3 of SEQ ID NO: 65; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 66, a CDR2 of SEQ ID NO: 67, and a CDR3 of SEQ ID NO: 68. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 75, or a sequence that has at least 80% identity to SEQ ID NO: 75. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 76 or a sequence that has at least 80% identity to SEQ ID NO: 76. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 87; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 90. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 79, a CDR2 of SEQ ID NO: 80, and a CDR3 of SEQ ID NO: 81; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 82, a CDR2 of SEQ ID NO: 83, and a CDR3 of SEQ ID NO: 84. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 91, or a sequence that has at least 80% identity to SEQ ID NO: 91. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 92 or a sequence that has at least 80% identity to SEQ ID NO: 92. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 103; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 106. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 95, a CDR2 of SEQ ID NO: 96, and a CDR3 of SEQ ID NO: 97; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 98, a CDR2 of SEQ ID NO: 99, and a CDR3 of SEQ ID NO: 100. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 107, or a sequence that has at least 80% identity to SEQ ID NO: 107. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 108 or a sequence that has at least 80% identity to SEQ ID NO: 108. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 119; and the TCR beta chain construct comprises a variable region having at least 80% sequence

identity to SEQ ID NO: 122. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 111, a CDR2 of SEQ ID NO: 112, and a CDR3 of SEQ ID NO: 113; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 114, a CDR2 of SEQ ID NO: 115, and a CDR3 of SEQ ID NO: 116. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 123, or a sequence that has at least 80% identity to SEQ ID NO: 123. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 124 or a sequence that has at least 80% identity to SEQ ID NO: 124. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 247; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 250. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 239, a CDR2 of SEQ ID NO: 240, and a CDR3 of SEQ ID NO: 241; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 242, a CDR2 of SEQ ID NO: 243, and a CDR3 of SEQ ID NO: 244. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 251, or a sequence that has at least 80% identity to SEQ ID NO: 251. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 252 or a sequence that has at least 80% identity to SEQ ID NO: 252. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 263; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 266. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 255, a CDR2 of SEQ ID NO: 256, and a CDR3 of SEQ ID NO: 257; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 258, a CDR2 of SEQ ID NO: 259, and a CDR3 of SEQ ID NO: 260. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 267, or a sequence that has at least 80% identity to SEQ ID NO: 267. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 268 or a sequence that has at least 80% identity to SEQ ID NO: 268. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 279; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 282. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 271, a CDR2 of SEQ ID NO: 272, and a CDR3 of SEQ ID NO: 273; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 274, a CDR2 of SEQ ID NO: 275, and a CDR3 of SEQ ID NO: 276. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 283, or a sequence that has at least 80% identity to SEQ ID NO: 283. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 284 or a sequence that has at least 80% identity to SEQ ID NO: 284. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 295; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 298. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 287, a CDR2 of SEQ ID NO: 288, and a CDR3 of SEQ ID NO: 289; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 290, a CDR2 of SEQ ID NO: 291, and a CDR3 of SEQ ID NO: 292. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 299, or a sequence

that has at least 80% identity to SEQ ID NO: 299. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 300 or a sequence that has at least 80% identity to SEQ ID NO: 300. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 311; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 314. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 303, a CDR2 of SEQ ID NO: 304, and a CDR3 of SEQ ID NO: 305; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 306, a CDR2 of SEQ ID NO: 307, and a CDR3 of SEQ ID NO: 308. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 315, or a sequence that has at least 80% identity to SEQ ID NO: 315. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 316 or a sequence that has at least 80% identity to SEQ ID NO: 316. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 327; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 330. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 319, a CDR2 of SEQ ID NO: 320, and a CDR3 of SEQ ID NO: 321; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 322, a CDR2 of SEQ ID NO: 323, and a CDR3 of SEQ ID NO: 324. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 331, or a sequence that has at least 80% identity to SEQ ID NO: 331. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 332 or a sequence that has at least 80% identity to SEQ ID NO: 332. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 343; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 346. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 335, a CDR2 of SEQ ID NO: 336, and a CDR3 of SEQ ID NO: 337; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 338, a CDR2 of SEQ ID NO: 339, and a CDR3 of SEQ ID NO: 340. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 347, or a sequence that has at least 80% identity to SEQ ID NO: 347. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 348 or a sequence that has at least 80% identity to SEQ ID NO: 348. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 359; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 362. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 351, a CDR2 of SEQ ID NO: 352, and a CDR3 of SEQ ID NO: 353; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 354, a CDR2 of SEQ ID NO: 355, and a CDR3 of SEQ ID NO: 356. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 363, or a sequence that has at least 80% identity to SEQ ID NO: 363. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 364 or a sequence that has at least 80% identity to SEQ ID NO: 364. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 375; and the TCR beta chain construct comprises a variable region having at least 80% sequence

identity to SEQ ID NO: 378. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 367, a CDR2 of SEQ ID NO: 368, and a CDR3 of SEQ ID NO: 369; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 370, a CDR2 of SEQ ID NO: 371, and a CDR3 of SEQ ID NO: 372. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 379, or a sequence that has at least 80% identity to SEQ ID NO: 379. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 380 or a sequence that has at least 80% identity to SEQ ID NO: 380. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 391; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 394. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 383, a CDR2 of SEQ ID NO: 384, and a CDR3 of SEQ ID NO: 385; the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 386, a CDR2 of SEQ ID NO: 387, and a CDR3 of SEQ ID NO: 388. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 395, or a sequence that has at least 80% identity to SEQ ID NO: 395. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 396 or a sequence that has at least 80% identity to SEQ ID NO: 396. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 407; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 410. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 399, a CDR2 of SEQ ID NO: 400, and a CDR3 of SEQ ID NO: 401; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 402, a CDR2 of SEQ ID NO: 403, and a CDR3 of SEQ ID NO: 404. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 411, or a sequence that has at least 80% identity to SEQ ID NO: 411. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 412 or a sequence that has at least 80% identity to SEQ ID NO: 412. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 423; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 426. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 415, a CDR2 of SEQ ID NO: 416, and a CDR3 of SEQ ID NO: 417; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 418, a CDR2 of SEQ ID NO: 419, and a CDR3 of SEQ ID NO: 420. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 427, or a sequence that has at least 80% identity to SEQ ID NO: 427. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 428 or a sequence that has at least 80% identity to SEQ ID NO: 428. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 391; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 394.

[0024] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from TMPRSS2:ERG in complex with a human MHC, wherein the TCR alpha chain construct and/or the TCR beta

chain construct comprises a complementarity determining region 3 (CDR3) having a sequence of SEQ ID NO: 144 and SEQ ID NO: 147 or a sequence having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 144 and SEQ ID NO: 147. In some embodiments, the TCR comprises an alpha chain having a sequence of SEQ ID NO: 154, or a sequence that has at least 80% identity to SEQ ID NO: 154. In some embodiments, the TCR comprises a beta chain having a sequence of SEQ ID NO: 155 or a sequence that has at least 80% identity to SEQ ID NO: 155.

[0025] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from TMPRSS2:ERG in complex with a human MHC, wherein the epitope from TMPRSS2:ERG comprises a region having at least 90% sequence identity to amino acid sequence SEQ ID NO: 156.

[0026] In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 150. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 153. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having a sequence of SEQ ID NO: 142 or a sequence having at least 90% sequence identity to SEQ ID NO: 142 and a sequence of SEQ ID NO: 145 or a sequence having at least 90% sequence identity to SEQ ID NO: 145 respectively. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to SEQ ID NO: 143 or SEQ ID NO: 146 respectively. In some embodiments, the TCR alpha chain construct comprises a variable region having a sequence of SEQ ID NO: 150 or at least 80% sequence identity to SEQ ID NO: 150; and the TCR beta chain construct comprises a variable region having a sequence of SEQ ID NO: 153 or at least 80% sequence identity to SEQ ID NO: 153. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 142, a CDR2 of SEQ ID NO: 143, and a CDR3 of SEQ ID NO: 144; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 145, a CDR2 of SEQ ID NO: 146, and a CDR3 of SEQ ID NO: 147.

[0027] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from GATA3 in complex with a human MHC, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 129, 132, 191, 194, 206 and 209.

[0028] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) capable of specifically binding to a mutant GATA3 peptide in complex with a protein encoded by an HLA allele of a subject with cancer, wherein the TCR comprises a TCR alpha chain construct and/or a TCR beta chain construct.

[0029] Provided herein is an isolated nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes a T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct, wherein the TCR specifically binds to a mutant GATA3 peptide in complex with an HLA-A02:01,

HLA-B07:02 or HLA-B08:01 protein; comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to SEQ ID NOs: 129, 132, 191, 194, 206 or 209; and/or specifically binds to a mutant GATA3 peptide comprising a region having a sequence of or having a sequence with at least 70% sequence identity to SEQ ID NO: 141, 203 or 218.

[0030] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from GATA3 in complex with a human MHC, wherein the epitope from GATA3 comprises a region having at least 90% sequence identity to amino acid sequence SEQ ID NO: 141, 203 or 218.

[0031] In some embodiments, the TCR alpha chain construct comprises a variable region having a sequence of SEQ ID NO: 135, 197 or 212; or a sequence with at least 80% sequence identity to SEQ ID NO: 135, 197 or 212. In some embodiments, the TCR beta chain construct comprises a variable region having a sequence of SEQ ID NO: 138, 200 or 215; or a sequence having at least 80% sequence identity to SEQ ID NO: 138, 200 or 215. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having an amino acid sequence of, having or at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 127, 130, 189, 192, 204 and 207. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having an amino acid sequence of, or having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 128, 131, 190, 193, 205 and 208. In some embodiments, the GATA3 binding TCR alpha chain comprises a variable region having a sequence of SEQ ID NO: 135, or a sequence having at least 80% identity to SEQ ID NO: 135; and a beta chain having a variable region having a sequence of SEQ ID NO: 138, or a sequence having at least 80% identity to SEQ ID NO: 138. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 127, a CDR2 of SEQ ID NO: 128, and a CDR3 of SEQ ID NO: 129; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 130, a CDR2 of SEQ ID NO: 131, and a CDR3 of SEQ ID NO: 132. In some embodiments, the TCR has an alpha chain having a sequence of SEQ ID NO: 139, or a sequence having at least 80% identity to SEQ ID NO: 139. In some embodiments, the TCR has a beta chain having a sequence of SEQ ID NO: 140, or a sequence having at least 80% identity to SEQ ID NO: 140. In some embodiments, the TCR alpha chain construct comprises a variable region having an amino acid sequence of, or having at least 80% sequence identity to SEQ ID NO: 197; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 200. In some embodiments the TCR alpha chain has a sequence of SEQ ID NO: 201 or a sequence having at least 80% identity to SEQ ID NO: 201. In some embodiments the TCR beta chain has a sequence of SEQ ID NO: 202 or a sequence having at least 80% identity to SEQ ID NO: 202. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 189, a CDR2 of SEQ ID NO: 190, and a CDR3 of SEQ ID NO: 191; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 192, a CDR2 of SEQ ID NO: 193, and a CDR3 of SEQ ID NO: 194. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 212; and the

TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 215. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 204, a CDR2 of SEQ ID NO: 205, and a CDR3 of SEQ ID NO: 206; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 207, a CDR2 of SEQ ID NO: 208, and a CDR3 of SEQ ID NO: 209. In some embodiments, the TCR comprises of an alpha chain having a sequence of SEQ ID NO: 216 or a sequence having at least 80% identity to SEQ ID NO: 216. In some embodiments, the TCR comprises of a beta chain having a sequence of SEQ ID NO: 217 or a sequence having at least 80% identity to SEQ ID NO: 217.

[0032] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from BTK in complex with a human MHC, wherein the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 161 and SEQ ID NO: 176, or wherein the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 164 and SEQ ID NO: 179.

[0033] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) capable of specifically binding to a mutant BTK peptide in complex with a protein encoded by an HLA allele of a subject with cancer, wherein the TCR comprises a TCR alpha chain construct and/or a TCR beta chain construct.

[0034] Provided herein is an isolated nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes a T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct, wherein the TCR specifically binds to a mutant BTK peptide in complex with an HLA-A02:01 protein; comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to SEQ ID NO: 161, 164, 176, or 179; and/or specifically binds to a mutant BTK peptide comprising a region with at least 70% sequence identity to SEQ ID NO: 173 or 188.

[0035] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from BTK in complex with a human MHC, wherein the epitope from BTK comprises a region having at least 90% sequence identity to amino acid sequence SEQ ID NO: 173 or 188.

[0036] In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 167 or 182. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 170 or 185. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 159, 162, 174, and 177. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 160, 163, 175 and 178. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 167 or

182; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 170 or 185. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 159 or 174, a CDR2 of SEQ ID NO: 160 or 175, and a CDR3 of SEQ ID NO: 161 or 176; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 162 or 177, a CDR2 of SEQ ID NO: 163 or 178, and a CDR3 of SEQ ID NO: 164 or 179.

[0037] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from EGFR in complex with a human MHC, wherein the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 449, SEQ ID NO: 466, SEQ ID NO: 483, SEQ ID NO: 500, and SEQ ID NO: 517, or wherein the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 452, SEQ ID NO: 469, SEQ ID NO: 486, SEQ ID NO: 503, and SEQ ID NO: 520.

[0038] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) capable of specifically binding to a mutant EGFR peptide in complex with a protein encoded by an HLA allele of a subject with cancer, wherein the TCR comprises a TCR alpha chain construct and/or a TCR beta chain construct.

[0039] Provided herein is an isolated nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes a T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct, wherein the TCR specifically binds to a mutant EGFR peptide in complex with an HLA-A02:01 protein; comprises a complementarity determining region 3 (CDR3) having a sequence of, or a sequence having at least 90% sequence identity to SEQ ID NO: 449, 466, 483, 500, 517, 452, 469, 486, 503, or 520; and/or specifically binds to a mutant EGFR peptide comprising a region having a sequence of, or having a sequence with at least 70% sequence identity to SEQ ID NO: 461, 462, 463, 478, 479, 480, 495, 496, 497, 512, 513, 514, 529, 530 or 531.

[0040] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from EGFR in complex with a human MHC, wherein the epitope from EGFR comprises a region having at least 90% sequence identity to amino acid sequence SEQ ID NO: 461, 462, 463, 478, 479, 480, 495, 496, 497, 512, 513, 514, 529, 530 or 531.

[0041] In some embodiments, the TCR alpha chain construct comprises a variable region having a sequence of, or a sequence having at least 80% sequence identity to SEQ ID NO: 449, 466, 483, 500 or 517. In some embodiments, the TCR beta chain construct comprises a variable region having a sequence of, or a sequence having at least 80% sequence identity to SEQ ID NO: 452, 469, 486, 503, or 520. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having a sequence of, or a sequence having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 447, 464, 481, 498, 515, 450, 467, 484, 501, and 518. In some

embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having a sequence of, or a sequence having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 448, 465, 482, 499, 516, 451, 468, 485, 502, and 519. In some embodiments, the TCR alpha chain construct comprises a variable region having a sequence of, or a sequence having at least 80% sequence identity to SEQ ID NO: 455, 472, 489, 506, or 523; and the TCR beta chain construct comprises a variable region having a sequence of, or a sequence having at least 80% sequence identity to SEQ ID NO: 458, 475, 492, 509 or 526. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 447, 464, 481, 498 or 515, a CDR2 of SEQ ID NO: 448, 465, 482, 499 or 516, and a CDR3 of SEQ ID NO: 449, 466, 483, 500 or 517; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 450, 467, 484, 501 or 518, a CDR2 of SEQ ID NO: 451, 468, 485, 502, or 519, and a CDR3 of SEQ ID NO: 452, 469, 486, 503, or 520.

[0042] In some embodiments, the epitope comprises a mutation selected from the group consisting of a point mutation, a splice-site mutation, a frameshift mutation, a read-through mutation, a resistance mutation, a gene fusion mutation and any combination thereof. In some embodiments, the human MHC is encoded by either HLA-A02:01 allele, or HLA-A03:01 allele or HLA-A11:01 allele. In some embodiments, the RAS epitope comprises a point mutation. In some embodiments, the point mutation is a G12V mutation. In some embodiments, the point mutation is a G12C mutation. In some embodiments, the point mutation is a G12D mutation. In some embodiments, the human MHC is encoded by HLA-A02:01 allele. In some embodiments, the TMPRSS2:ERG epitope comprises a gene fusion mutation. In some embodiments, the human MHC is encoded by HLA-A02:01, HLA-B07:02 or HLA-B08:01 allele. In some embodiments, the epitope comprises a frameshift mutation. In some embodiments, the human MHC is encoded by HLA-A02:01 allele. In some embodiments, the BTK epitope comprises a point mutation. In some embodiments, the point mutation is C481S mutation. In some embodiments, the human MHC is encoded by HLA-A02:01 allele. In some embodiments, the EGFR epitope comprises a point mutation. In some embodiments, the point mutation is T790M.

[0043] In some embodiments, the epitope has a length of at least 8 amino acids. In some embodiments, the epitope has a length of at least 16 amino acids. In some embodiments, the epitope has a length of from 8-25 amino acids. In some embodiments, the epitope has a length of from 8-12 amino acids. In some embodiments, the epitope has a length of from 16-25 amino acids. In some embodiments, the epitope has a length of 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acids.

[0044] In some embodiments, the epitope binds to the human MHC with a greater affinity than a corresponding wild-type epitope. In some embodiments, the epitope binds to the human MHC with a K_D or an IC_{50} less than 500 nM, 250 nM, 150 nM, 100 nM, 50 nM, 25 nM or 10 nM.

[0045] In some embodiments, the mutation is not present in non-cancer cells of a subject. In some embodiments, the epitope is encoded by a gene or an expressed gene of a subject's cancer cells.

[0046] In some embodiments, the TCR binds to a MHC-peptide complex with a K_D or an IC_{50} of less than 500 nM, 250 nM, 150 nM, 100 nM, 50 nM, 25 nM or 10 nM.

[0047] In some embodiments, the nucleic acid is operably linked to a promoter.

[0048] Provided herein is a vector comprising a nucleic acid described herein. In some embodiments, the vector is a self-amplifying RNA replicon, plasmid, phage, transposon, cosmid, virus, or virion. In some embodiments, wherein the vector is a viral vector. In some embodiments, wherein the vector is derived from a retrovirus, lentivirus, adenovirus, adeno-associated virus, herpes virus, pox virus, alpha virus, vaccinia virus, hepatitis B virus, human papillomavirus or a pseudotype thereof. In some embodiments, the vector is a non-viral vector. In some embodiments, the non-viral vector is a nanoparticle, a cationic lipid, a cationic polymer, a metallic nanopolymer, a nanorod, a liposome, a micelle, a microbubble, a cell-penetrating peptide, or a liposphere.

[0049] Provided herein is a protein encoded by the nucleic acid of any one sections described above.

[0050] Provided herein is a host cell comprising the nucleic acid described above, the vector of described above, or the protein described above. In some embodiments, the host cell is a CD4⁺ T cell. In some embodiments, the host cell is a CD8⁺ T cell. In some embodiments, the host cell is an autologous cell. In some embodiments, the host cell is an allogeneic cell. In some embodiments, the host cell is a natural killer cell, a B cell, or an immortalized cell line. In some embodiments, the host cell is a human cell.

[0051] Provided herein is a pharmaceutical composition comprising a nucleic acid described herein, a vector described herein, a protein described herein, or a host cell described herein; and a pharmaceutically acceptable excipient or diluent. In some embodiments, the pharmaceutical composition further comprises an immunomodulatory agent or an adjuvant. In some embodiments, the immunomodulatory agent in the pharmaceutical composition is a cytokine. In some embodiments, the adjuvant in the pharmaceutical composition is poly I:C. In some embodiments, the pharmaceutical compositions are for use in treating an immune disease or cancer.

[0052] Provided herein is the use of the pharmaceutical composition described above, for treating an immune disease or cancer.

[0053] Provided herein is a vector described herein, a protein described herein, or a host cell described herein for manufacture of a medicament for treating an immune disease or cancer. In some embodiments, the medicament is an adoptive T cell therapy or a TCR gene therapy.

[0054] Provided herein is a method of treating a subject with a disease or condition, comprising administering to the subject a pharmaceutical composition disclosed herein.

[0055] Provided herein is a method of treating a subject with cancer, comprising administering to the subject a pharmaceutical composition disclosed herein.

[0056] Provided herein is a method of treating a subject with cancer comprising administering to the subject a pharmaceutical composition In some embodiments, ; wherein the subject is identified as expressing or expresses a protein encoded by an HLA-A02:01 allele, an HLA-B07:02, an HLA-B08:01, an HLA-A03:01 allele, an HLA-A11:01 allele, an HLA-A03:02 allele, an HLA-A30:01 allele, an HLA-A31:01 allele, an HLA-A33:01 allele, an HLA-A33:03 allele, an HLA-A68:01 allele, or an HLA-A74:01 allele of the subject's genome.

[0057] Provided herein is a method of treating a subject with cancer comprising administering a TCR or T cell expressing the TCR to the subject, wherein the TCR specifically binds to a mutant RAS peptide in complex with a protein encoded by an HLA-A02:01, an HLA-A03:01 allele, an HLA-A11:01 allele, an HLA-A03:02 allele, an HLA-A30:01 allele, an HLA-A31:01 allele, an HLA-A33:01 allele, an HLA-A33:03 allele, an HLA-A68:01 allele, or an HLA-A74:01; wherein the subject is identified as expressing or expresses a protein encoded by an HLA-A03:01 allele, an HLA-A11:01 allele, an HLA-A03:02 allele, an HLA-A30:01 allele, an HLA-A31:01 allele, an HLA-A33:01 allele, an HLA-A33:03 allele, an HLA-A68:01 allele, or an HLA-A74:01 allele, wherein the subject expresses the HLA allele.

[0058] Provided herein is a method of treating a subject with cancer comprising administering to the subject a pharmaceutical composition described herein; wherein the TCR binds to a mutant RAS peptide comprising a mutation at G12 in complex with an HLA-A02:01, an HLA-A03:01 allele, an HLA-A11:01 allele, an HLA-A03:02 allele, an HLA-A30:01 allele, an HLA-A31:01 allele, an HLA-A33:01 allele, an HLA-A33:03 allele, an HLA-A68:01 allele, or an HLA-A74:01; wherein the subject is identified as expressing a protein encoded by an HLA-A03:01 allele, an HLA-A11:01 allele, an HLA-A03:02 allele, an HLA-A30:01 allele, an HLA-A31:01 allele, an HLA-A33:01 allele, an HLA-A33:03 allele, an HLA-A68:01 allele, or an HLA-A74:01 allele.

[0059] Provided herein is a method of treating a subject with cancer comprising administering to the subject a composition comprising a T cell receptor (TCR) specific for a mutant GATA3 peptide in complex with an HLA protein; wherein the mutant GATA3 peptide comprises at least one mutant amino acid and is fragment of at least 8 contiguous amino acids of a mutant GATA3 protein arising from a mutation in a GATA3 gene of a cancer cell; wherein the mutant GATA3 peptide binds to a protein encoded by an HLA-A02:01, HLA-B07:02 or HLA-B08:01 allele.

[0060] Provided herein is a method of treating a subject with cancer comprising administering to the subject a composition comprising a T cell receptor (TCR) specific for a mutant GATA3 peptide in complex with an HLA protein; wherein the mutant GATA3 peptide comprises one or more mutant GATA3 amino acids encoded by a GATA3 neoORF sequence, wherein the mutant GATA3 peptide binds to a protein encoded by an HLA-A02:01, HLA-B07:02 or HLA-B08:01 allele.

[0061] Provided herein is a method of treating a subject with cancer comprising administering a TCR or T cell expressing the TCR to the subject; wherein the TCR specifically binds to a mutant GATA3 peptide in complex with a protein encoded by an HLA-A02:01, HLA-B07:02 or HLA-B08:01 allele; wherein the subject is identified as expressing or expresses a protein encoded by an HLA-A02:01, HLA-B07:02 or HLA-B08:01 allele.

[0062] Provided herein is a method of treating a subject with cancer comprising administering to the subject a composition comprising a T cell receptor (TCR) specific for a mutant TMPRSS2:ERG peptide in complex with an HLA protein; wherein the mutant TMPRSS2:ERG peptide comprises at least one mutant amino acid and is a fragment of a TMPRSS2:ERG gene fusion mutation; wherein the mutant TMPRSS2:ERG peptide binds to a protein encoded by an HLA-A02:01 allele.

[0063] Provided herein is a method of treating a subject with cancer comprising administering to the subject a composition comprising a T cell receptor (TCR) specific for a mutant BTK peptide in complex with an HLA protein; wherein the mutant BTK peptide comprises at least one mutant amino acid; wherein the mutant BTK peptide binds to a protein encoded by an HLA-A02:01 allele.

[0064] Provided herein is a method of treating a subject with cancer comprising administering to the subject a composition comprising a T cell receptor (TCR) specific for a mutant BTK peptide in complex with an HLA protein; wherein the mutant BTK peptide comprises a resistance mutation or a point mutation; wherein the mutant BTK peptide binds to a protein encoded by an HLA-A02:01 allele.

[0065] Provided herein is a method of treating a subject with cancer comprising administering to the subject a composition comprising a T cell receptor (TCR) specific for a mutant BTK peptide in complex with an HLA protein; wherein the mutant BTK peptide comprises a C481S mutation; wherein the mutant BTK peptide binds to a protein encoded by an HLA-A02:01 allele.

[0066] Provided herein is a method of treating a subject with cancer comprising administering to the subject a composition comprising a T cell receptor (TCR) or a T cell expressing the TCR to the subject, wherein the TCR specifically binds to a mutant EGFR peptide in complex with a protein encoded by an HLA-A02:01; wherein the mutant EGFR peptide comprises a resistance mutation or a point mutation, wherein the subject is identified as expressing or expresses a protein encoded by an HLA-A02:01 allele. In some embodiments, the mutant EGFR peptide comprises a T790M mutation.

[0067] Provided herein is a method of preventing resistance to a cancer therapy, the method comprising administering to a subject in need thereof a pharmaceutical composition described herein.

[0068] Provided herein is a method of inducing an immune response, the method comprising administering to a subject in need thereof a pharmaceutical composition described herein.

[0069] Provided herein is a method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising identifying the subject as a subject that expresses a protein encoded by an HLA-A02:01 allele, an HLA-A03:01 allele, an HLA-A11:01 allele, an HLA-A03:02 allele, an HLA-A30:01 allele, an HLA-A31:01 allele, an HLA-A33:01 allele, an HLA-A33:03 allele, an HLA-A68:01 allele, or an HLA-A74:01 allele, wherein the therapeutic is a pharmaceutical composition described herein.

[0070] Provided herein is a method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising identifying the subject as one that expresses a protein encoded by an HLA-A02:01, HLA-B07:02 or HLA-B08:01 allele, wherein the therapeutic comprises a T cell receptor (TCR) specific for a mutant GATA3 peptide in complex with an HLA protein; wherein the mutant GATA3 peptide comprises at least one mutant amino acid and is fragment of at least 8 contiguous amino acids of a mutant GATA3 protein arising from a mutation in a GATA3 gene of a cancer cell; wherein the mutant GATA3 peptide binds to a protein encoded by an HLA-A02:01, HLA-B07:02 or HLA-B08:01 allele.

[0071] Provided herein is a method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising identifying the subject as one that expresses a protein encoded by an HLA-A03:01 allele,

an HLA-A11:01 allele, an HLA-A03:02 allele, an HLA-A30:01 allele, an HLA-A31:01 allele, an HLA-A33:01 allele, an HLA-A33:03 allele, an HLA-A68:01 allele, or an HLA-A74:01 allele, wherein the therapeutic comprises a T cell receptor (TCR) specific for a mutant RAS peptide comprising a mutation at G12 in complex with an HLA protein; wherein the mutant RAS peptide binds to a protein encoded by an HLA-A03:01 allele, an HLA-A11:01 allele, an HLA-A03:02 allele, an HLA-A30:01 allele, an HLA-A31:01 allele, an HLA-A33:01 allele, an HLA-A33:03 allele, an HLA-A68:01 allele, or an HLA-A74:01 allele.

[0072] Provided herein is a method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising identifying the subject as one that expresses a protein encoded by an HLA-A02:01 allele, wherein the therapeutic comprises a T cell receptor (TCR) specific for a mutant TMPRSS2:ERG peptide in complex with an HLA protein; wherein the mutant TMPRSS2:ERG peptide comprises at least one mutant amino acid and is a fragment of a TMPRSS2:ERG gene fusion mutation; wherein the mutant TMPRSS2:ERG peptide binds to a protein encoded by an HLA-A02:01 allele.

[0073] Provided herein is a method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising identifying the subject as one that expresses a protein encoded by an HLA-A02:01 allele, wherein the therapeutic comprises a T cell receptor (TCR) specific for a mutant BTK peptide in complex with an HLA protein; wherein the mutant BTK peptide comprises at least one mutant amino acid; wherein the mutant BTK peptide binds to a protein encoded by an HLA-A02:01 allele.

[0074] Provided herein is a method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising identifying the subject as one that expresses a protein encoded by an HLA-A02:01 allele, wherein the therapeutic a T cell receptor (TCR) specific for a mutant BTK peptide in complex with an HLA protein; wherein the mutant BTK peptide comprises a resistance mutation or a point mutation; wherein the mutant BTK peptide binds to a protein encoded by an HLA-A02:01 allele.

[0075] Provided herein is a method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising identifying the subject as one that expresses a protein encoded by an HLA-A02:01 allele, wherein the therapeutic a T cell receptor (TCR) specific for a mutant BTK peptide in complex with an HLA protein; wherein the mutant BTK peptide comprises a C481S mutation; wherein the mutant BTK peptide binds to a protein encoded by an HLA-A02:01 allele.

[0076] Provided herein is a method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising identifying the subject as one that expresses a protein encoded by an HLA-A02:01 allele, wherein the therapeutic comprises a T cell receptor (TCR) specific for a mutant EGFR peptide in complex with an HLA protein; wherein the mutant EGFR peptide comprises at least one mutant amino acid T790M; wherein the mutant EGFR peptide binds to a protein encoded by an HLA-A02:01 allele.

[0077] In some embodiments, the cancer is selected from the group consisting of breast cancer, lung cancer, non-small cell lung cancer, pancreatic cancer, colorectal cancer, uterine cancer, melanoma, ovarian cancer, prostate cancer, endometrial cancer, chronic lymphocytic leukemia (CLL) and liver cancer. In some embodiments, the subject has a breast cancer that is resistant to anti-estrogen therapy, is an MSI breast cancer,

is a metastatic breast cancer, is a Her2 negative breast cancer, is a Her2 positive breast cancer, is an ER negative breast cancer, is an ER positive breast cancer is a recurrent breast cancer, is a metastatic breast cancer, or any combination thereof. In some embodiments, the breast cancer expresses an estrogen receptor with a mutation.

[0078] In some embodiments, the subject has a breast cancer that is resistant to anti-estrogen therapy. In some embodiments, the breast cancer expresses an estrogen receptor with a mutation. In some embodiments, the subject has a CLL that is resistant to ibrutinib therapy. In some embodiments, the CLL expresses a Bruton tyrosine kinase (BTK) with a mutation, such as a C481S mutation. In some embodiments, the subject has a lung cancer that is resistant to a tyrosine kinase inhibitor. In some embodiments, the lung cancer expresses an epidermal growth factor receptor (EGFR) with a mutation, such as a T790M, L792F, or C797S mutation.

[0079] In some embodiments, an immune response is elicited in the subject. In some embodiments, the immune response is a humoral response. In some embodiments, the immune response is a cytotoxic T cell response.

[0080] In some embodiments, the method further comprises administering at least one additional therapeutic agent or modality. In some embodiments, the at least one additional therapeutic agent or modality is surgery, a checkpoint inhibitor, an antibody or fragment thereof, a chemotherapeutic agent, radiation, a vaccine, a small molecule, a T cell, a vector, and APC, a polynucleotide, an oncolytic virus or any combination thereof. In some embodiments, the at least one additional therapeutic agent is an anti-PD-1 agent and anti-PD-L1 agent, an anti-CTLA-4 agent, or an anti-CD40 agent. In some embodiments, the additional therapeutic agent is administered before, simultaneously, or after administering a pharmaceutical composition described herein.

[0081] In some embodiments, administering comprises administering subcutaneously or intravenously.

[0082] In some embodiments, the subject is a subject that has had disease progression following endocrine therapy in combination with a CDK 4/6 inhibitor.

[0083] Provided herein is a method comprising: identifying neoantigen-specific T cells from a sample comprising a population of T cells; identifying one or more peptides of a peptide-MHC complex that are presented by an antigen presenting cell (APC); identifying a variable sequence of a T cell receptor (TCR) from the neoantigen-specific T cells; expressing a recombinant TCR comprising the variable sequence of the TCR identified in a TCR cell; and performing a functional assay, wherein the functional assay comprises contacting the TCR cell to a peptide-MHC complex comprising a peptide of the one or more peptides identified.

[0084] In some embodiments, the method comprises obtaining the sample comprising the population of cells comprising the neoantigen-specific T cells. In some embodiments, obtaining the sample comprises obtaining a T cell sample from a healthy subject or from a subject with cancer. In some embodiments, the T cell sample is from a healthy donor. In some embodiments, the T cell sample is a peripheral blood mononuclear cell (PBMC) sample.

[0085] In some embodiments, in identifying neoantigen-specific T cells comprises contacting the population of T cells to at least one peptide-MHC multimer complex comprising a neoantigen peptide. In some embodiments, identifying neoantigen-specific T cells comprises contacting the population of T cells to a peptide-MHC complex comprising a neoantigen peptide. In some embodiments, identifying neoantigen-specific

T cells comprises contacting the population of T cells to an APC comprising the peptide-MHC complex. In some embodiments, identifying neoantigen-specific T cells further comprises isolating T cells of the T cell population specific to the peptide-MHC complex. In some embodiments, identifying neoantigen-specific T cells further comprises identifying or predicting T cells of the of the T cell population specific to the peptide-MHC complex based on TCR clonality. In some embodiments, identifying a variable sequence of a TCR from the neoantigen-specific T cells is performed before identifying neoantigen-specific T cells. In some embodiments, identifying a variable sequence of a TCR from the neoantigen-specific T cells comprises sequencing DNA, RNA, or amplified products thereof from one or more neoantigen-specific T cells that encode the variable sequence. In some embodiments, identifying a variable sequence of a TCR from the neoantigen-specific T cells comprises sequencing DNA, RNA, or amplified products thereof from a single neoantigen-specific T cell that encodes the variable sequence. In some embodiments, identifying a variable sequence of a TCR from the neoantigen-specific T cells comprises sequencing barcoded DNA or barcoded RNA, or amplified products thereof, from one or more neoantigen-specific T cells that encode the variable sequence. In some embodiments, identifying a variable sequence of a TCR from the neoantigen-specific T cells comprises pairing a TCR-alpha chain with a TCR-beta chain.

[0086] In some embodiments, expressing a recombinant TCR comprises expressing the variable sequence identified from a polynucleotide comprising a sequence encoding the variable sequence identified. In some embodiments, the polynucleotide is a vector. In some embodiments, the vector is a viral vector. In some embodiments, the viral vector is a lentiviral vector. In some embodiments, expressing a recombinant TCR comprises transducing or transfecting the polynucleotide into cells. In some embodiments, the cells are a T cell line or healthy donor PMBCs.

[0087] In some embodiments, identifying one or more peptides of a peptide-MHC complex that are presented by an APC comprises expressing the one or more peptides in cells. In some embodiments, identifying one or more peptides of a peptide-MHC complex that are presented by an APC comprises loading the one or more peptides onto MHCs of cells. In some embodiments, identifying one or more peptides of a peptide-MHC complex that are presented by an APC comprises eluting or isolating a peptide of the one or more peptides from a peptide MHC complex. In some embodiments, identifying one or more peptides of a peptide-MHC complex that are presented by an APC comprises performing mass spectrometry on a peptide of the one or more peptides that was isolated or eluted from a peptide-MHC complex. In some embodiments, performing a functional assay comprises determining expression of one or more cell markers. In some embodiments, the one or more cell markers comprise TNF- α , IFN- γ , LAMP-1, 4-1BB, IL-2, IL-17A, Granzyme B, PD-1, CD25, CD69, TIM3, LAG3, CTLA-4, CD62L, CD45RA, CD45RO, FoxP3, or any combination thereof.

INCORPORATION BY REFERENCE

[0088] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0089] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0090] **FIG. 1** depicts a workflow for antigen-specific TCR identification and analysis. PBMCs from healthy donors can be stimulated with the antigen of interest, after which antigen-specific T cells can be identified with peptide-MHC multimers (left). Antigen-specific T cells can be isolated and the TCR can be sequenced and analyzed (middle left). The TCR can be synthesized and expressed in a cell line or PBMCs, and the specificity can be again confirmed by peptide-MHC multimer (middle right). The TCR-expressing cell line or PBMCs can then be co-cultured with antigen-expressing cell lines to confirm the functionality of the TCR (right).

[0091] **FIG. 2** an example schematic of an antigen-specific CD8⁺ T cell expansion. PBMCs can be stimulated with the antigen of interest and cytokines. After expansion antigen-specific CD8⁺ T cells can be identified with peptide-MHC multimers.

[0092] **FIG. 3A** is an example schematic of recombinant TCR constructs and vector design for expression of the TCR constructs in cells.

[0093] **FIG. 3B** is an example schematic of a viral vector encoding recombinant TCRs for transduction or transfection into cells.

[0094] **FIG. 4A** depicts an example flow cytometry analysis of RAS antigen specific CD8⁺ T cell expansion in response to stimulation with a RAS peptide.

[0095] **FIG. 4B** depicts an example flow cytometry analysis of RAS antigen specific Jurkat cells after sorting of top 10% of multimer positive cells expressing a recombinant TCR after puromycin selection.

[0096] **FIG. 5** depicts an example flow cytometry analysis of RAS-peptide-HLA-A11:01 complex specific CD8⁺ T cell expansion in response to stimulation with RAS G12V peptide (left), RAS-peptide-HLA-A11:01 complex specific CD8⁺ T cell expansion in response to stimulation with RAS G12C peptide (middle), and RAS-peptide-HLA-A11:01 complex specific CD8⁺ T cell expansion in response to stimulation with RAS G12D peptide (right).

[0097] **FIG. 6A** depicts example flow cytometry analyses of RAS-peptide-HLA-A11:01 complex specific CD8⁺ T cell expansion in response to stimulation with a G12V or G12C mutant RAS peptides (left), TCR clone abundance analysis after sequencing the TCR from pooled hits (middle), and confirmation of mutant versus wild-type specificity of the top 2 retrieved clones after recombinant TCR expression in Jurkat cells (right).

[0098] FIG. 6B depicts experimental results of TCR functional assays to assess the specificity (left) and avidity (right) of three RAS TCRs (RAS TCR-3, RAS TCR-4, RAS TCR-11). Graphs showing IL-2 production after co-culturing RAS TCR-transduced Jurkat cells with A375 cells expressing HLA-A11:01 loaded with either RAS wild-type or RAS-mutant peptide (left) or increasing amounts of RAS-mutant peptide (right).

[0099] FIG. 7A depicts experimental results of a TCR functional avidity assay (peptide titration). A graph showing IL-2 production after co-culturing RAS TCR-transduced Jurkat cells with A375 cells expressing HLA-A11:01 loaded with increasing amounts of RAS-wild type or RAS-mutant peptide.

[0100] FIG. 7B depicts an example graph showing IL-2 production after co-culturing RAS TCR-4-transduced Jurkat cells with A375 cells modified to express HLA-A11:01 only, modified to express HLA-A11:01 and the KRAS G12V mutation, or modified to express HLA-A11:01 and an irrelevant mutation.

[0101] FIG. 8A depicts an example graph showing IFN γ secretion from RAS TCR-4-transduced PBMCs after co-culture with the naturally RAS G12V mutant SW620 colon cancer cell line without manipulation, with expression of HLA-A11:01 plus RAS G12V peptide added, and with expression of HLA-A11:01 only.

[0102] FIG. 8B depicts an example graph showing Caspase-3 activation after co-culture with RAS TCR-transduced PBMCs in the naturally RAS G12V mutant SW620 colon cancer cell line without manipulation, with expression of HLA-A11:01 plus RAS G12V peptide added, and with expression of HLA-A11:01 only.

[0103] FIG. 8C depicts experimental results of a cytotoxicity assay in which PBMCs transduced with an irrelevant TCR (left) or RAS TCR-4 (right) are co-cultured with SW620 target tumor cells expressing HLA-A11:01 and GFP over an increasing range of PBMC to target ratios. Graphs depicting the growth of the target cells over 72 hours as measured by GFP signal (top) and the death of the target cells as measured by Annexin V signaling (bottom) show that the RAS TCR-transduced PBMCs kill the target cells effectively.

[0104] FIG. 8D depicts experimental results of a cytotoxicity assay in which PBMCs transduced with an irrelevant TCR (left) or RAS TCR-4 (right) are co-cultured with SNG-M target tumor cells over an increasing range of PBMC to target ratios. Graphs depicting the death of the target cells as measured by Annexin V signaling over 72 hours show that the RAS TCR-transduced PBMCs kill the target cells.

[0105] FIG. 8E depicts experimental results of a safety screen of RAS TCR-4. Depicted on the left is a graph showing IL-2 production after co-culturing RAS TCR-transduced Jurkat cells with A375 cells expressing HLA-A11:01 loaded with the cognate RAS G12V epitope or peptides in which one position of the cognate epitope is changed to an alanine. Depicted in the center is a graph showing IL-2 production after co-culturing RAS TCR-transduced Jurkat cells with A375 cells expressing HLA-A11:01 loaded with the RAS G12V epitope or peptides identified from the initial safety screen. Depicted on the right is a graph showing IL-2 production after co-culturing RAS TCR-transduced Jurkat cells with A375 cells expressing HLA-A11:01 transduced with Perilipin4 and loaded with RAS G12V peptide or Perilipin4 peptide or no peptide (right).

[0106] FIG. 8F depicts the workflow used to identify RAS TCR-26 and RAS TCR-27. Depicted on the top left is a flow cytometry analysis of RAS-peptide-HLA-A11:01 complex specific CD8⁺ T cell expansion in response to stimulation with RAS G12V peptide. Depicted on the top right is the measurement of the cell growth

of target A375 cells expressing HLA-A11:01 and GFP over 54 hours after co-culture with the expanded CD8⁺ T cells. In this experiment, T cells expanded in the presence of the peptides were incubated with the A375 cells that were loaded with indicated amounts of peptides. Depicted on the bottom left is the specific cytotoxicity calculated at 48 hours comparing target cells loaded with increasing amounts or mutant-RAS peptide normalized to a control with wild-type peptide. Depicted on the bottom right are the relative abundances of TCR alpha and TCR beta CDR3 regions after single-cell TCR sequencing the multimer-positive cells.

[00107] **FIG. 8G** depicts the workflow used to identify RAS TCR-28. Depicted on the top left is a flow cytometry analysis of RAS-peptide-HLA-A11:01 complex specific CD8⁺ T cell expansion in response to stimulation with RAS G12V peptide. Depicted on the top right is the measurement of the cell growth of target A375 cells expressing HLA-A11:01 and GFP and loaded with varying doses of the peptide, over 54 hours after co-culture with the expanded CD8⁺ T cells. The data show good inverse correlation of cell growth with peptide dose, which demonstrates the TCR specificity to the peptide. Depicted on the bottom left is the specific cytotoxicity calculated at 48 hours comparing target cells loaded with increasing amounts or mutant-RAS peptide normalized to a control with wild-type peptide. Depicted on the bottom right are the relative abundances of TCR alpha and TCR beta CDR3 regions after single-cell TCR sequencing the multimer-positive cells.

[00108] **FIG. 9** depicts an example flow cytometry analysis of RAS-peptide-HLA-A03:01 complex specific CD8⁺ T cell expansion in response to stimulation with RAS G12V peptide (left) and RAS-peptide-HLA-A03:01 complex specific CD8⁺ T cell expansion in response to stimulation with RAS G12C peptide (right).

[00109] **FIG. 10A** depicts a workflow for antigen-specific TCR identification and analysis of a sample depicted in **FIG. 9**.

[00110] **FIG. 10B** depicts a workflow for antigen-specific TCR identification of a sample depicted in **FIG. 9**.

[00111] **FIG. 10C** depicts experimental results of TCR functional avidity assays (peptide titration). Depicted on the left is a graph showing IL-2 production after co-culturing RAS TCR-5-transduced Jurkat cells with A375 cells expressing HLA-A03:01 loaded with increasing amounts of RAS-wild type or RAS-mutant peptide. Depicted on the right is a graph showing IL-2 production after co-culturing RAS TCR-6-transduced Jurkat cells with A375 cells expressing HLA-A03:01 loaded with increasing amounts of RAS-wild type or RAS-mutant peptide.

[00112] **FIG. 10D** depicts experimental results of a cytotoxicity assay in which PBMCs transduced with an irrelevant TCR (left), RAS TCR-5 (middle), or RAS TCR-6 (right) are co-cultured with A375 target tumor cells expressing HLA-A03:01 and GFP over an increasing range of PBMC to target ratios. Graphs of the growth of the target cells over 72 hours as measured by GFP signal show that the RAS TCR-transduced PBMCs kill the target cells effectively.

[00113] **FIG. 10E** depicts depicts experimental results of a cytotoxicity assay in which PBMCs transduced with an irrelevant TCR, RAS TCR-5, or RAS TCR-6 are co-cultured with NCI-H441 target tumor cells. Increased Annexin V signal in target cells over 48 hours shows that the RAS TCRs are able to recognize and kill this target tumor cell.

[00114] FIG. 10F depicts experimental results of a safety screen of RAS TCR-5 (top) and RAS TCR-6 (bottom). Graphs showing IL-2 production after co-culturing RAS TCR-transduced Jurkat cells with A375 cells expressing HLA-A11:01 loaded with the cognate RAS G12V epitope or peptides in which one position of the cognate epitope is changed to an alanine.

[00115] FIG. 11 depicts an example workflow for GATA3 antigen-specific TCR identification and analysis. Depicted on the left is an example flow cytometry analysis of GATA3-peptide-HLA-A02:01 complex specific CD8⁺ T cell expansion in response to stimulation with a GATA3 mutant peptide.

[00116] FIG. 12A depicts results of a TCR functional avidity assay (peptide titration). A graph showing IL-2 production after co-culturing GATA3 TCR-1-transduced T cells with cells loaded or transduced with increasing amounts of GATA3 mutant peptide.

[00117] FIG. 12B depicts a graph showing IL-2 production after co-culturing GATA3 TCR-transduced Jurkat cells with cells loaded with an irrelevant peptide or the mutant GATA3 peptide, and cells transduced with an irrelevant vector or a vector encoding the GATA3 neoORF mutation.

[00118] FIG. 12C depicts a graph showing upregulation of IFN γ production in 2 cell samples expressing control peptide or a GATA3 mutant peptide.

[00119] FIG. 12D depicts a graph showing percent CD8 and CD107a positive cells in 2 cell samples expressing control peptide or a GATA3 mutant peptide.

[00120] FIG. 12E depicts a graph showing percent live caspase 3 positive cells in 2 cell samples expressing control peptide or a GATA3 mutant peptide.

[00121] FIG. 13 depicts an example workflow for TMPRSS2:ERG antigen-specific TCR identification and analysis. Depicted on the left is an example flow cytometry analysis of TMPRSS2:ERG-peptide-HLA-A02:01 complex specific CD8⁺ T cell expansion in response to stimulation with a TMPRSS2:ERG mutant peptide.

[00122] FIG. 14 depicts an example graph showing IL-2 production after co-culturing TMPRSS2:ERG TCR-1-transduced Jurkat cells with 293T cells either unmanipulated, loaded with irrelevant peptide, or loaded with the TMPRSS2:ERG peptide.

[00123] FIG. 15 depicts an example workflow for BTK antigen-specific TCR identification and analysis. Depicted on the left is an example flow cytometry analysis of BTK-peptide-HLA-A02:01 complex specific CD8⁺ T cell expansion in response to stimulation with a BTK mutant peptide.

[00124] FIG. 16A depicts an example flow cytometry analysis of EGFR-peptide-HLA-A02:01 complex specific CD8⁺ T cell expansion in response to stimulation with EGFR T790M peptide. Each plot on FIG. 16A represents a representative T cell expansion sample (well) with the EGFR T790M peptide. The TCRs from the cells were sequenced.

[00125] FIG. 16B depicts an example flow cytometry analysis of potential EGFR-peptide-HLA-A02:01 complex specific CD8⁺ T cell populations in response to stimulation with EGFR T790M peptide, the TCRs of which remain to be sequenced. Each plot on FIG. 16B represents a representative T cell expansion sample (well) in response to the EGFR T790M peptide.

DETAILED DESCRIPTION

[00126] The term “about” or “approximately” means within an acceptable error range for the particular value as determined by one of ordinary skill in the art, which will depend in part on how the value is measured or determined, i.e., the limitations of the measurement system. For example, “about” can mean within 1 or more than 1 standard deviation, per the practice in the art. Alternatively, “about” can mean a range of up to 20%, up to 10%, up to 5%, or up to 1% of a given value. Alternatively, particularly with respect to biological systems or processes, the term can mean within an order of magnitude, preferably within 5-fold, and more preferably within 2-fold, of a value. Where particular values are described in the application and claims, unless otherwise stated the term “about” meaning within an acceptable error range for the particular value should be assumed.

[00127] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Although any methods and materials similar or equivalent to those described herein can also be used in the practice or testing of the present disclosure, the preferred methods and materials are now described. The details of one or more particular embodiments are set forth in the description below.

I. Definitions

[00128] Unless otherwise stated, the term “TCR” should be understood to encompass full TCRs as well as antigen-binding portions or antigen-binding fragments (also called MHC-peptide binding fragments) thereof. In some embodiments, the TCR is an intact or full-length TCR. In some embodiments, the TCR is an antigen-binding portion that is less than a full-length TCR but that binds to a specific antigenic peptide bound to (i.e., in the context of) an MHC molecule, i.e., an MHC-peptide complex. In some cases, an antigen-binding portion or fragment of a TCR can contain only a portion of the structural domains of a full-length or intact TCR, but yet is able to bind the epitope (e.g., MHC-peptide complex) to which the full TCR binds. In some cases, an antigen-binding portion or fragment of a TCR contains the variable domains of a TCR, such as variable α chain and variable β chain of a TCR, sufficient to form a binding site for binding to a specific MHC-peptide complex, such as generally where each chain contains three complementarity determining regions. Polypeptides or proteins having a binding domain which is an antigen-binding domain or is homologous to an antigen-binding domain are included. Complementarity determining region (CDR) grafted TCRs and other humanized TCRs (including CDR modifications and framework region modifications) are also contemplated by these terms. It should be noted that while reference may be made only to immunoglobulin chains (e.g., heavy chains and light chains), the disclosed invention can be applied to multiple other different types of paired sequences, e.g., T cell receptor chain pairs (TCR α and TCR β chains and TCR γ and TCR δ chains), and is not limited to immunoglobulins.

[00129] The terms “complementarity determining region,” and “CDR,” synonymous with “hypervariable region” or “HVR,” are known in the art to refer to non-contiguous sequences of amino acids within TCR variable regions, which confer specificity and/or binding affinity to an MHC-peptide complex. In general, there are three CDRs in each alpha chain variable region (CDR-H1, CDR-H2, CDR-H3) and three CDRs in each beta chain

variable region (CDR-L1, CDR-L2, CDR-L3). “Framework regions” and “FR” are known in the art to refer to the non-CDR portions of the variable regions of the alpha and beta chains. In general, there are four FRs in each full-length alpha chain variable region (FR-H1, FR-H2, FR-H3, and FR-H4), and four FRs in each full-length beta chain variable region (FR-L1, FR-L2, FR-L3, and FR-L4).

[00130] The term “variable region” or “variable domain” refers to the domain of a TCR alpha, beta, gamma or delta chain, that is involved in binding the TCR to antigen-MHC complexes. The variable domains of the alpha chain and beta chain ($V\alpha$ and $V\beta$, respectively), and the gamma chain and delta chain ($V\gamma$ and $V\delta$, respectively) of a native TCR generally have similar structures, with each domain comprising four conserved framework regions (FRs) and three CDRs. A single $V\alpha$ or $V\beta$ domain, or $V\gamma$ or $V\delta$ domain, may be sufficient to confer binding specificity to a peptide-MHC complex.

[00131] Also provided herein are TCR fragments, including antigen-binding fragments. In some embodiments, the TCR is an antigen-binding portion thereof, such as a variant of a full-length TCR not containing the transmembrane and/or cytoplasmic region(s) thereof, which may be referred to as a full soluble TCR. In some embodiments, the TCR is a dimeric TCR (dTTCR). In some embodiments, the TCR is a single-chain TCR (scTCR), such as a scTCR having a structure as described in PCT patent publication numbers WO2003/020763, WO2004/033685, or WO2011/044186. In certain embodiments, the TCR is a single-chain TCR fragment comprising an alpha chain variable region linked to a beta chain variable region, such as a scTv. In some embodiments, a scTv is also referred to as a scFv. A single-chain Tv or scTv refers in some aspects to TCR fragments that comprise the variable alpha or gamma chain ($V\alpha$ or $V\gamma$) and variable beta or delta chain ($V\beta$ or $V\delta$) domains of a TCR, wherein these domains are present in a single polypeptide chain. Generally, the Tv polypeptide further comprises a polypeptide linker between the $V\alpha$ and $V\beta$ domains or $V\gamma$ and $V\delta$ domains which enables the scTv to form the desired structure for antigen binding. A diabody refers in some aspects to TCR fragments with two antigen-binding sites, which fragments comprise a $V\alpha$ connected to a $V\beta$ in the same polypeptide chain ($V\alpha$ - $V\beta$) or a $V\gamma$ connected to a $V\delta$ in the same polypeptide chain ($V\gamma$ - $V\delta$). By using a linker that is too short to allow pairing between the two domains on the same chain, the domains are forced to pair with the complementary domains of another chain and create two antigen-binding sites. Exemplary diabodies are described more fully in, for example, EP404097 and WO93111161. Fv refers in some aspects to a TCR fragment which contains a complete peptide-MHC complex recognition and peptide-MHC complex binding site. This region consists of a dimer of one TCR α chain and one TCR β chain or one TCR γ chain and one TCR δ chain in tight, non-covalent association. It is in this configuration that the three CDRs of each variable domain interact to define a peptide-MHC complex binding site on the surface of the $V\alpha$ - $V\beta$ dimer or $V\gamma$ - $V\delta$ dimer. Collectively, a combination of one or more of the CDRs from each of the $V\alpha$ - $V\beta$ chains or $V\gamma$ - $V\delta$ chains confers peptide-MHC complex binding specificity to the TCR. For example, it would be understood that, for example, the CDR α 3 and CDR β 3 or CDR γ 3 and CDR δ 3 could be sufficient to confer antigen-binding specificity to a TCR when transferred to $V\alpha$ and $V\beta$ chains or $V\gamma$ - $V\delta$ chains of a recipient selected TCR or antigen-binding fragment thereof and this combination of CDRs can be tested for binding, affinity, etc. Furthermore, although

the two domains of a Tv fragment ($V\alpha$ and $V\beta$ or $V\gamma$ and $V\delta$), are coded for by separate genes, they can be joined using recombinant methods by a synthetic linker that enables them to be made as a single protein chain in which the $V\alpha$ and $V\beta$ or $V\gamma$ and $V\delta$ chain regions pair to form monovalent molecules (known as single chain Tv (scTv)). Such scTvs are also intended to be encompassed within the peptide-MHC complex binding portion of a TCR.

[00132] A “bispecific TCR” refers in some aspects to a TCR that shows specificities to two different peptide-MHC complexes or two different types of peptide-MHC complexes. The terms as used herein specifically include, without limitation, TCRs which show binding specificity for a target peptide-MHC complex and to another peptide-MHC complex that facilitates delivery to a particular tissue. Similarly, multi-specific TCRs have two or more binding specificities. A linear TCR refers in some aspects to a pair of tandem Fd segments (*e.g.*, $V\alpha$ - $C\alpha_1$ - $V\alpha$ - $C\alpha_1$) which form a pair of antigen binding regions. Linear TCRs can be bispecific or monospecific.

[00133] An “antigen-binding domain” refers in some aspects to one or more fragments of a TCR that retain the ability to specifically bind to a peptide-MHC complex. Non-limiting examples of TCR fragments included within such terms include, but are not limited to, (i) a Tab fragment, a monovalent fragment consisting of the $V\beta$, $V\alpha$, $C\beta$ and $C\alpha$ domains; (ii) a $T(ab')_2$ fragment, a bivalent fragment containing two Tab fragments linked by a disulfide bridge at the hinge region; (iii) a Td fragment consisting of the $V\alpha$ and $C\alpha_1$ domains; (iv) a Tv fragment containing the $V\beta$ and $V\alpha$ domains of a single arm of a TCR, including scTvs, (v) a dAb fragment (Ward et al., (1989) Nature 341:544 546), which contains a $V\alpha$ domain; and (vi) an isolated CDR. Included in this definition are TCRs with a single alpha chain or a single beta chain.

[00134] Among the provided TCRs are humanized and human TCRs. A “humanized” TCR is a TCR in which all or substantially all CDR amino acid residues are derived from non-human CDRs and all or substantially all FR amino acid residues are derived from human FRs. A humanized TCR optionally may include at least a portion of a TCR constant region derived from a human TCR. A “humanized form” of a non-human TCR, refers to a variant of the non-human TCR that has undergone humanization, typically to reduce immunogenicity to humans, while retaining the specificity and affinity of the parental non-human TCR. In some embodiments, some FR residues in a humanized TCR are substituted with corresponding residues from a non-human TCR (*e.g.*, the TCR from which the CDR residues are derived), *e.g.*, to restore or improve TCR specificity or affinity. A “human TCR” is a TCR with an amino acid sequence corresponding to that of a TCR produced by a human or a human cell, or non-human source that utilizes human TCR repertoires or other human TCR-encoding sequences, including human TCR libraries. The term excludes humanized forms of non-human TCRs comprising non-human peptide-MHC complex binding regions, such as those in which all or substantially all CDRs are non-human. Human TCRs may be prepared by administering an immunogen to a transgenic animal that has been modified to produce intact human TCRs or intact TCRs with human variable regions in response to antigenic challenge. Such animals typically contain all or a portion of the human TCR loci, which replace the endogenous TCR loci, or which are present extrachromosomally or integrated randomly into the animal's

chromosomes. In such transgenic animals, the endogenous TCR loci have generally been inactivated. Human TCRs also may be derived from human TCR libraries, including phage display and cell-free libraries, containing TCR-encoding sequences derived from a human repertoire.

[00135] The term “cancer neoantigen” or “neoantigen” or “neoepitope” can refer to antigens that are not encoded in a normal, non-mutated host genome. A neoantigen can relate to an antigen including one or more amino acid modifications compared to the parental antigen. For example, a neoantigen may be a tumor-associated neoantigen, wherein the term “tumor-associated neoantigen” can include a peptide or protein including amino acid modifications due to tumor-specific mutations. In some instances, a neoantigen represents either oncogenic viral proteins or abnormal proteins that arise as a consequence of somatic mutations. For example, a neoantigen can arise by the disruption of cellular mechanisms through the activity of viral proteins. Another example can be an exposure of a carcinogenic compound, which in some cases can lead to a somatic mutation. This somatic mutation can ultimately lead to the formation of a tumor/cancer. A neoantigen can be a class of tumor antigens which arise from tumor-specific changes in proteins. Neoantigens encompass, but are not limited to, tumor antigens which arise from, for example, a substitution in a protein sequence, a frame shift mutation, a fusion polypeptide, an in-frame deletion, an insertion, and expression of an endogenous retroviral polypeptide. A neoepitope can be an epitope that is not present in a reference, such as a non-diseased cell, e.g., a non-cancerous cell or a germline cell, but is found in a diseased cell, e.g., a cancer cell. This includes situations where a corresponding epitope is found in a normal non-diseased cell or a germline cell but, due to one or more mutations in a diseased cell, e.g., a cancer cell, the sequence of the epitope is changed so as to result in the neoepitope.

[00136] An “epitope” refers in some aspects to a portion of an antigen or other macromolecule capable of forming a binding interaction with the variable region binding pocket of a TCR. In some aspects, an epitope refers to a portion of a peptide-MHC complex capable of forming a binding interaction with the variable region binding pocket of a TCR. Such binding interactions can be manifested as an intermolecular contact with one or more amino acid residues of one or more CDRs. Peptide-MHC complex binding can involve, for example, a CDR3, a CDR3 pair, or in some instances, interactions of up to all six CDRs of the V α and V β chains or V γ or V δ chains. An epitope can be a linear peptide sequence (i.e., “continuous”) or can be composed of noncontiguous amino acid sequences (i.e., “conformational” or “discontinuous”). A TCR can recognize one or more amino acid sequences. Therefore an epitope can define more than one distinct amino acid sequence. In some aspects, a TCR can recognize one or more amino acid sequences or epitopes in the context of an MHC. Epitopes recognized by TCRs can be determined by peptide mapping and sequence analysis techniques well known to one of skill in the art. Binding interactions are manifested as intermolecular contacts with one or more amino acid residues of a CDR. An epitope can refer to an antigenic determinant in a molecule such as an antigen, i.e., to a part in or fragment of the molecule that is recognized by the immune system, for example, that is recognized by a T cell, in particular when presented in the context of MHC molecules. An epitope of a protein such as a tumor antigen can comprise a continuous or discontinuous portion of the protein and can be between

5 and 100, 5 and 50, 8 and 30, or 10 and 25 amino acids in length, for example, the epitope may be 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25 amino acids in length.

[00137] The term “binding” refers to a direct association between two molecules, due to, for example, covalent, electrostatic, hydrophobic, and ionic and/or hydrogen-bond interactions under physiological conditions, and includes interactions such as salt bridges and water bridges, as well as any other conventional means of binding.

[00138] In some embodiments, reference to a TCR with “specific binding” refers to a situation in which a TCR will not show any significant binding to molecules other than the peptide-MHC complex containing the epitope recognized by the TCR. The term is also applicable where for example, an antigen binding domain is specific for a particular epitope which is carried by a number of peptide-MHC complexes, in which case the selected TCR or peptide-MHC complex binding fragment thereof carrying the peptide-MHC complex binding domain will be able to bind to the various peptide-MHC complexes carrying the epitope. The terms “preferentially binds” or “specifically binds” mean that the TCRs or fragments thereof bind to an epitope with greater affinity than it binds unrelated amino acid sequences, and, if cross-reactive to other polypeptides containing the epitope, are not toxic at the levels at which they are formulated for administration to human use. In one aspect, such affinity is at least 1-fold greater, at least 2-fold greater, at least 3-fold greater, at least 4-fold greater, at least 5-fold greater, at least 6-fold greater, at least 7-fold greater, at least 8-fold greater, at least 9-fold greater, 10-fold greater, at least 20-fold greater, at least 30-fold greater, at least 40-fold greater, at least 50-fold greater, at least 60-fold greater, at least 70-fold greater, at least 80-fold greater, at least 90-fold greater, at least 100-fold greater, or at least 1000-fold greater than the affinity of the TCR or fragment thereof for unrelated amino acid sequences.

[00139] The term “affinity” refers to a measure of the strength of binding between two members of a binding pair (e.g., a human leukocyte antigen (HLA)-binding peptide and a class I or II HLA, or a peptide-HLA complex and a T cell receptor (TCR)). Affinity can be expressed as an equilibrium constant of the reversible binding of two agents and can be expressed as K_D , K_A , K_{off} or K_{on} . K_D refers to the dissociation constant between two members of a binding pair and has units of molarity. K_A refers to the affinity constant between two members of a binding pair is the inverse of the dissociation constant. Affinity may be determined experimentally, for example by surface plasmon resonance (SPR) using commercially available Biacore SPR units. K_{off} refers to the off-rate constant of two members of a binding pair, (e.g., the off-rate constant of an HLA-binding peptide and a class I or II HLA, or a peptide-HLA complex and a TCR). K_{on} refers to the on-rate constant of two members of a binding pair, (e.g., the on-rate constant of an HLA-binding peptide and a class I or II HLA, or a peptide-HLA complex and a TCR). Affinity of a binding protein to a ligand such as affinity of a TCR for an epitope can be, for example, from about 100 nanomolar (nM) to about 0.1 nM, from about 100 nM to about 1 picomolar (pM), or from about 100 nM to about 1 femtomolar (fM). The term “avidity” refers to the resistance of a complex of two or more agents to dissociation after dilution.

[00140] Throughout this disclosure, “binding data” results may be expressed in terms of an “ IC_{50} .” Affinity may also be expressed as the inhibitory concentration 50 (IC_{50}), or the concentration at which 50% of a first member of a binding pair (e.g., a peptide) is displaced. Likewise, $\ln(IC_{50})$ refers to the natural log of the IC_{50} .

For example, an IC_{50} may be the concentration of a tested peptide in a binding assay at which 50% inhibition of binding of a labeled reference peptide is observed. Given the conditions in which the assays are run (e.g., limiting HLA protein concentrations and/or labeled reference peptide concentrations), these values can approximate K_D values. Assays for determining binding are well known in the art and are described in detail, for example, in PCT publications WO 94/20127 and WO 94/03205, and other publications such as Sidney et al., *Current Protocols in Immunology* 18.3.1 (1998); Sidney, et al., *J. Immunol.* 154:247 (1995); and Sette, et al., *Mol. Immunol.* 31:813 (1994). Alternatively, binding can be expressed relative to binding by a reference standard peptide. Binding can also be determined using other assay systems including those using: live cells (e.g., Ceppellini et al., *Nature* 339:392 (1989); Christnick et al., *Nature* 352:67 (1991); Busch et al., *Int. Immunol.* 2:443 (1990); Hill et al., *J. Immunol.* 147:189 (1991); del Guercio et al., *J. Immunol.* 154:685 (1995)), cell free systems using detergent lysates (e.g., Cerundolo et al., *J. Immunol.* 21:2069 (1991)), immobilized purified MHC (e.g., Hill et al., *J. Immunol.* 152, 2890 (1994); Marshall et al., *J. Immunol.* 152:4946 (1994)), ELISA systems (e.g., Reay et al., *EMBO J.* 11:2829 (1992)), surface plasmon resonance (e.g., Khilko et al., *J. Biol. Chem.* 268:15425 (1993)), high flux soluble phase assays (Hammer et al., *J. Exp. Med.* 180:2353 (1994)), and measurement of class I MHC stabilization or assembly (e.g., Ljunggren et al., *Nature* 346:476 (1990); Schumacher et al., *Cell* 62:563 (1990); Townsend et al., *Cell* 62:285 (1990); Parker et al., *J. Immunol.* 149:1896 (1992)).

[00141] The terms “major histocompatibility complex” and the abbreviation “MHC” can include MHC class I and MHC class II molecules and relate to a complex of genes which occurs in all vertebrates. MHC proteins or molecules can be important for signaling between lymphocytes and antigen presenting cells or diseased cells in immune reactions, wherein the MHC proteins or molecules bind peptides and present them for recognition by T cell receptors. The proteins encoded by the MHC can be expressed on the surface of cells, and display both self-antigens (peptide fragments from the cell itself) and non-self-antigens (e.g., fragments of invading microorganisms) to a T cell. The MHC region can be divided into three subgroups, class I, class II, and class III. MHC class I proteins can contain an α -chain and β 2-microglobulin (not part of the MHC encoded by chromosome 15). They can present antigen fragments to cytotoxic T cells. MHC class II proteins can contain α - and β -chains and they can present antigen fragments to T-helper cells. MHC class III region can encode for other immune components, such as complement components and cytokines. The MHC can be both polygenic (there are several MHC class I and MHC class II genes) and polymorphic (there are multiple alleles of each gene).

[00142] The term “haplotype” can refer to the human leukocyte antigen (HLA) alleles found on one chromosome and the proteins encoded thereby. Haplotype may also refer to the allele present at any one locus within the MHC. Each class of MHC is represented by several loci: e.g., HLA-A (Human Leukocyte Antigen-A), HLA-B, HLA-C, HLA-E, HLA-F, HLA-G, HLA-H, HLA-I, HLA-J, HLA-K, HLA-L, HLA-P and HLA-V for class I and HLA-DRA, HLA-DRB1-9, HLA-DQA1, HLA-DQB1, HLA-DPA1, HLA-DPB1, HLA-DPB2, HLA-

DMA, HLA-DMB, HLA-DOA, and HLA-DOB for class II. The terms “HLA allele” and “MHC allele” are used interchangeably herein.

[00143] The terms “polynucleotide”, “nucleotide”, “nucleotide sequence”, “nucleic acid” and “oligonucleotide” are used interchangeably. They can refer to a polymeric form of nucleotides of any length, either deoxyribonucleotides or ribonucleotides, or analogs thereof. Polynucleotides may have any three dimensional structure, and may perform any function, known or unknown. The following are non-limiting examples of polynucleotides: coding or non-coding regions of a gene or gene fragment, loci (locus) defined from linkage analysis, exons, introns, messenger RNA (mRNA), transfer RNA (tRNA), ribosomal RNA (rRNA), short interfering RNA (siRNA), short-hairpin RNA (shRNA), micro-RNA (miRNA), ribozymes, cDNA, recombinant polynucleotides, branched polynucleotides, plasmids, vectors, isolated DNA of any sequence, isolated RNA of any sequence, nucleic acid probes, and primers. A polynucleotide may comprise one or more modified nucleotides, such as methylated nucleotides and nucleotide analogs. If present, modifications to the nucleotide structure may be imparted before or after assembly of the polymer. Polynucleotides can include nonstandard nucleotides, such as nucleotide analogs or modified nucleotides. In some embodiments, nonstandard nucleotides can stabilize hybrid formation. In some embodiments, nonstandard nucleotides can destabilize hybrid formation. In some embodiments, nonstandard nucleotides can enhance hybridization specificity. In some embodiments, nonstandard nucleotides can reduce hybridization specificity. Examples of nonstandard nucleotide modifications include 2' O-Me, 2' O-allyl, 2' O-propargyl, 2' O-alkyl, 2' fluoro, 2' arabino, 2' xylo, 2' fluoro arabino, phosphorothioate, phosphorodithioate, phosphoroamidates, 2' Amino, 5-alkyl-substituted pyrimidine, 3' deoxyguanosine, 5-halo-substituted pyrimidine, alkyl-substituted purine, halo-substituted purine, bicyclic nucleotides, 2'MOE, PNA molecules, LNA-molecules, LNA-like molecules, diaminopurine, S2T, 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xantine, 4-acetylcytosine, 5-(carboxyhydroxymethyl)uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N⁶-adenine, 7-methyl guanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-D46-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxy acetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, 2,6-diaminopurine, and derivatives thereof. The sequence of nucleotides may be interrupted by non-nucleotide components. A polynucleotide may be further modified after polymerization, such as by conjugation with a labeling component.

[00144] “Complementarity” can refer to the ability of a nucleic acid to form hydrogen bond(s) with another nucleic acid sequence by either traditional Watson-Crick or other non-traditional types. A percent complementarity can indicate the percentage of residues in a nucleic acid molecule which can form hydrogen

bonds (e.g., Watson-Crick base pairing) with a second nucleic acid sequence (e.g., 5, 6, 7, 8, 9, 10 out of 10 being 50%, 60%, 70%, 80%, 90%, and 100% complementary, respectively). “Perfectly complementary” can mean that all the contiguous residues of a nucleic acid sequence will hydrogen bond with the same number of contiguous residues in a second nucleic acid sequence. “Substantially complementary” refers to a degree of complementarity that is at least 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 97%, 98%, 99%, or 100% over a region of 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 45, 50, or more nucleotides, or can refer to two nucleic acids that hybridize under stringent conditions. Sequence identity, such as for the purpose of assessing percent complementarity, may be measured by any suitable alignment algorithm, including but not limited to the Needleman-Wunsch algorithm (e.g., the EMBOSS Needle aligner available at www.ebi.ac.uk/Tools/psa/emboss_needle/nucleotide.html, optionally with default settings), the BLAST algorithm (see e.g., the BLAST alignment tool available at blast.ncbi.nlm.nih.gov/Blast.cgi, optionally with default settings), or the Smith-Waterman algorithm. Optimal alignment may be assessed using any suitable parameters of a chosen algorithm, including default parameters.

[00145] The terms “polypeptide” and “protein” are used interchangeably to refer to a polymer of amino acid residues, and, are not limited to a minimum length. For example, a polypeptide can comprise at least about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, 40, 50, 60, 70, 80, 90, 100, 200, 300, 400, 500, 600, 700, 800, 900, or 1000 peptides or amino acids. Examples of polypeptides include, but are not limited to, amino acid chains, proteins, peptides, hormones, polypeptide saccharides, lipids, glycolipids, phospholipids, antibodies, enzymes, kinases, receptors, transcription factors, and ligands. Polypeptides, including the provided TCRs and TCR chains and other peptides, e.g., linkers and binding peptides, may include amino acid residues including natural and/or non-natural amino acid residues. The terms also include post-expression modifications of the polypeptide, for example, glycosylation, sialylation, acetylation, phosphorylation, and the like. In some aspects, the polypeptides may contain modifications with respect to a native or natural sequence, as long as the protein maintains the desired activity. These modifications may be deliberate, as through site-directed mutagenesis, or may be accidental, such as through mutations of hosts which produce the proteins or errors due to PCR amplification.

[00146] As used herein, the twenty conventional amino acids and their abbreviations known to one skilled in the art follow conventional usage. Stereoisomers (e.g., D-amino acids) of the twenty conventional amino acids, unnatural amino acids such as α -, α -disubstituted amino acids, N-alkyl amino acids, lactic acid, and other unconventional amino acids may also be suitable components for polypeptides of the present invention. Examples of unconventional amino acids include: 4-hydroxyproline, γ -carboxyglutamate, ϵ -N,N,N-trimethyllysine, ϵ -N-acetyllysine, O-phosphoserine, N-acetylserine, N-formylmethionine, 3-methylhistidine, 5-hydroxylysine, σ -N-methylarginine, and other similar amino acids and imino acids (e.g., 4-hydroxyproline). In the polypeptide notation used herein, the left hand direction is the amino terminal direction and the right hand direction is the carboxy-terminal direction, in accordance with standard usage and convention. Percent (%) sequence identity with respect to a reference polypeptide sequence (or nucleic acid sequence) is the percentage

of amino acid residues (or nucleotides in case of nucleic acid sequence) in a candidate sequence that are identical with the amino acid residues (or nucleotides) in the reference polypeptide sequence (or nucleic acid sequence), after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for aligning sequences, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared. For purposes herein, however, % amino acid sequence identity values are generated using the sequence comparison computer program ALIGN-2. The ALIGN-2 sequence comparison computer program was authored by Genentech, Inc., and the source code has been filed with user documentation in the U.S. Copyright Office, Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXU510087. The ALIGN-2 program is publicly available from Genentech, Inc., South San Francisco, Calif., or may be compiled from the source code. The ALIGN-2 program should be compiled for use on a UNIX operating system, including digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary. In situations where ALIGN-2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows: 100 times the fraction X/Y , where X is the number of amino acid residues scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A. Unless specifically stated otherwise, all % amino acid sequence identity values used herein are obtained as described in the immediately preceding paragraph using the ALIGN-2 computer program.

[00147] A “germline sequence” refers to a genetic sequence from the haploid gametes and those diploid cells from which they are formed. Germline DNA contains multiple gene segments that encode a single TCR α or TCR β chain, or a single TCR γ or TCR δ chain. These gene segments are carried in the germ cells but cannot be transcribed and translated until they are arranged into functional genes. During T cell differentiation in the bone marrow, these gene segments are randomly shuffled by a dynamic genetic system capable of generating more than 10^8 specificities.

[00148] Inhibition, “treatment” and “treating” are used interchangeably and refer to, for example, stasis of symptoms, prolongation of survival, partial or full amelioration of symptoms, and partial or full eradication of a condition, disease or disorder associated with excess levels of protein or correlated with protein activity. For example, treatment of cancer includes, but is not limited to, stasis, partial or total elimination of a cancerous

growth or tumor. Treatment or partial elimination includes, for example, a fold reduction in growth or tumor size and/or volume such as about 2-fold, about 3-fold, about 4-fold, about 5-fold, about 10-fold, about 20-fold, about 50-fold, or any fold reduction in between. Similarly, treatment or partial elimination can include a percent reduction in growth or tumor size and/or volume of about 1%, 2%, 3%, 4%, 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or any percentage reduction in between. Prevention refers to prophylaxis, prevention of onset of symptoms, prevention of progression of a disease or disorder associated with excess levels of protein or correlated with protein activity.

[00149] A “subject”, “individual”, “host” or “patient” refers to living organisms such as mammals. Examples of subjects and hosts include, but are not limited to, horses, cows, camels, sheep, pigs, goats, dogs, cats, rabbits, guinea pigs, rats, mice (*e.g.*, humanized mice), gerbils, non-human primates (*e.g.*, macaques), humans and the like, non-mammals, including, *e.g.*, non-mammalian vertebrates, such as birds (*e.g.*, chickens or ducks) fish (*e.g.*, sharks) or frogs (*e.g.*, *Xenopus*), and non-mammalian invertebrates, as well as transgenic species thereof. In certain aspects, a subject refers to a single organism (*e.g.*, human). In certain aspects, or a group of individuals composing a small cohort having either a common immune factor to study and/or disease, and/or a cohort of individuals without the disease (*e.g.*, negative/normal control) are provided. A subject from whom samples are obtained can either be inflicted with a disease and/or disorder (*e.g.*, one or more allergies, infections, cancers or autoimmune disorders or the like) and can be compared against a negative control subject which is not affected by the disease.

[00150] A “kit” refers to a delivery system for delivering materials or reagents for carrying out a method disclosed herein. In some embodiments, kits include systems that allow for the storage, transport, or delivery of reaction reagents (*e.g.*, probes, enzymes, etc. in the appropriate containers) and/or supporting materials (*e.g.*, buffers, written instructions for performing the assay etc.) from one location to another. For example, kits include one or more enclosures (*e.g.*, boxes) containing the relevant reaction reagents and/or supporting materials. Such contents may be delivered to the intended recipient together or separately. For example, a first container may contain an enzyme for use in an assay, while a second container contains a plurality of primers. A packaging material refers to a physical structure housing the components of the kit. The packaging material can maintain the components sterile and can be made of material commonly used for such purposes (*e.g.*, paper, corrugated fiber, glass, plastic, foil, ampules, etc.). The label or packaging insert can include appropriate written instructions. Kits, therefore, can additionally include labels or instructions for using the kit components in any method of the invention. A kit can include a compound in a pack, or dispenser together with instructions for administering the compound in a method described herein.

[00151] The term “resistance mutation” refers to a mutation in a gene that allows the gene or the host cell containing the gene to become resistant to treatment with a drug. For example, BTK C481S mutation is a resistance mutation which can confer ibrutinib resistance.

II. Overview

[00152] The present disclosure provides T cell receptors (TCRs) against neoantigens, isolated nucleic acid molecules encoding TCRs against neoantigens, T cells expressing said TCRs, and pharmaceutical compositions for use in the treatment of diseases involving malignant cells expressing said neoantigens.

[00153] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from RAS in complex with a human MHC, wherein the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 84% sequence identity to an amino acid sequence selected from SEQ ID NOs: 3, 18, 33, 49, 65, 81, 97, and 113, and/or wherein the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 84% sequence identity to an amino acid sequence selected from SEQ ID NOs: 6, 21, 36, 52, 68, 84, 100, and 116.

[00154] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from RAS in complex with a human MHC, wherein the epitope from RAS comprises a region having at least 70% sequence identity to an amino acid sequence selected from SEQ ID NOs: 15, 30, 45, 46, 61, 62, 77, 78, 93, 94, 109, 110, 125, 126 and 219-222.

[00155] Provided herein is an isolated nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct, wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A03:01 allele.

[00156] In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to an amino acid sequence selected from SEQ ID NOs: 9, 24, 39, 55, 71, 87, 103, and 119. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80% sequence identity to an amino acid sequence selected from SEQ ID NOs: 12, 27, 42, 58, 74, 90, 106, and 122. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 1, 16, 31, 47, 63, 79, 95, and 111. In some embodiments, the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 4, 19, 34, 50, 66, 82, 98, and 114. In some embodiments, the TCR alpha chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 2, 17, 32, 48, 64, 80, 96, and 112. In some embodiments, the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 5, 20, 35, 51, 67, 83, 99, and 115. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 9; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 12. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 1, a CDR2 of SEQ ID NO: 2, and a CDR3 of SEQ ID NO: 3; and the TCR beta chain

construct comprises a CDR1 of SEQ ID NO: 4, a CDR2 of SEQ ID NO: 5, and a CDR3 of SEQ ID NO: 6. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 24; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 27. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 16, a CDR2 of SEQ ID NO: 17, and a CDR3 of SEQ ID NO: 18; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 19, a CDR2 of SEQ ID NO: 20, and a CDR3 of SEQ ID NO: 21. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 39; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 42. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 31, a CDR2 of SEQ ID NO: 32, and a CDR3 of SEQ ID NO: 33; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 34, a CDR2 of SEQ ID NO: 35, and a CDR3 of SEQ ID NO: 36. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 55; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 58. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 47, a CDR2 of SEQ ID NO: 48, and a CDR3 of SEQ ID NO: 49; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 50, a CDR2 of SEQ ID NO: 51, and a CDR3 of SEQ ID NO: 52.

[00157] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from TMPRSS2:ERG in complex with a human MHC, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 144 and SEQ ID NO: 147.

[00158] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from TMPRSS2:ERG in complex with a human MHC, wherein the epitope from TMPRSS2:ERG comprises a region having at least 90% sequence identity to amino acid sequence SEQ ID NO: 156.

[00159] In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 150. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 153. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to SEQ ID NO: 142 or SEQ ID NO: 145. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to SEQ ID NO: 143 or SEQ ID NO: 146. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 150; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 153. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO:

142, a CDR2 of SEQ ID NO: 143, and a CDR3 of SEQ ID NO: 144; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 145, a CDR2 of SEQ ID NO: 146, and a CDR3 of SEQ ID NO: 147.

[00160] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from GATA3 in complex with a human MHC, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 129 and SEQ ID NO: 132.

[00161] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) capable of specifically binding to a mutant GATA3 peptide in complex with a protein encoded by an HLA allele of a subject with cancer, wherein the TCR comprises a TCR alpha chain construct and/or a TCR beta chain construct.

[00162] Provided herein is an isolated nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes a T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct, wherein the TCR specifically binds to a mutant GATA3 peptide in complex with an HLA-A02:01 protein; comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to SEQ ID NO: 129 or SEQ ID NO: 132; and/or specifically binds to a mutant GATA3 peptide comprising a region with at least 70% sequence identity to SEQ ID NO: 141.

[00163] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from GATA3 in complex with a human MHC, wherein the epitope from GATA3 comprises a region having at least 90% sequence identity to amino acid sequence SEQ ID NO: 141.

[00164] In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 135. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 138. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 127 and SEQ ID NO: 130. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 128 and SEQ ID NO: 131. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 135; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 138. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 127, a CDR2 of SEQ ID NO: 128, and a CDR3 of SEQ ID NO: 129; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 130, a CDR2 of SEQ ID NO: 131, and a CDR3 of SEQ ID NO: 132.

[00165] In another aspect, provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from BTK in complex with a human MHC, wherein the TCR alpha chain construct comprises a

complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 161 and SEQ ID NO: 176, or wherein the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 164 and SEQ ID NO: 179. In another aspect, provided herein is a nucleic acid encoding at least one T cell receptor (TCR) capable of specifically binding to a mutant BTK peptide in complex with a protein encoded by an HLA allele of a subject with cancer, wherein the TCR comprises a TCR alpha chain construct and/or a TCR beta chain construct. In another aspect, provided herein is an isolated nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes a T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct, wherein the TCR specifically binds to a mutant BTK peptide in complex with an HLA-A02:01 protein; comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to SEQ ID NO: 161, 164, 176, or 179; and/or specifically binds to a mutant BTK peptide comprising a region with at least 70% sequence identity to SEQ ID NO: 173 or 188. In another aspect, provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from BTK in complex with a human MHC, wherein the epitope from BTK comprises a region having at least 90% sequence identity to amino acid sequence SEQ ID NO: 173 or 188. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 167 or 182. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 170 or 185. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 159, 162, 174, and 177. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 160, 163, 175 and 178. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 167 or 182; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 170 or 185. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 159 or 174, a CDR2 of SEQ ID NO: 160 or 175, and a CDR3 of SEQ ID NO: 161 or 176; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 162 or 177, a CDR2 of SEQ ID NO: 163 or 178, and a CDR3 of SEQ ID NO: 164 or 179.

[00166] In yet another aspect, the present disclosure provides a host cell comprising the nucleic acid encoding a TCR against a neoantigen provided herein, a vector containing the nucleic acid sequence, or a protein encoded by the nucleic acid provided herein. In some embodiments, the host cell is a CD4⁺ T cell. In some embodiments, the host cell is a CD8⁺ T cell. The host cell may be a natural killer (NK) cell or a B cell. The host cell may be an immortalized cell line.

[00167] In yet another aspect, the present disclosure provides pharmaceutical compositions comprising the nucleic acid encoding a TCR against a neoantigen provided herein, a host cell comprising the nucleic acid

encoding a TCR against a neoantigen provided herein, a vector containing the nucleic acid sequence, or a protein encoded by the nucleic acid provided herein. In some embodiments, provided herein also comprises a method of using the pharmaceutical compositions disclosed herein.

[00168] Also provided herein in an additional aspect is a method of treating a subject with a disease or condition, comprising administering to the subject a pharmaceutical composition disclosed herein. In some embodiments, the subject has cancer.

III. T Cell Receptors (TCRs)

[00169] The ability of T cells to recognize antigens associated with various cancers or infectious organisms is conferred by its TCR, which is made up of both an alpha (α) chain and a beta (β) chain or a gamma (γ) and a delta (δ) chain. The proteins which make up these chains are encoded by DNA, which employs a unique mechanism for generating the tremendous diversity of the TCR. This multi-subunit immune recognition receptor associates with the CD3 complex and binds peptides presented by the MHC class I and II proteins on the surface of antigen-presenting cells (APCs). Binding of a TCR to the antigenic peptide on the APC is a central event in T cell activation, which occurs at an immunological synapse at the point of contact between the T cell and the APC.

[00170] Each TCR contains variable complementarity determining regions (CDRs), as well as framework regions (FRs) and a constant region. The amino acid sequence of the third complementarity-determining region (CDR3) loops of the α and β chain variable domains largely determines the sequence diversity of $\alpha\beta$ T cells arising from recombination between variable ($V\beta$), diversity ($D\beta$), and joining ($J\beta$) gene segments in the β chain locus, and between analogous $V\alpha$ and $J\alpha$ gene segments in the α chain locus, respectively. The existence of multiple such gene segments in the TCR α and β chain loci allows for a large number of distinct CDR3 sequences to be encoded. Independent addition and deletion of nucleotides at the $V\beta$ - $D\beta$, $D\beta$ - $J\beta$, and $V\alpha$ - $J\alpha$ junctions during the process of TCR gene rearrangement further increases CDR3 sequence diversity. In this respect, immunocompetence is reflected in the diversity of TCRs. The $\gamma\delta$ TCR is distinctive from the $\alpha\beta$ TCR in that it encodes a receptor that interacts closely with the innate immune system. $TCR\gamma\delta$, is expressed early in development, has specialized anatomical distribution, has unique pathogen and small-molecule specificities, and has a broad spectrum of innate and adaptive cellular interactions. Early in ontogeny, as the restricted subsets of $TCR\gamma\delta$ cells populate various tissues prenatally, a biased pattern of $TCR\gamma$ V and J segment expression is established.

[00171] The TCRs provided herein target may be engineered TCRs, for example, chimeric antigen receptors (CARs). CARs can be composed of three regions: an ectodomain, a transmembrane domain and an endodomain.

[00172] An ectodomain can be the region of the receptor that is exposed to the extracellular fluid and can consist of an antigen recognition region. In some embodiments, an ectodomain further comprises a spacer. In some embodiments, an ectodomain further comprises a signal peptide. A signal peptide can direct the nascent protein into the endoplasmic reticulum. A signal protein in a CAR may be a single-chain variable fragment (scFv). A fusion protein may be a protein that is formed by merging two or more genes that code

originally for different proteins but when they are translated in the cell, the translation produces one or more polypeptides with functional properties derived for each of the original genes. A scFv is a chimeric protein made up of a light chain domain and heavy chain variable domain connected with a short linker peptide. The linker may comprise hydrophilic residues with stretches of glycine and/or serine residues. The linker may comprise stretches of glutamate and lysine residues, which can improve solubility.

[00173] A transmembrane domain can be a hydrophobic domain that spans the membrane. In some embodiments, a transmembrane domain comprises an alpha-helical domain. A transmembrane domain may be functional for the stability of the receptor as a whole. In some embodiments, a transmembrane domain comprises a transmembrane domain from the most membrane proximal component of an endodomain. In some embodiments, a transmembrane domain comprises a CD3-zeta transmembrane domain. In some embodiments, a transmembrane domain allows for incorporation of an artificial TCR into a native TCR complex. In some embodiments, a transmembrane domain comprises a CD28 transmembrane domain.

[00174] An endodomain can be a functional intracellular portion of a receptor, such as a TCR or CAR. After antigen recognition, receptors cluster and a signal may be transmitted to the cell. In some embodiments, an endodomain comprises a CD3-zeta intracellular domain. In some embodiments, an endodomain comprises at least one ITAM. In some embodiments, an endodomain comprises at least 3 or at least 3 ITAMs. In some embodiments, an endodomain comprises a CD28 intracellular domain. In some embodiments, an endodomain comprises an OX40 intracellular domain. In some embodiments, an endodomain comprises a chimeric intracellular domain. For example, an endodomain can comprises a CD28 intracellular domain, an OX40 intracellular domain and a CD3-zeta intracellular domain.

IV. T cells

[00175] T cells belong to a group of white blood cells known as lymphocytes, and play a central role in cell-mediated immunity. T cells include CD4⁺ T cells (helper T cells) and CD8⁺ T cells (cytotoxic T cells). CD4⁺ T cells can assist other white blood cells in immunologic processes, including maturation of B-cells and activation of cytotoxic T cells and macrophages. CD4⁺ T cells are activated when presented with peptide antigens by MHC class II molecules expressed on the surface of antigen presenting cells (APCs). Once activated, the T cells can divide rapidly and secrete cytokines that regulate the active immune response. CD8⁺ T cells can destroy virally infected cells and tumor cells, and, can also be implicated in transplant rejection. CD8⁺ T cells can recognize their targets by binding to antigen associated with MHC class I, which is present on the surface of nearly every cell of the body. Most T cells have a T cell receptor (TCR). The ability of T cells to recognize antigens associated with various cancers or infectious organisms is conferred by its TCR, which is made up of both an alpha (α) chain and a beta (β) chain or a gamma (γ) and a delta (δ) chain. The proteins which make up these chains are encoded by DNA, which employs a unique mechanism for generating the diversity of the TCR. This multi-subunit immune recognition receptor can associate with the CD3 complex and bind peptides presented by the MHC class I and II proteins on the surface of antigen-presenting cells (APCs). The first signal in activation of T cells can be provided by binding of the T cell receptor to a short peptide presented by the MHC on another

cell. This ensures that only a T cell with a TCR specific to that peptide is activated. The partner cell is usually an antigen presenting cell such as a professional antigen presenting cell, usually a dendritic cell in the case of naive responses, although B-cells and macrophages can be important APCs. Binding of a TCR to the antigenic peptide on the APC can be a central event in T cell activation, which occurs at an immunological synapse at the point of contact between the T cell and the APC.

[00176] T cells can be prepared according to methods known in the art. T cells can be an enriched T cell preparation, an APC-depleted cell preparation, or a substantially purified T cell preparation. T cells can be a mixed T cell population or a purified T cell subset. T cells can be an enriched T cell preparation containing a number or percentage of T cells that is increased with respect to an isolated population of T cells.

[00177] T cells, or a subset of T cells, can be obtained from various lymphoid tissues. T cells can be obtained from a number of sources, including peripheral blood mononuclear cells (PBMCs), bone marrow, thymus, tissue biopsy, tumor, lymph node tissue, gut associated lymphoid tissue, mucosa associated lymphoid tissue, spleen tissue, lymphoid tissue, and tumors. The term “peripheral blood lymphocytes” (PBL) and its grammatical equivalents as used herein can refer to lymphocytes that circulate in the blood (e.g., peripheral blood). Peripheral blood lymphocytes can refer to lymphocytes that are not localized to organs. Peripheral blood lymphocytes can comprise T cells, NK cells, B cell, or any combinations thereof.

[00178] The method can comprise isolating T cells from a subject. The method can comprise obtaining T cells isolated from a subject. T cells can be obtained from T cell lines. T cells can be obtained from autologous sources. T cells can be obtained from allogeneic sources. T cells may also be obtained from a xenogeneic source, for example, from mouse, rat, non-human primate, and pig.

[00179] T cells can be an APC-depleted cell preparation. T cells can be substantially free of APCs. For example, T cells can comprise T cells separated from over 75% of APCs. In an exemplary embodiment, peripheral blood mononuclear cells (PBMCs) can be obtained from blood, e.g., in heparinized vials. PBMCs can be separated from red blood cells by centrifugation and PBMCs recovered from the interface. The recovered PBMCs optionally can be washed (e.g., with PBS).

[00180] T cell purification can be achieved, for example, by positive or negative selection including, but not limited to, the use of antibodies directed to CD2, CD3, CD4, CD5, CD8, CD14, CD19, and/or MHC class II molecules. A specific T cell subset, such as CD28⁺, CD4⁺, CD8⁺, CD45RA⁺, and/or CD45RO⁺ T cells, can be isolated by positive or negative selection techniques. For example, CD3⁺, CD28⁺ T cells can be positively selected using CD3/CD28 conjugated magnetic beads. In one aspect of the present invention, enrichment of a T cell population by negative selection can be accomplished with a combination of antibodies directed to surface markers unique to the negatively selected cells.

[00181] For example, a T cell sample can comprise cells from a subject's circulating blood and can be obtained by apheresis or leukopheresis. A T cell sample may contain lymphocytes, including T cells, monocytes, granulocytes, B cells, other nucleated white blood cells, red blood cells, and/or platelets. Undesirable components of the T cell sample can be removed and the remaining T cells can be suspended in culture media.

For example, cells can be washed to remove the plasma fraction. For example, T cells can be isolated from peripheral blood lymphocytes by lysing the red blood cells and by centrifugation through a PERCOLL™ gradient.

[00182] In some embodiments, a T cell comprises at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from RAS in complex with a human MHC. In some embodiments, a T cell comprises at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from TMPRSS2:ERG in complex with a human MHC. In some embodiments, a T cell comprises at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from GATA3 in complex with a human MHC. In some embodiments, a host cell comprises at least one TCR disclosed herein, wherein the host cell is a CD4+ T cell. In some embodiments, the host cell is a CD8+ T cell. In some embodiments, the host cell is an autologous cell. In some embodiments, the host cell is an allogeneic cell. In some embodiments, the host cell is a human cell. In some other cases, a host cell may be natural killer (NK) cell, a B cell, or an immortalized cell line.

[00183] In some embodiments, T cells can be obtained by positive selection and/or negative selection. In positive selection, an affinity agent (such as an antibody, an antibody fragment, and aptamer) can be used to bind a cell surface marker expressed on the population of cells, for example, CD3 for T cells. Using the affinity agent, the T cells can be labeled. The labeled T cells can then be enriched using various methods that are well-known in the art. Non-limiting examples of those methods include fluorescent-activated cell sorting (FACS) and (para)magnetic particle-based cell separation (e.g. MACS cell separation kits from Miltenyi Biotec).

[00184] In negative selection, affinity agents can be used to bind cell surface markers expressed on blood cells other than the desired population. For example, when attempting to isolate T cells, a cocktail of affinity agents can be used to label B cells, NK cells, monocytes, platelets, dendritic cells, granulocytes and erythrocytes. The labeled cells can then be depleted, leaving the T cells enriched. The exemplary methods to deplete labeled cells include FACS and (para)magnetic particle-based cell separation.

[00185] In addition to labeling-based isolation, special growth condition may be used to promote the growth of one particular cell population. For example, the special growth condition can be obtained using special cytokines or growth factors. For another example, in culture media containing phytohemagglutinin (PHA), IL-2, and/or IL-15, T cells may preferentially proliferate.

[00186] In some situations, non-functional markers may be used to isolate T cells since binding of functional markers such as binding of CD3 by anti-CD3 antibody (alone or conjugated to magnetic particles) may trigger unwanted signaling events on T cells. Therefore, a cocktail of antibodies against CD14, CD15, CD16, CD19, CD34, CD36, CD56, CD123, and CD235a (glycophorin A) can be used to isolate T cells.

[00187] Detailed protocol can be found in published literatures (e.g. see Lefort et al., *J Vis Exp.* 2010; (40): 2017) which are incorporated by reference herein. T cell isolation kits can be obtained from, for example, STEMCELL Technologies, Thermofisher, and Miltenyi Biotec.

[00188] The T cell described herein may be an allogeneic T cell.

[00189] In some embodiments, the T cell may be a genetically-modified cell comprising in its genome a modified human T cell receptor (TCR) alpha chain gene and/or a modified human TCR beta chain gene, wherein the cell has reduced cell-surface expression of the endogenous TCR.

[00190] Gene-editing nucleases may be employed in order to disrupt components of the TCR. The TCR alpha chain (TCR α) is encoded by a single TRAC gene and pairs with the TCR beta chain (TCR β) encoded by two TRCB genes. Since the TCR α/β dimer can produce a fully functioning TCR complex, disrupting TCR α and/or TCR β function may reduce (even eliminate) endogenous TCR expression.

[00191] Various methods may be used to disrupt endogenous TCR α or TCR β genes. For example, four classes of gene editing proteins exist that share a common mode of action in binding a user defined sequence of DNA and mediating a double stranded DNA break (DSB). Zinc finger nucleases (ZFN) are heterodimeric arrays that co-localize at a target DNA site. ZFNs include individual finger subunits that bind DNA and are tethered to the FokI nuclease domain that cleaves DNA. Transcription activator-like effector nucleases (TALEN) include repeating units that bind DNA by virtue of a hypervariable two amino acid sequence (repeat variable diresidue; RVD) that governs DNA base recognition. Similar to ZFNs, TALENs function as dimeric proteins that are fused to the FokI endonuclease domain for DSB generation. Meganucleases (MN) are monomeric proteins with innate nuclease activity that are derived from bacterial homing endonucleases and engineered for a unique target site. The clustered regularly interspaced short palindromic repeats (CRISPR) and associated Cas9 nuclease platform involves a small guide RNA (gRNA) transcript that contacts a target DNA sequence via Watson-Crick base pairing and the Cas9 nuclease that cleaves the DNA.

[00192] In some embodiments, introducing the genome-editing nuclease into the T cell includes introducing into the T cell a polynucleotide that encodes the genome-editing nuclease.

[00193] In some embodiments, introducing the genome-editing nuclease into the T cell includes introducing into the T cell a Cas9 polypeptide. In some embodiments, the genome-editing nuclease includes a TALEN nuclease, a CRISPR/Cas9 nuclease, or a megaTAL nuclease.

[00194] In some embodiments, the CRISPR/Cas9 nuclease is derived from either *Streptococcus pyogenes* or *Staphylococcus aureus*. In some of these embodiments, the CRISPR/Cas9 nuclease includes a nuclease-resistant gRNA such as, for example, at least one 2'-OMe-phosphorothioate modified base, at least one 2'-O-methyl modified base, or at least one 2'-O-methyl 3' thioPACE modified base.

[00195] In some embodiments, the TALEN nuclease or the megaTAL nuclease is encoded by an RNA that has an exogenous polyadenylation signal.

[00196] In some embodiments, the method described herein may further include culturing the T cell under conditions effective for expanding the population of genome-modified T cells.

[00197] In some embodiments, disrupting expression of TCR α and/or TCR β further disrupts assembly of TCR α and TCR β . In some embodiments, disrupting expression of TCR α further disrupts formation of a complex

between TCR and CD3. In some embodiments, disrupting expression of TCR α involves further disrupting assembly of TCR α and TCR β .

[00198] In some embodiments, a genetically-modified T cell comprises a disrupted TCR alpha chain and/or beta chain and an inactivated gene encoding immune checkpoint protein such as PD1 and CTLA-4. This may be made possible by gene inactivation using specific TALE-nucleases directed against TCRalpha or TCRbeta coupled with inactivation of genes encoding immune checkpoint protein such as PD1 and CTLA-4.

[00199] In some embodiments, the genetic modification relies on the inactivation of one gene, or two genes selected from the group consisting of PD1, CTLA-4, LAG3, Tim3, BTLA, BY55, TIGIT, B7H5, LAIR1, SIGLEC10, 2B4, TCR alpha and TCR beta. In some embodiments, the genetic modification relies on the inactivation of two genes selected from the group consisting of PD1 and TCR alpha, PD1 and TCR beta, CTLA-4 and TCR alpha, CTLA-4 and TCR beta, LAG 3 and TCR alpha, LAG 3 and TCR beta, Tim3 and TCR alpha, Tim3 and TCR beta, BTLA and TCR alpha, BTLA and TCR beta, BY55 and TCR alpha, BY55 and TCR beta, TIGIT and TCR alpha, TIGIT and TCR beta, B7H5 and TCR alpha, B7H5 and TCR beta, LAIR1 and TCR alpha, LAIR1 and TCR beta, SIGLEC10 and TCR alpha, SIGLEC10 and TCR beta, 2B4 and TCR alpha, 2B4 and TCR beta. In some embodiments, the genetic modification relies on the inactivation of more than two genes. The genetic modification may be operated ex-vivo.

V. TCRs Specific to RAS peptide-MHC complexes

[00200] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from RAS in complex with a human MHC, wherein the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 84% sequence identity to an amino acid sequence selected from SEQ ID NOs: 3, 18, 33, 49, 65, 81, 97, 113, 241, 257, 273, 289, 305, 321, 337, 353, 369, 385, 401, 417, and 433 and/or wherein the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 84% sequence identity to an amino acid sequence selected from SEQ ID NOs: 6, 21, 36, 52, 68, 84, 100, 116, 244, 260, 276, 292, 308, 324, 340, 356, 372, 388, 404, 420, and 436.

[00201] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from RAS in complex with a human MHC, wherein the epitope from RAS comprises a region having at least 70% sequence identity to an amino acid sequence selected from SEQ ID NOs: 15, 30, 45, 46, 61, 62, 77, 78, 93, 94, 109, 110, 125, 126, 219-222, 253, 254, 269, 270, 285, 286, 301, 302, 317, 318, 333, 334, 349, 350, 365, 366, 381, 382, 397, 398, 413, 414, 429, 430, 445 and 446.

[00202] Provided herein is an isolated nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct; wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A03:01 allele. In some embodiments, the alpha chain construct comprises a variable region having at least 80% sequence identity to an amino acid sequence selected from SEQ ID NOs: 71, 87,

103, 295, 311, 327, 343, 359 and 391, wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A03:01 allele. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80% sequence identity to an amino acid sequence selected from SEQ ID NOs: 74, 90, 106, 298, 314, 330, 346, 362 and 394, wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A03:01 allele.

[00203] In some embodiments, the TCR alpha chain construct as described above comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 63, 79, 95, 287, 303, 319, 335, 351 and 383. In some embodiments, the TCR beta chain construct as described above comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 66, 82, 98, 290, 306, 322, 338, 354 and 386. In some embodiments, the TCR alpha chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 64, 80, 96, 288, 304, 320, 336, 352 and 384. In some embodiments, the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 67, 83, 99, 291, 307, 323, 339, 355 and 387. In some embodiments, the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 65, 81, 97, 289, 305, 321, 337, 353 and 385. In some embodiments, the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 68, 84, 100, 292, 308, 324, 340, 356 and 388.

[00204] Provided herein is an isolated nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct; wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A02:01 allele. In some embodiments, the alpha chain construct comprises a variable region having at least 80% sequence identity to an amino acid sequence selected from SEQ ID NOs: 9 and 24 wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A02:01 allele. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80% sequence identity to an amino acid sequence selected from SEQ ID NOs: 12 and 27, wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A02:01 allele.

[00205] In some embodiments, the TCR alpha chain construct as described above comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 1 and 16. In some embodiments, the TCR beta chain construct as described above comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 4 and 19. In some embodiments, the TCR alpha chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 2 and 17. In some embodiments TCR beta chain construct comprises a

complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 5 and 20. In some embodiments, the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 3 and 18. In some embodiments, the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 6 and 21.

[00206] Provided herein is an isolated nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct; wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A11:01 allele. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to an amino acid sequence selected from SEQ ID NOs: 39, 55, 122, 247, 263, 279, 375, 407, 423 and 439, wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A11:01 allele. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80% sequence identity to an amino acid sequence selected from SEQ ID NOs: 42, 58, 125, 250, 266, 282, 378, 413, 426 and 442, wherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A11:01 allele.

[00207] In some embodiments, the TCR alpha chain construct as described above comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 31, 47, 111, 239, 255, 271, 367, 399, 415, and 431. In some embodiments, the TCR beta chain construct as described above comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 34, 50, 114, 242, 258, 274, 370, 402, 418, and 434. In some embodiments, the TCR alpha chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 32, 48, 112, 240, 256, 272, 368, 400, 416, and 432. In some embodiments, the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 35, 51, 115, 243, 259, 275, 371, 403, 419, and 435. In some embodiments, the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 33, 49, 113, 241, 257, 273, 369, 401, 417, and 433. In some embodiments, the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 36, 52, 116, 228, 244, 260, 276, 372, 404, 420, and 434. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 9; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 12. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 1, a CDR2 of SEQ ID NO: 2, and a CDR3 of SEQ ID NO: 3; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 4, a CDR2 of SEQ ID NO: 5, and a CDR3 of SEQ ID NO: 6. In some embodiments, the TCR alpha

chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 24; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 27. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 16, a CDR2 of SEQ ID NO: 17, and a CDR3 of SEQ ID NO: 18; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 19, a CDR2 of SEQ ID NO: 20, and a CDR3 of SEQ ID NO: 21. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 39; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 42. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 31, a CDR2 of SEQ ID NO: 32, and a CDR3 of SEQ ID NO: 33; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 34, a CDR2 of SEQ ID NO: 35, and a CDR3 of SEQ ID NO: 36. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 55; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 58. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 47, a CDR2 of SEQ ID NO: 48, and a CDR3 of SEQ ID NO: 49; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 50, a CDR2 of SEQ ID NO: 51, and a CDR3 of SEQ ID NO: 52. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 71; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 74. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 63, a CDR2 of SEQ ID NO: 64, and a CDR3 of SEQ ID NO: 65; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 66, a CDR2 of SEQ ID NO: 67, and a CDR3 of SEQ ID NO: 68. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 87; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 90. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 79, a CDR2 of SEQ ID NO: 80, and a CDR3 of SEQ ID NO: 81; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 82, a CDR2 of SEQ ID NO: 83, and a CDR3 of SEQ ID NO: 84. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 103; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 106. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 95, a CDR2 of SEQ ID NO: 96, and a CDR3 of SEQ ID NO: 97; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 98, a CDR2 of SEQ ID NO: 99, and a CDR3 of SEQ ID NO: 100. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 119; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 122. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 111, a CDR2 of SEQ ID NO: 112, and a CDR3 of SEQ ID NO: 113; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 114, a CDR2 of SEQ ID NO: 115, and a CDR3 of SEQ ID NO: 116. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO:

263; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 266. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 255, a CDR2 of SEQ ID NO: 256, and a CDR3 of SEQ ID NO: 257; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 258, a CDR2 of SEQ ID NO: 259, and a CDR3 of SEQ ID NO: 260. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 279; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 282. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 271, a CDR2 of SEQ ID NO: 272, and a CDR3 of SEQ ID NO: 273; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 274, a CDR2 of SEQ ID NO: 275, and a CDR3 of SEQ ID NO: 276. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 295; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 298. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 287, a CDR2 of SEQ ID NO: 288, and a CDR3 of SEQ ID NO: 289; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 290, a CDR2 of SEQ ID NO: 291, and a CDR3 of SEQ ID NO: 292. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 311; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 314. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 303, a CDR2 of SEQ ID NO: 304, and a CDR3 of SEQ ID NO: 305; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 306, a CDR2 of SEQ ID NO: 307, and a CDR3 of SEQ ID NO: 308. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 327; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 330. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 319, a CDR2 of SEQ ID NO: 320, and a CDR3 of SEQ ID NO: 321; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 322, a CDR2 of SEQ ID NO: 323, and a CDR3 of SEQ ID NO: 324. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 343; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 346. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 335, a CDR2 of SEQ ID NO: 336, and a CDR3 of SEQ ID NO: 337; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 338, a CDR2 of SEQ ID NO: 339, and a CDR3 of SEQ ID NO: 340. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 343; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 346. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 351, a CDR2 of SEQ ID NO: 352, and a CDR3 of SEQ ID NO: 353; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 354, a CDR2 of SEQ ID NO: 355, and a CDR3 of SEQ ID NO: 356. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 343; and the TCR beta chain

construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 346. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 367, a CDR2 of SEQ ID NO: 368, and a CDR3 of SEQ ID NO: 369; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 370, a CDR2 of SEQ ID NO: 371, and a CDR3 of SEQ ID NO: 372. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 391; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 394. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 383, a CDR2 of SEQ ID NO: 384, and a CDR3 of SEQ ID NO: 385; the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 386, a CDR2 of SEQ ID NO: 387, and a CDR3 of SEQ ID NO: 388. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 391; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 394. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 399, a CDR2 of SEQ ID NO: 400, and a CDR3 of SEQ ID NO: 401; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 402, a CDR2 of SEQ ID NO: 403, and a CDR3 of SEQ ID NO: 404. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 423; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 426. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 415, a CDR2 of SEQ ID NO: 416, and a CDR3 of SEQ ID NO: 417; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 418, a CDR2 of SEQ ID NO: 419, and a CDR3 of SEQ ID NO: 420. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 391; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 394. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 431, a CDR2 of SEQ ID NO: 432, and a CDR3 of SEQ ID NO: 433; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 434, a CDR2 of SEQ ID NO: 435, and a CDR3 of SEQ ID NO: 426.

[00208] In various embodiments, the nucleic acid sequence encoding a TCR is codon optimized.

[00209] Mutations in any one of the three *ras* genes, *H-ras*, *K-ras* and *N-ras* are one of the most common events in human tumorigenesis. About 30% of all human tumors are found to carry at least one mutation in any of the canonical *ras* genes. Ras mutations are evident in, for example, adenocarcinoma of the biliary tract, transitional cell carcinoma of the bladder, breast carcinoma, cervical adenocarcinoma, colon adenocarcinoma, colon adenoma, neuroblastoma (autonomic ganglia), acute myeloid leukemia, chronic myeloid leukemia, chronic myelomonocytic leukemia, juvenile myelomonocytic leukemia, acute lymphoblastic leukemia, Burkitt's lymphoma, Hodgkin's lymphoma, plasma cell myeloma, hepatocellular carcinoma, large cell carcinoma, non-small cell carcinoma, ductal carcinoma, endocrine tumor, prostate adenocarcinoma, basal cell carcinoma, squamous cell carcinoma, malignant melanoma, angiosarcoma, leiomyosarcoma, liposarcoma, rhabdomyosarcoma, myxoma, malignant fibrous histiocytoma, pleomorphic sarcoma, germinoma, seminoma, anaplastic carcinoma, follicular carcinoma, papillary carcinoma and Hurthle cell carcinoma. Ras mutations are

found in cancers affecting many tissues and organs of the body, for example, lung, liver, breast, bladder, colon, cervix, pancreas, prostate gland, stomach, thyroid, testis, soft tissue, skin and blood.

[00210] In various embodiments, the TCR binds to an MHC:RAS peptide complex, wherein the RAS peptide comprises a G12V mutation. In various embodiments, the TCR binds to an MHC:RAS peptide complex, wherein the RAS peptide comprises a G12C mutation. In various embodiments, the TCR binds to an MHC:RAS peptide complex, wherein the RAS peptide comprises a G12D mutation. In various embodiments, the TCR binds to an MHC:RAS peptide complex, wherein the RAS peptide comprises a mutation at Q61. In various embodiments, the TCR binds to an MHC:RAS peptide complex, wherein the RAS peptide comprises a sequence of VVGAVGVGK, VVVGAVGVGK, VVGADGVGK, VVVGADGVGK, VVGACGVGK, VVVGACGVGK, KLVVVGACGV, LVVVGACGV, KLVVVGADGV, LVVVGADGV, KLVVVGAVGV or LVVVGAVGV.

[00211] In various embodiments, the TCR binds to an MHC:RAS peptide complex, wherein the human MHC is encoded by an HLA-A02:01 allele. In various embodiments, the TCR binds to an MHC:RAS peptide complex, wherein the human MHC is encoded by an HLA-A03:01 allele. In various embodiments, the TCR binds to an MHC:RAS peptide complex, wherein the human MHC is encoded by an HLA-A11:01 allele.

[00212] In various embodiments, the TCR binds to an MHC:RAS peptide complex, wherein the human MHC is encoded by an HLA-A02:01 allele and wherein the RAS peptide comprises a sequence of VVGAVGVGK, VVVGAVGVGK, VVGADGVGK, VVVGADGVGK, VVGACGVGK, VVVGACGVGK, KLVVVGACGV, LVVVGACGV, KLVVVGADGV, LVVVGADGV, KLVVVGAVGV or LVVVGAVGV. In various embodiments, the TCR binds to an MHC:RAS peptide complex, wherein the human MHC is encoded by an HLA-A03:01 allele and wherein the RAS peptide comprises a sequence of VVGAVGVGK, VVVGAVGVGK, VVGADGVGK, VVVGADGVGK, VVGACGVGK, VVVGACGVGK, KLVVVGACGV, LVVVGACGV, KLVVVGADGV, LVVVGADGV, KLVVVGAVGV or LVVVGAVGV. In various embodiments, the TCR binds to an MHC:RAS peptide complex, wherein the human MHC is encoded by an HLA-A11:01 allele and wherein the RAS peptide comprises a sequence of VVGAVGVGK, VVVGAVGVGK, VVGADGVGK, VVVGADGVGK, VVGACGVGK, VVVGACGVGK, KLVVVGACGV, LVVVGACGV, KLVVVGADGV, LVVVGADGV, KLVVVGAVGV or LVVVGAVGV.

[00213] In some embodiments, one TCR as disclosed herein, exhibits a specific binding affinity to an epitope peptide containing a point mutation found in cancer when the epitope peptide is in complex with an MHC encoded by the specific allele; and additionally the TCR may exhibit a different binding affinity to another epitope peptide containing a different point mutation of the same cancer protein, when the epitope peptide is in complex with an MHC encoded by the specific allele, but do not exhibit binding affinity to the WT peptide which does not contain any mutation.

VI. TCRs Specific to Tmprss2:ERG peptide-MHC complexes

[00214] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from

TMPRSS2:ERG in complex with a human MHC, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 144 and SEQ ID NO: 147.

[00215] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from TMPRSS2:ERG in complex with a human MHC, wherein the epitope from TMPRSS2:ERG comprises a region having at least 90% sequence identity to amino acid sequence SEQ ID NO: 156.

[00216] In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 150. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 153. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to SEQ ID NO: 142 or SEQ ID NO: 145. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to SEQ ID NO: 143 or SEQ ID NO: 146. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 150; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 153. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 142, a CDR2 of SEQ ID NO: 143, and a CDR3 of SEQ ID NO: 144; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 145, a CDR2 of SEQ ID NO: 146, and a CDR3 of SEQ ID NO: 147.

[00217] In some embodiments, a TCR comprises a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from TMPRSS2:ERG in complex with a human MHC, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to SEQ ID NO: 144 or 147.

[00218] In some embodiments, a TCR comprises a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from TMPRSS2:ERG in complex with a human MHC, wherein the epitope from TMPRSS2:ERG comprises a region having at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to SEQ ID NO: 156.

[00219] In some embodiments, the TCR alpha chain construct and or TCR beta chain construct comprises a variable region having at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to SEQ ID NO: 150 or 153.

[00220] In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to SEQ ID NO: 142 or 145.

[00221] In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to SEQ ID NO: 143 or 146.

[00222] In some embodiments, the nucleic acid encoding a TCR alpha chain construct and/or TCR beta chain comprises a nucleic acid sequence with at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to any one of SEQ ID NOs: 148, 149, 151, and 152. In various embodiments, the nucleic acid sequence encoding a TCR is codon optimized.

[00223] In various embodiments, the TCR binds to an MHC:TMPRSS2::ERG peptide complex, wherein the TMPRSS2::ERG peptide comprises a gene fusion mutation. In various embodiments, the TCR binds to an MHC:TMPRSS2::ERG peptide complex, wherein the TMPRSS2::ERG peptide comprises a gene fusion mutation comprising at least two consecutive amino acids wherein the at least two consecutive amino acids comprise at least one amino acid of TMPRSS2 and at least one amino acid of ERG. In various embodiments, the TCR binds to an MHC:TMPRSS2::ERG peptide complex, wherein the TMPRSS2::ERG peptide comprises a sequence of ALNSEALSV.

[00224] In various embodiments, the human MHC is encoded by an HLA-A02:01 allele. In various embodiments, the TCR binds to an MHC:TMPRSS2::ERG peptide complex, wherein the human MHC is encoded by an HLA-A02:01 allele.

[00225] In various embodiments, the human MHC is encoded by an HLA-A02:01 allele. In various embodiments, the TCR binds to an MHC:TMPRSS2::ERG peptide complex, wherein the human MHC is encoded by an HLA-A02:01 allele wherein the TMPRSS2::ERG peptide comprises a sequence of ALNSEALSV.

VII. TCRs Specific to GATA3 peptide-MHC complexes

[00226] In some other embodiments, a TCR comprises a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from GATA3 in complex with a human MHC, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to SEQ ID NO: 129, 132, 191, 194, 206 or 209.

[00227] In some embodiments, a TCR comprises a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from GATA3 in complex with a human MHC, wherein the epitope from GATA3 comprises a region having at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to SEQ ID NO: 141, 203 or 218.

[00228] In some embodiments, the TCR alpha chain construct and or TCR beta chain construct comprises a variable region having at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to SEQ ID NO: 135, 138, 197, 200, 212 or 215.

[00229] In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to SEQ ID NO: 127, 130, 189, 192, 204 or 207.

[00230] In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity SEQ ID NO: 128, 131, 190, 193, 205 or 208.

[00231] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from GATA3 in complex with a human MHC, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 129, 132, 191, 194, 206 or 209.

[00232] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) capable of specifically binding to a mutant GATA3 peptide in complex with a protein encoded by an HLA-A02:01, HLA-B07:02 or HLA-B08:01 allele of a subject with cancer, wherein the TCR comprises a TCR alpha chain construct and/or a TCR beta chain construct.

[00233] Provided herein is an isolated nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes a T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct, wherein the TCR specifically binds to a mutant GATA3 peptide in complex with an HLA-A02:01, HLA-B07:02 or HLA-B08:01 protein; comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to SEQ ID NO: 129, 132, 191, 194, 206 or 209; and/or specifically binds to a mutant GATA3 peptide comprising a region with at least 70% sequence identity to SEQ ID NO: 141, 203 or 218.

[00234] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from GATA3 in complex with a human MHC, wherein the epitope from GATA3 comprises a region having at least 90% sequence identity to amino acid sequence SEQ ID NO: 141, 203 or 218.

[00235] In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 135, 197 or 212. In some embodiments, the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 138, 200 or 215. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 127, 130, 189, 192, 204 and 207. In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 128, 131, 190, 193, 205 and 208.

[00236] In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 135; and the TCR beta chain construct comprises a variable region having at

least 80% sequence identity to SEQ ID NO: 138. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 197; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 200. In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 212; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 215.

[00237] In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 127, a CDR2 of SEQ ID NO: 128, and a CDR3 of SEQ ID NO: 129; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 130, a CDR2 of SEQ ID NO: 131, and a CDR3 of SEQ ID NO: 132. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 189, a CDR2 of SEQ ID NO: 190, and a CDR3 of SEQ ID NO: 191; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 192, a CDR2 of SEQ ID NO: 193, and a CDR3 of SEQ ID NO: 194. In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 204, a CDR2 of SEQ ID NO: 205, and a CDR3 of SEQ ID NO: 206; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 207, a CDR2 of SEQ ID NO: 208, and a CDR3 of SEQ ID NO: 209.

[00238] In some embodiments, the nucleic acid encoding a TCR alpha chain construct and/or TCR beta chain comprises a nucleic acid sequence with at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to any one of SEQ ID NOs: 133, 134, 136 or 137. In some embodiments, the nucleic acid encoding a TCR alpha chain construct and/or TCR beta chain comprises a nucleic acid sequence with at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to any one of SEQ ID NOs: 195, 196, 198 or 199. In some embodiments, the nucleic acid encoding a TCR alpha chain construct and/or TCR beta chain comprises a nucleic acid sequence with at least 60%, at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 98% sequence identity to any one of SEQ ID NOs: 210, 211, 213 or 214.

[00239] In various embodiments, the nucleic acid sequence encoding a TCR is codon optimized.

[00240] In various embodiments, the TCR binds to an MHC:GATA3 peptide complex, wherein the GATA peptide comprises at least one amino acid encoded by a GATA3 neoORF sequence. In various embodiments, the TCR binds to an MHC:GATA3 peptide complex, wherein the GATA peptide comprises at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25 amino acids encoded by a GATA3 neoORF sequence. In various embodiments, the TCR binds to an MHC:GATA3 peptide complex, wherein the GATA peptide comprises at least one amino acid encoded by a GATA3 neoORF sequence and at least one amino acid encoded by a GATA3 wild type sequence. In various embodiments, the TCR binds to an MHC:GATA3 peptide complex, wherein the GATA peptide comprises at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25 amino acids encoded by a GATA3 neoORF sequence and at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25 amino acids encoded by a GATA3 wild type sequence. In various embodiments, the TCR binds to an MHC:GATA3 peptide complex,

wherein the GATA peptide comprises at least one amino acid encoded by a GATA3 neoORF sequence and at least one amino acid not encoded by a GATA3 neoORF sequence. In various embodiments, the TCR binds to an MHC:GATA3 peptide complex, wherein the GATA peptide comprises at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25 amino acids encoded by a GATA3 neoORF sequence and at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25 amino acids not encoded by a GATA3 neoORF sequence. In various embodiments, the TCR binds to an MHC:GATA3 peptide complex, wherein each amino acid of the GATA peptide is an amino acid encoded by a GATA3 neoORF sequence. In various embodiments, the TCR binds to an MHC:GATA3 peptide complex, wherein the GATA3 peptide comprises a sequence of MLTGPPARV, KPKRDGYMF or ESKIMFATL.

[00241] In various embodiments, the human MHC is encoded by an HLA-A02:01, HLA-B07:02 or HLA-B08:01 allele. In various embodiments, the TCR binds to an MHC:GATA3 peptide complex, wherein the human MHC is encoded by an HLA-A02:01 allele. In various embodiments, the TCR binds to an MHC:GATA3 peptide complex, wherein the human MHC is encoded by an HLA-B07:02 allele. In various embodiments, the TCR binds to an MHC:GATA3 peptide complex, wherein the human MHC is encoded by an HLA-B08:01 allele.

[00242] In various embodiments, the TCR binds to an MHC:GATA3 peptide complex, wherein the human MHC is encoded by an HLA-B08:01 allele and wherein the GATA3 peptide comprises a sequence of MLTGPPARV, KPKRDGYMF or ESKIMFATL.

VIII. TCRs Specific to BTK peptide-MHC complexes

[00243] The *BTK* gene can encode a Bruton tyrosine kinase (BTK) protein, which can be related to the development and maturation of B cells. The BTK protein can transmit chemical signals that instruct B cells to mature and produce antibodies.

[00244] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from BTK in complex with a human MHC, wherein the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 161 and SEQ ID NO: 176, or wherein the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 164 and SEQ ID NO: 179.

[00245] Also provided herein is an isolated nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes a T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct, wherein the TCR specifically binds to a mutant BTK peptide in complex with an HLA-A02:01 protein; comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to SEQ ID NO: 161, 164, 176, or 179; and/or specifically binds to a mutant BTK peptide comprising a region with at least 70% sequence identity to SEQ ID NO: 173 or 188.

[00246] Also provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from BTK

in complex with a human MHC, wherein the epitope from BTK comprises a region having at least 90% sequence identity to amino acid sequence SEQ ID NO: 173 or 188.

[00247] In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 167 or 182.

[00248] In some embodiments, the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 170 or 185.

[00249] In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 159, 162, 174, and 177.

[00250] In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 160, 163, 175 and 178.

[00251] In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 167 or 182; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 170 or 185.

[00252] In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 159 or 174, a CDR2 of SEQ ID NO: 160 or 175, and a CDR3 of SEQ ID NO: 161 or 176; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 162 or 177, a CDR2 of SEQ ID NO: 163 or 178, and a CDR3 of SEQ ID NO: 164 or 179.

[00253] In some embodiments, the epitope comprises a point mutation. In some embodiments, the point mutation is C481S mutation.

[00254] In various embodiments, the nucleic acid sequence encoding a TCR is codon optimized.

[00255] In various embodiments, the TCR binds to an MHC:BTK peptide complex, wherein the BTK peptide comprises a point mutation. In various embodiments, the TCR binds to an MHC:BTK peptide complex, wherein the BTK peptide comprises a C481S point mutation. In various embodiments, the TCR binds to an MHC:BTK peptide complex, wherein the BTK peptide comprises a sequence of SLLNYLREM.

[00256] In some embodiments, the human MHC is encoded by HLA-A02:01 allele. In various embodiments, the human MHC is encoded by an HLA-A02:01 allele. In various embodiments, the TCR binds to an MHC:BTK peptide complex, wherein the human MHC is encoded by an HLA-A02:01 allele.

[00257] In various embodiments, the TCR binds to an MHC:BTK peptide complex, wherein the human MHC is encoded by an HLA-A02:01 allele and wherein the BTK peptide comprises a sequence of SLLNYLREM.

IX. TCRs Specific to EGFR peptide-MHC complexes

[00258] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from EGFR in complex with a human MHC, wherein the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO:

449, SEQ ID NO: 466, SEQ ID NO: 483, SEQ ID NO: 500, and SEQ ID NO: 517, or wherein the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 452, SEQ ID NO: 469, SEQ ID NO: 486, SEQ ID NO: 503, and SEQ ID NO: 520.

[00259] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) capable of specifically binding to a mutant EGFR peptide in complex with a protein encoded by an HLA allele of a subject with cancer, wherein the TCR comprises a TCR alpha chain construct and/or a TCR beta chain construct.

[00260] Provided herein is an isolated nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes a T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct, wherein the TCR specifically binds to a mutant EGFR peptide in complex with an HLA-A02:01 protein; comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to SEQ ID NO: 449, 466, 483, 500, 517, 452, 469, 486, 503, or 520; and/or specifically binds to a mutant EGFR peptide comprising a region with at least 70% sequence identity to SEQ ID NO: 461, 462, 463, 478, 479, 480, 495, 496, 497, 512, 513, 514, 529, 530 or 531.

[00261] Provided herein is a nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from EGFR in complex with a human MHC, wherein the epitope from EGFR comprises a region having at least 90% sequence identity to amino acid sequence SEQ ID NO: 461, 462, 463, 478, 479, 480, 495, 496, 497, 512, 513, 514, 529, 530 or 531.

[00262] In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 449, 466, 483, 500 or 517.

[00263] In some embodiments, the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 452, 469, 486, 503, or 520.

[00264] In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 447, 464, 481, 498, 515, 450, 467, 484, 501, and 518.

[00265] In some embodiments, the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NOs: 448, 465, 482, 499, 516, 451, 468, 485, 502, and 519.

[00266] In some embodiments, the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 455, 472, 489, 506, or 523; and the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 458, 475, 492, 509 or 526.

[00267] In some embodiments, the TCR alpha chain construct comprises a CDR1 of SEQ ID NO: 447, 464, 481, 498 or 515, a CDR2 of SEQ ID NO: 448, 465, 482, 499 or 516, and a CDR3 of SEQ ID NO: 449, 466, 483, 500 or 517; and the TCR beta chain construct comprises a CDR1 of SEQ ID NO: 450, 467, 484, 501 or

518, a CDR2 of SEQ ID NO: 451, 468, 485, 502, or 519, and a CDR3 of SEQ ID NO: 452, 469, 486, 503, or 520.

[00268] In some embodiments, the epitope comprises a point mutation. In some embodiments, the point mutation is a T790M mutation. In some embodiments, the human MHC is encoded by an HLA-A02:01 allele.

[00269] In various embodiments, the nucleic acid sequence encoding a TCR is codon optimized.

[00270] In various embodiments, the TCR binds to an MHC:EGFR peptide complex, wherein the EGFR peptide comprises a point mutation. In various embodiments, the TCR binds to an MHC:EGFR peptide complex, wherein the EGFR peptide comprises a T790M point mutation. In various embodiments, the TCR binds to an MHC:EGFR peptide complex, wherein the EGFR peptide comprises a sequence of QLIMQLMPF, LIMQLMPFGC or MQLMPFGCLL.

[00271] In various embodiments, the human MHC is encoded by an HLA-A02:01 allele. In various embodiments, the TCR binds to an MHC:EGFR peptide complex, wherein the human MHC is encoded by an HLA-A02:01 allele.

[00272] In various embodiments, the TCR binds to an MHC:EGFR peptide complex, wherein the human MHC is encoded by an HLA-A02:01 allele and wherein the EGFR peptide comprises a sequence of QLIMQLMPF, LIMQLMPFGC or MQLMPFGCLL.

[00273] Delivery of Nucleic Acid or Vector

[00274] Nucleic acids encoding TCRs or vectors containing such nucleic acids can be delivered to host cells for expression and processing.

[00275] Terms such as “transferring”, “introducing” or “transfecting” are used interchangeably herein and relate to the introduction of nucleic acids, in particular exogenous or heterologous nucleic acids, into a cell.

[00276] Cells can be transfected with any carriers with which nucleic acid can be associated, e.g., by forming complexes with the nucleic acid or forming vesicles in which the nucleic acid is enclosed or encapsulated, resulting in increased stability of the nucleic acid compared to naked nucleic acid. Carriers useful according to the present disclosure include, for example, lipid-containing carriers such as cationic lipids, liposomes, in particular cationic liposomes, and micelles, and nanoparticles. Cationic lipids may form complexes with negatively charged nucleic acids. Any cationic lipid may be used according to the present disclosure.

[00277] In various embodiments, a nucleic acid encoding a TCR disclosed herein is operably linked to a promoter. Furthermore, the present disclosure provides a vector, e.g. a plasmid, shuttle vector, phagemide, cosmid, expression vector, retroviral vector, adenoviral vector or particle and/or vector to be used in gene therapy, which comprises one or more of the nucleic acids as disclosed above. A “vector” is a nucleic acid molecule that is capable of transporting another nucleic acid. The vector comprises the nucleic acid insert, which encodes the polypeptide or protein desired for expression in a cell, such as a host cell. For the purposes of the disclosure, an insert may be a nucleic acid encoding a TCR; an alpha chain or a beta chain or both of a TCR. The term “incorporating” a nucleic acid sequence in a vector may mean preparing a suitable expression vector with an insert comprising said nucleic acid sequence. An “expression vector” is a vector that can direct the expression

of a protein encoded by one or more genes carried by the vector when it is present in the appropriate environment. "Retroviruses" are viruses having an RNA genome. "Gammaretrovirus" refers to a genus of the retroviridae family. Exemplary gammaretroviruses include, but are not limited to, mouse stem cell virus, murine leukemia virus, feline leukemia virus, feline sarcoma virus, and avian reticuloendotheliosis viruses. "Lentivirus" refers to a genus of retroviruses that are capable of infecting dividing and non-dividing cells. Several examples of lentiviruses include HIV (human immunodeficiency virus: including HIV type 1, and HIV type 2); equine infectious anemia virus; feline immunodeficiency virus (FIV); bovine immune deficiency virus (BIV); and simian immunodeficiency virus (SIV). A vector that encodes a core virus is also known as a "viral vector." There are a large number of available viral vectors that are suitable for use with the invention, including those identified for human gene therapy applications, such as those described by Pfeifer and Verma (Pfeifer, A. and I. M. Verma. 2001. *Ann. Rev. Genomics Hum. Genet.* 2:177-211). Suitable viral vectors include vectors based on RNA viruses, such as retrovirus-derived vectors, e.g., Moloney murine leukemia virus (MLV)-derived vectors, and include more complex retrovirus-derived vectors, e.g., lentivirus-derived vectors. HIV-1-derived vectors belong to this category. Other examples include lentivirus vectors derived from HIV-2, FIV, equine infectious anemia virus, SIV, and maedi/visna virus. Methods of using retroviral and lentiviral viral vectors and packaging cells for transducing mammalian target cells with viral particles containing TCRs transgenes are well known in the art and have been previously described, for example, in U.S. Pat. No. 8,119,772; Walchli et al., 2011, *PLoS One* 6:327930; Zhao et al., *J. Immunol.*, 2005, 174:4415-4423; Engels et al., 2003, *Hum. Gene Ther.* 14:1155-68; Frecha et al., 2010, *Mol. Ther.* 18:1748-57; Verhoeven et al., 2009, *Methods Mol. Biol.* 506:97-114. Retroviral and lentiviral vector constructs and expression systems are also commercially available. In some embodiments, a viral vector is used to introduce the non-endogenous nucleic acid sequence encoding TCR α chain specific for the peptide antigen into the hematopoietic progenitor cells. The viral vector may be a retroviral vector or a lentiviral vector. The viral vector may also include a nucleic acid sequence encoding a marker for transduction. Transduction markers for viral vectors are known in the art and include selection markers, which may confer drug resistance, or detectable markers, such as fluorescent markers or cell surface proteins that can be detected by methods such as flow cytometry. Where the viral vector genome comprises more than one nucleic acid sequence to be expressed in the host cell as separate transcripts, the viral vector may also comprise additional sequence between the two (or more) transcripts allowing bicistronic or multicistronic expression. Examples of such sequences used in viral vectors include internal ribosome entry sites (IRES), furin cleavage sites, viral 2A peptide. Other vectors also can be used for polynucleotide delivery including DNA viral vectors, including, for example adenovirus-based vectors and adeno-associated virus (AAV)-based vectors; vectors derived from herpes simplex viruses (HSVs), including amplicon vectors, replication-defective HSV and attenuated HSV (Krisky et al., 1998, *Gene Ther.* 5: 1517-30). Other vectors include those derived from baculoviruses and alpha-viruses. (Jolly D J. 1999. *Emerging viral vectors*. pp 209-40 in Friedmann T. ed. 1999. *The development of human gene therapy*. New York: Cold Spring Harbor Lab).

[00278] A vector may include nucleic acid sequences that permit the nucleic acid to replicate in a host cell, such as an origin of replication. A vector may also include one or more selectable marker genes and other genetic elements known to those of ordinary skill in the art. A vector preferably is an expression vector that includes a nucleic acid according to the present invention operably linked to sequences allowing for the expression of said nucleic acid.

[00279] In some embodiments, provided herein is a vector comprising a nucleic acid encoding a TCR disclosed herein. In some embodiments, the vector is a self-amplifying RNA replicon, plasmid, phage, transposon, cosmid, virus, or virion. In some embodiments, the vector is a viral vector. In some embodiments, the vector is derived from a retrovirus, lentivirus, adenovirus, adeno-associated virus, herpes virus, pox virus, alpha virus, vaccinia virus, hepatitis B virus, human papillomavirus or a pseudotype thereof. In some embodiments, the vector is a non-viral vector. In some embodiments, the non-viral vector is a nanoparticle, a cationic lipid, a cationic polymer, a metallic nanopolymer, a nanorod, a liposome, a micelle, a microbubble, a cell-penetrating peptide, or a liposphere.

[00280] Presented herein are constructs, for example, nucleic acid constructs that encode an alpha chain and a beta chain of a TCR for expression in a cell. In some embodiments, the constructs comprise one or more polynucleotides encoding a TCR alpha chain and a TCR beta chain. In some embodiments, the polynucleotides are incorporated in a suitable vector. In some embodiments, the polynucleotides encoding the alpha chain and the beta chain are incorporated in the same vector. In some embodiments, the polynucleotides encoding the alpha chain and the beta chain are incorporated in different vectors, and both vectors are delivered for expression in the single cell.

[00281] In some embodiments, a cell may be transduced or transfected with a nucleic acid encoding a TCR, wherein the cell is capable of expressing the TCR and the cell is used as a therapeutic. In some embodiments the cell is derived from a subject or a host, wherein the subject or the host is a human. In some embodiments, the subject or the host comprises a cell having a mutation in an epitope, and the TCR expressed in the cell is capable of binding specifically to the epitope having the mutation. In some embodiments, the cell is a lymphocyte cell. In some embodiments, the T-lymphocyte. In some embodiments, the cell is a lymphocytic precursor cell. In some embodiments, the cell is a T lymphocyte precursor cell. In some embodiments, the cell is a T lymphocyte progenitor cell. In some embodiments the cell is a thymocyte.

[00282] In some embodiments, the T cells are immature T cells. In some embodiments, the T cells are antigen naive T cells. The host cell may be cultured *ex vivo* for 1, 2, 3, 4, 5 or more days for monitoring and recover after transfection or transduction with the polynucleotide(s) encoding the TCR.

X. Neoantigens

[00283] The TCRs disclosed herein are specific to immunogenic neoantigens. In some embodiments, the neoantigen peptide is from RAS. In some embodiments, the neoantigen peptide is from GATA3. In some embodiments, the neoantigen peptide is from BTK. In some embodiments, the neoantigen peptide is from Tmprss2:ERG. In some embodiments, one or more neoantigen peptides are loaded on to APCs, wherein the

peptide loaded APCs are then used to stimulate T cells to produce antigen specific T cells. In some embodiments, the APCs used for peptide loading are dendritic cells. Immunogenic neoantigen sequences can be identified by any suitable method known in the art.

[00284] In various embodiments, the neoantigen comprises an epitope. In both animals and humans, mutated epitopes can be potentially effective in inducing an immune response or activating T cells. In some embodiments, the epitope comprises a mutation. In some embodiments, the mutation is selected from the group consisting of a point mutation, a splice-site mutation, a frameshift mutation, a read-through mutation, a gene fusion mutation and any combination thereof.

[00285] In some embodiments, the epitope has a length of at least 8 amino acids. In some embodiments, the epitope has a length of at least 16 amino acids. In some embodiments, the epitope has a length of from 8-25 amino acids. In some embodiments, the epitope has a length of from 8-12 amino acids. In some embodiments, the epitope has a length of from 16-25 amino acids. In some embodiments, the epitope has a length of 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acids.

[00286] In certain embodiments, a neoantigen or epitope thereof can comprise, but is not limited to, about 5, about 6, about 7, about 8, about 9, about 10, about 11, about 12, about 13, about 14, about 15, about 16, about 17, about 18, about 19, about 20, about 21, about 22, about 23, about 24, about 25, about 26, about 27, about 28, about 29, about 30, about 31, about 32, about 33, about 34, about 35, about 36, about 37, about 38, about 39, about 40, about 41, about 42, about 43, about 44, about 45, about 46, about 47, about 48, about 49, about 50, about 60, about 70, about 80, about 90, about 100, about 110, about 120 or greater amino acid residues, and any range derivable therein. In specific embodiments, a neoantigen or epitope thereof is equal to or less than 100 amino acids.

[00287] In some embodiments, a neoantigen or epitope thereof for MHC Class I is 13 residues or less in length and usually consists of between about 8 and about 11 residues, particularly 9 or 10 residues. In some embodiments, a neoantigen or epitope thereof for MHC Class II is 9-24 residues in length.

[00288] In some embodiments, neoantigens bind an HLA protein (e.g., HLA class I or HLA class II). In specific embodiments neoantigens bind an HLA protein with greater affinity than a corresponding wild-type peptide. In specific embodiments, the neoantigenic peptide or polypeptide has an IC₅₀ of at least less than 5000 nM, at least less than 500 nM, at least less than 100 nM, at least less than 50 nM or less.

[00289] In some embodiments, the epitope binds to the human MHC with a greater affinity than a corresponding wild-type epitope. In some embodiments, the epitope binds to the human MHC with a K_D or an IC₅₀ less than 500 nM, 250 nM, 150 nM, 100 nM, 50 nM, 25 nM or 10 nM. In some embodiments, the epitope comprises a mutation, wherein the mutation is not present in non-cancer cells of a subject. In some embodiments, the epitope is encoded by a gene or an expressed gene of a subject's cancer cells. In some embodiments, the TCR binds to an HLA-peptide complex with a K_D or an IC₅₀ of less than 500 nM, 250 nM, 150 nM, 100 nM, 50 nM, 25 nM or 10 nM.

[00290] In some embodiments, the neoantigenic peptide can be from about 8 and about 50 amino acid residues in length, or from about 8 and about 30, from about 8 and about 20, from about 8 and about 18, from about 8 and about 15, or from about 8 and about 12 amino acid residues in length. In some embodiments, the neoantigenic peptide can be from about 8 and about 500 amino acid residues in length, or from about 8 and about 450, from about 8 and about 400, from about 8 and about 350, from about 8 and about 300, from about 8 and about 250, from about 8 and about 200, from about 8 and about 150, from about 8 and about 100, from about 8 and about 50, or from about 8 and about 30 amino acid residues in length.

[00291] In some embodiments, the neoantigenic peptide can be at least 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, or more amino acid residues in length. In some embodiments, the neoantigenic peptide can be at least 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 55, 60, 70, 80, 90, 100, 150, 200, 250, 300, 350, 400, 450, 500 or more amino acid residues in length. In some embodiments, the neoantigenic peptide can be at most 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, or less amino acid residues in length. In some embodiments, the neoantigenic peptide can be at most 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 55, 60, 70, 80, 90, 100, 150, 200, 250, 300, 350, 400, 450, 500, or less amino acid residues in length.

[00292] In some embodiments, the neoantigenic peptide has a total length of at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, at least 20, at least 21, at least 22, at least 23, at least 24, at least 25, at least 26, at least 27, at least 28, at least 29, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90, at least 100, at least 150, at least 200, at least 250, at least 300, at least 350, at least 400, at least 450, or at least 500 amino acids.

[00293] In some embodiments, the neoantigenic peptide has a total length of at most 8, at most 9, at most 10, at most 11, at most 12, at most 13, at most 14, at most 15, at most 16, at most 17, at most 18, at most 19, at most 20, at most 21, at most 22, at most 23, at most 24, at most 25, at most 26, at most 27, at most 28, at most 29, at most 30, at most 40, at most 50, at most 60, at most 70, at most 80, at most 90, at most 100, at most 150, at most 200, at most 250, at most 300, at most 350, at most 400, at most 450, or at most 500 amino acids.

[00294] In some embodiments, the neoantigenic peptide can have a pI value of about 0.5 and about 12, about 2 and about 10, or about 4 and about 8. In some embodiments, the neoantigenic peptide can have a pI value of at least 4.5, 5, 5.5, 6, 6.5, 7, 7.5, or more. In some embodiments, the neoantigenic peptide can have a pI value of at most 4.5, 5, 5.5, 6, 6.5, 7, 7.5, or less.

[00295] In some embodiments, the neoantigenic peptide can have an HLA binding affinity of between about 1pM and about 1mM, about 100pM and about 500μM, about 500pM and about 10μM, about 1nM and about 1μM, or about 10nM and about 1μM. In some embodiments, the neoantigenic peptide can have an HLA binding affinity of at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100,

150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 700, 800, 900 μ M, or more. In some embodiments, the neoantigenic peptide can have an HLA binding affinity of at most 2, 3, 4, 5, 6, 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 700, 800, 900 μ M.

[00296] In some embodiments, a neoantigenic peptide described herein can comprise carriers such as those well known in the art, e.g., thyroglobulin, albumins such as human serum albumin, tetanus toxoid, polyamino acid residues such as poly L-lysine, poly L-glutamic acid, influenza virus proteins, hepatitis B virus core protein, and the like.

[00297] In some embodiments, a neoantigenic peptide described herein can be modified by terminal-NH₂ acylation, e.g., by alkanoyl (C1-C20) or thioglycolyl acetylation, terminal-carboxyl amidation, e.g., ammonia, methylamine, etc. In some embodiments, these modifications can provide sites for linking to a support or other molecule.

[00298] In some embodiments, a neoantigenic peptide described herein can contain modifications such as but not limited to glycosylation, side chain oxidation, biotinylation, phosphorylation, addition of a surface active material, e.g. a lipid, or can be chemically modified, e.g., acetylation, etc. Moreover, bonds in the peptide can be other than peptide bonds, e.g., covalent bonds, ester or ether bonds, disulfide bonds, hydrogen bonds, ionic bonds, etc.

[00299] In some embodiments, a neoantigenic peptide described herein can contain substitutions to modify a physical property (e.g., stability or solubility) of the resulting peptide. For example, neoantigenic peptides can be modified by the substitution of a cysteine (C) with α -amino butyric acid ("B"). Due to its chemical nature, cysteine has the propensity to form disulfide bridges and sufficiently alter the peptide structurally so as to reduce binding capacity. Substituting α -amino butyric acid for C not only alleviates this problem, but actually improves binding and cross-binding capability in certain instances. Substitution of cysteine with α -amino butyric acid can occur at any residue of a neoantigenic peptide, e.g., at either anchor or non-anchor positions of an epitope or analog within a peptide, or at other positions of a peptide.

[00300] In some embodiments, a neoantigenic peptide described herein can comprise amino acid mimetics or unnatural amino acid residues, e.g. D- or L-naphylalanine; D- or L-phenylglycine; D- or L-2-thienylalanine; D- or L-1, -2, 3-, or 4-pyrenylalanine; D- or L-3 thienylalanine; D- or L-(2-pyridinyl)-alanine; D- or L-(3-pyridinyl)-alanine; D- or L-(2-pyrazinyl)-alanine; D- or L-(4-isopropyl)-phenylglycine; D-(trifluoromethyl)-phenylglycine; D-(trifluoro-methyl)-phenylalanine; D- ρ -fluorophenylalanine; D- or L- ρ -biphenyl-phenylalanine; D- or L- ρ -methoxybiphenylphenylalanine; D- or L-2-indole(allyl)alanines; and, D- or L-alkylalanines, where the alkyl group can be a substituted or unsubstituted methyl, ethyl, propyl, hexyl, butyl, pentyl, isopropyl, iso-butyl, sec-isotyl, iso-pentyl, or a non-acidic amino acid residues. Aromatic rings of a non-natural amino acid include, e.g., thiazolyl, thiophenyl, pyrazolyl, benzimidazolyl, naphthyl, furanyl, pyrrolyl, and pyridyl aromatic rings. Modified peptides that have various amino acid mimetics or unnatural amino acid

residues are particularly useful, as they tend to manifest increased stability in vivo. Such peptides can also possess improved shelf-life or manufacturing properties.

[00301] Peptide stability can be assayed in a number of ways. For instance, peptidases and various biological media, such as human plasma and serum, have been used to test stability. See, e.g., Verhoef, et al., *Eur. J. Drug Metab. Pharmacokinetics* 11:291 (1986). Half-life of the peptides described herein is conveniently determined using a 25% human serum (v/v) assay. The protocol is as follows: pooled human serum (Type AB, non-heat inactivated) is delipidated by centrifugation before use. The serum is then diluted to 25% with RPMI-1640 or another suitable tissue culture medium. At predetermined time intervals, a small amount of reaction solution is removed and added to either 6% aqueous trichloroacetic acid (TCA) or ethanol. The cloudy reaction sample is cooled (4°C) for 15 minutes and then spun to pellet the precipitated serum proteins. The presence of the peptides is then determined by reversed-phase HPLC using stability-specific chromatography conditions.

[00302] In some embodiments, a neoantigenic peptide described herein can be prepared synthetically, by recombinant DNA technology or chemical synthesis, or can be isolated from natural sources such as native tumors or pathogenic organisms. Epitopes can be synthesized individually or joined directly or indirectly in a peptide. Although a neoantigenic peptide described herein will be substantially free of other naturally occurring host cell proteins and fragments thereof, in some embodiments, the peptide can be synthetically conjugated to be joined to native fragments or particles.

[00303] In some embodiments, a neoantigenic peptide described herein can be prepared in a wide variety of ways. In some embodiments, the peptides can be synthesized in solution or on a solid support according to conventional techniques. Various automatic synthesizers are commercially available and can be used according to known protocols. (See, for example, Stewart & Young, *SOLID PHASE PEPTIDE SYNTHESIS*, 2D. ED., Pierce Chemical Co., 1984). Further, individual peptides can be joined using chemical ligation to produce larger peptides that are still within the bounds of the invention.

[00304] Alternatively, recombinant DNA technology can be employed wherein a nucleotide sequence which encodes a peptide inserted into an expression vector, transformed or transfected into an appropriate host cell and cultivated under conditions suitable for expression. These procedures are generally known in the art, as described generally in Sambrook et al., *MOLECULAR CLONING, A LABORATORY MANUAL*, Cold Spring Harbor Press, Cold Spring Harbor, N.Y. (1989). Thus, recombinant peptides, which comprise or consist of one or more epitopes described herein, can be used to present the appropriate T cell epitope.

XI. Pharmaceutical Compositions

[00305] Pharmaceutical compositions can be formulated using one or more physiologically acceptable carriers including excipients and auxiliaries which facilitate processing of the active agents into preparations which can be used pharmaceutically. Proper formulation can be dependent upon the route of administration chosen. Any of the well-known techniques, carriers, and excipients can be used as suitable and as understood in the art.

[00306] In some cases, a pharmaceutical composition is formulated as cell based therapeutic, e.g., a T cell therapeutics. In some embodiments, a pharmaceutical composition comprises a peptide-based therapy, a nucleic

acid-based therapy, an antibody-based therapy, and/or a cell-based therapy. In some embodiments, a pharmaceutical composition comprises a peptide-based therapeutic, or nucleic acid based therapeutic in which the nucleic acid encodes the polypeptides. A composition can comprise T cells specific for two or more immunogenic antigen or neoantigen peptides. In some embodiments, the T cell specific therapeutic may be supplemented by one or more additional therapies.

[00307] In some embodiments, a pharmaceutical composition comprising: a nucleic acid encoding a TCR targeting a neoantigen disclosed herein, a vector containing the nucleic acid, the protein encoded by the nucleic acid, or a host cell comprising the nucleic acid, the protein or the vector; and a pharmaceutically acceptable excipient or diluent. In some embodiments, the pharmaceutical composition further comprises an immunomodulatory agent or an adjuvant. In some embodiments, the immunomodulatory agent is a cytokine. In some embodiments, the adjuvant is poly I:C.

[00308] Also provided herein is the use of the pharmaceutical compositions in treating an immune disease or cancer.

[00309] Pharmaceutical compositions can include, in addition to active ingredient, a pharmaceutically acceptable excipient, carrier, buffer, stabilizer or other materials well known to those skilled in the art. Such materials should be non-toxic and should not interfere with the efficacy of the active ingredient. The precise nature of the carrier or other material will depend on the route of administration. Acceptable carriers, excipients, or stabilizers are those that are non-toxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid and methionine; preservatives (such as octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride, benzethonium chloride; phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol; and m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming counter-ions such as sodium; metal complexes (e.g., Zn-protein complexes); and/or non-ionic surfactants such as TWEEN®, PLURONICS® or polyethylene glycol (PEG).

[00310] Acceptable carriers are physiologically acceptable to the administered patient and retain the therapeutic properties of the compounds with/in which it is administered. Acceptable carriers and their formulations are generally described in, for example, Remington's Pharmaceutical Sciences (18th ed. A. Gennaro, Mack Publishing Co., Easton, PA 1990). One example of carrier is physiological saline. A pharmaceutically acceptable carrier is a pharmaceutically acceptable material, composition or vehicle, such as a liquid or solid filler, diluent, excipient, solvent or encapsulating material, involved in carrying or transporting the subject compounds from the administration site of one organ, or portion of the body, to another organ, or portion of the body, or in an in vitro assay system. Acceptable carriers are compatible with the other ingredients of the

formulation and not injurious to a subject to whom it is administered. Nor should an acceptable carrier alter the specific activity of the other ingredients.

[00311] In one aspect, provided herein are pharmaceutically acceptable or physiologically acceptable compositions including solvents (aqueous or non-aqueous), solutions, emulsions, dispersion media, coatings, isotonic and absorption promoting or delaying agents, compatible with pharmaceutical administration. Pharmaceutical compositions or pharmaceutical formulations therefore refer to a composition suitable for pharmaceutical use in a subject. Compositions can be formulated to be compatible with a particular route of administration (i.e., systemic or local). Thus, compositions include carriers, diluents, or excipients suitable for administration by various routes.

[00312] In some embodiments, a pharmaceutical composition can further comprise an acceptable additive in order to improve the stability of the composition. Acceptable additives may not alter the specific activity of the active agent, *e.g.* immune cells. Examples of acceptable additives include, but are not limited to, a sugar such as mannitol, sorbitol, glucose, xylitol, trehalose, sorbose, sucrose, galactose, dextran, dextrose, fructose, lactose and mixtures thereof. Acceptable additives can be combined with acceptable carriers and/or excipients such as dextrose. Alternatively, examples of acceptable additives include, but are not limited to, a surfactant such as polysorbate 20 or polysorbate 80 to increase stability of the peptide and decrease gelling of the solution. The surfactant can be added to the composition in an amount of 0.01% to 5% of the solution. Addition of such acceptable additives increases the stability and half-life of the composition in storage.

[00313] In some embodiments the pharmaceutical composition comprises a therapeutic which is a T cell expressing one or more polynucleotides, encoding a T cell receptor. In some embodiments, the pharmaceutical composition comprises physiologically acceptable carrier suitable for a cell suspension.

[00314] The pharmaceutical composition can be administered, for example, by injection. Pharmaceutical compositions for injection include aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, or phosphate buffered saline (PBS). The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. Fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Antibacterial and antifungal agents include, for example, parabens, chlorobutanol, phenol, ascorbic acid and thimerosal. Isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, and sodium chloride can be included in the composition. The resulting solutions can be packaged for use as is, or lyophilized; the lyophilized preparation can later be combined with a sterile solution prior to administration. For intravenous, injection, or injection at the site of affliction, the active ingredient will be in the form of a parenterally acceptable aqueous solution which is pyrogen-free and has suitable pH, isotonicity and stability. Those of relevant skill in the art are well able to prepare suitable solutions using, for example, isotonic vehicles such as Sodium Chloride Injection, Ringer's

Injection, Lactated Ringer's Injection. Preservatives, stabilizers, buffers, antioxidants and/or other additives can be included, as needed. Sterile injectable solutions can be prepared by incorporating an active ingredient in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active ingredient into a sterile vehicle which contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation can be vacuum drying and freeze drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

[00315] Pharmaceutical compositions can be conventionally administered intravenously, such as by injection of a unit dose, for example. For injection, an active ingredient can be in the form of a parenterally acceptable aqueous solution which is substantially pyrogen-free and has suitable pH, isotonicity and stability. One can prepare suitable solutions using, for example, isotonic vehicles such as Sodium Chloride Injection, Ringer's Injection, Lactated Ringer's Injection. Preservatives, stabilizers, buffers, antioxidants and/or other additives can be included, as required. Additionally, compositions can be administered via aerosolization.

[00316] When the pharmaceutical compositions are considered for use in medicaments or any of the methods provided herein, it is contemplated that the composition can be substantially free of pyrogens such that the composition will not cause an inflammatory reaction or an unsafe allergic reaction when administered to a human patient. Testing compositions for pyrogens and preparing compositions substantially free of pyrogens are well understood to one of ordinary skill of the art and can be accomplished using commercially available kits.

[00317] Acceptable carriers can contain a compound that stabilizes, increases or delays absorption, or increases or delays clearance. Such compounds include, for example, carbohydrates, such as glucose, sucrose, or dextrans; low molecular weight proteins; compositions that reduce the clearance or hydrolysis of peptides; or excipients or other stabilizers and/or buffers. Agents that delay absorption include, for example, aluminum monostearate and gelatin. Detergents can also be used to stabilize or to increase or decrease the absorption of the pharmaceutical composition, including liposomal carriers. To protect from digestion the compound can be complexed with a composition to render it resistant to acidic and enzymatic hydrolysis, or the compound can be complexed in an appropriately resistant carrier such as a liposome. Means of protecting compounds from digestion are known in the art (e.g., Fix (1996) *Pharm Res.* 13:1760-1764; Samanen (1996) *J. Pharm. Pharmacol.* 48:119-135; and U.S. Pat. No. 5,391,377).

[00318] The pharmaceutical compositions can be administered in a manner compatible with the dosage formulation, and in a therapeutically effective amount. The quantity to be administered depends on the subject to be treated, capacity of the subject's immune system to utilize the active ingredient, and degree of binding capacity desired. Precise amounts of active ingredient required to be administered depend on the judgment of the practitioner and are peculiar to each individual. Suitable regimes for initial administration and booster shots are also variable, but, are typified by an initial administration followed by repeated doses at one or more hour

intervals by a subsequent injection or other administration. Alternatively, continuous intravenous infusions sufficient to maintain concentrations in the blood are contemplated.

[00319] In some embodiments, the present disclosure is directed to an immunogenic composition, e.g., a pharmaceutical composition capable of raising a neoantigen-specific response (e.g., a humoral or cell-mediated immune response). In some embodiments, the immunogenic composition comprises neoantigen therapeutics (e.g., peptides, polynucleotides, TCR, CAR, cells containing TCR or CAR, dendritic cell containing polypeptide, dendritic cell containing polynucleotide, antibody, etc.) described herein corresponding to a tumor specific antigen or neoantigen.

[00320] In some embodiments, a pharmaceutical composition described herein is capable of raising a specific cytotoxic T cells response, specific helper T cell response, or a B cell response.

[00321] In some embodiments, antigen polypeptides or polynucleotides can be provided as antigen presenting cells (e.g., dendritic cells) containing such polypeptides or polynucleotides. In other embodiments, such antigen presenting cells are used to stimulate T cells for use in patients. In some embodiments, the antigen presenting cells are dendritic cells. In related embodiments, the dendritic cells are autologous dendritic cells that are pulsed with the neoantigen peptide or nucleic acid. The neoantigen peptide can be any suitable peptide that gives rise to an appropriate T cell response. In some embodiments, the T cell is a CTL. In some embodiments, the T cell is an HTL. Thus, one embodiment of the present disclosure is an immunogenic composition containing at least one antigen presenting cell (e.g., a dendritic cell) that is pulsed or loaded with one or more neoantigen polypeptides or polynucleotides described herein. In some embodiments, such APCs are autologous (e.g., autologous dendritic cells). Alternatively, peripheral blood mononuclear cells (PBMCs) isolated from a patient can be loaded with neoantigen peptides or polynucleotides ex vivo. In related embodiments, such APCs or PBMCs are injected back into the patient. The polynucleotide can be any suitable polynucleotide that is capable of transducing the dendritic cell, thus resulting in the presentation of a neoantigen peptide and induction of immunity. In some embodiments, such antigen presenting cells (APCs) (e.g., dendritic cells) or peripheral blood mononuclear cells (PBMCs) are used to stimulate a T cell (e.g., an autologous T cell, or an allogeneic T cell). In related embodiments, the T cell is a CTL. In other related embodiments, the T cell is an HTL. In some embodiments, the T cells are CD8⁺ T cells. In some embodiments, the T cells are CD4⁺ T cells. Such T cells are then injected into the patient. In some embodiments, CTL is injected into the patient. In some embodiments, HTL is injected into the patient. In some embodiments, both CTL and HTL are injected into the patient. Administration of either therapeutic can be performed simultaneously or sequentially and in any order.

[00322] In some embodiments, pharmaceutical compositions (e.g., immunogenic compositions) described herein for therapeutic treatment can be formulated for parenteral, topical, nasal, oral or local administration. In some embodiments, the pharmaceutical compositions described herein are administered parenterally, e.g., intravenously, subcutaneously, intradermally, or intramuscularly. In some embodiments, the composition can be administered intratumorally. The compositions can be administered at the site of surgical excision to induce a local immune response to the tumor. In some embodiments, described herein are compositions for parenteral

administration which comprise a solution of the neoantigen peptides and immunogenic compositions are dissolved or suspended in an acceptable carrier, for example, an aqueous carrier. A variety of aqueous carriers can be used, e.g., water, buffered water, 0.9% saline, 0.3% glycine, hyaluronic acid and the like. These compositions can be sterilized by conventional, well known sterilization techniques, or can be sterile filtered. The resulting aqueous solutions can be packaged for use as is, or lyophilized, the lyophilized preparation being combined with a sterile solution prior to administration. The compositions can contain pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions, such as pH adjusting and buffering agents, tonicity adjusting agents, wetting agents and the like, for example, sodium acetate, sodium lactate, sodium chloride, potassium chloride, calcium chloride, sorbitan monolaurate, triethanolamine oleate, etc.

[00323] The ability of an adjuvant to increase the immune response to an antigen is typically manifested by a significant increase in immune-mediated reaction, or reduction in disease symptoms. For example, an increase in humoral immunity can be manifested by a significant increase in the titer of antibodies raised to the antigen, and an increase in T cell activity can be manifested in increased cell proliferation, or cellular cytotoxicity, or cytokine secretion. An adjuvant can also alter an immune response, for example, by changing a primarily humoral or T helper 2 response into a primarily cellular, or T helper 1 response.

[00324] Suitable adjuvants are known in the art (see, WO 2015/095811) and include, but are not limited to poly(I:C), poly-ICLC, STING agonist, 1018 ISS, aluminum salts, Amplivax, AS15, BCG, CP-870,893, CpG7909, CyaA, dSLIM, GM-CSF, IC30, IC31, Imiquimod, ImuFact IMP321, IS Patch, ISS, ISCOMATRIX, JuvImmune, LipoVac, MF59, monophosphoryl lipid A, Montanide IMS 1312, Montanide ISA 206, Montanide ISA 50V, Montanide ISA-51, OK-432, OM-174, OM-197-MP-EC, ONTAK, PepTel® vector system, PLG microparticles, resiquimod, SRL172, virosomes and other virus-like particles, YF-17D, VEGF trap, R848, β -glucan, Pam3Cys, Pam3CSK4, Aquila's QS21 stimulon (Aquila Biotech, Worcester, Mass., USA) which is derived from saponin, mycobacterial extracts and synthetic bacterial cell wall mimics, and other proprietary adjuvants such as Ribi's Detox. Quil or Superfos. Several immunological adjuvants (e.g., MF59) specific for dendritic cells and their preparation have been described (Dupuis M, et al., *Cell Immunol.* 1998; 186(1):18-27; Allison A C; *Dev Biol Stand.* 1998; 92:3-11) (Mosca et al. *Frontiers in Bioscience*, 2007; 12:4050-4060) (Gamvrellis et al. *Immunol & Cell Biol.* 2004; 82: 506-516). Also cytokines can be used. Several cytokines have been directly linked to influencing dendritic cell migration to lymphoid tissues (e.g., TNF- α), accelerating the maturation of dendritic cells into efficient antigen-presenting cells for T-lymphocytes (e.g., GM-CSF, PGE1, PGE2, IL-1, IL-1 β , IL-4, IL-6 and CD40L) (U.S. Pat. No. 5,849,589 incorporated herein by reference in its entirety) and acting as immunoadjuvants (e.g., IL-12) (Gabrilovich D I, et al., *J Immunother Emphasis Tumor Immunol.* 1996 (6):414-418).

[00325] CpG immunostimulatory oligonucleotides have also been reported to enhance the effects of adjuvants in a therapeutic setting. Without being bound by theory, CpG oligonucleotides act by activating the innate (non-adaptive) immune system via Toll-like receptors (TLR), mainly TLR9. CpG triggered TLR9 activation

enhances antigen-specific humoral and cellular responses to a wide variety of antigens, including peptide or protein antigens, live or killed viruses, dendritic cell immunogenic pharmaceutical compositions, autologous cellular immunogenic pharmaceutical compositions and polysaccharide conjugates in both prophylactic and therapeutic immunogenic pharmaceutical compositions. Importantly, it enhances dendritic cell maturation and differentiation, resulting in enhanced activation of TH1 cells and strong cytotoxic T-lymphocyte (CTL) generation, even in the absence of CD4+ T cell help. The TH1 bias induced by TLR9 stimulation is maintained even in the presence of adjuvants such as alum or incomplete Freund's adjuvant (IFA) that normally promote a TH2 bias. CpG oligonucleotides show even greater adjuvant activity when formulated or co-administered with other adjuvants or in formulations such as microparticles, nanoparticles, lipid emulsions or similar formulations, which are especially useful for inducing a strong response when the antigen is relatively weak. They can also accelerate the immune response and enabled the antigen doses to be reduced with comparable antibody responses to the full-dose immunogenic pharmaceutical composition without CpG in some experiments (Arthur M. Krieg, *Nature Reviews, Drug Discovery*, 5, June 2006, 471-484). U.S. Pat. No. 6,406,705 describes the combined use of CpG oligonucleotides, non-nucleic acid adjuvants and an antigen to induce an antigen-specific immune response. A commercially available CpG TLR9 antagonist is dSLIM (double Stem Loop Immunomodulator) by Mologen (Berlin, DE), which is a component of the pharmaceutical composition described herein. Other TLR binding molecules such as RNA binding TLR7, TLR8 and/or TLR9 can also be used.

[00326] Other examples of useful adjuvants include, but are not limited to, chemically modified CpGs (e.g. CpR, Idera), Poly(I:C)(e.g., polyI:CI2U), polyIC:LC, non-CpG bacterial DNA or RNA, ssRNA40 for TLR8, as well as immunoactive small molecules and antibodies such as cyclophosphamide, sunitinib, bevacizumab, celebrex, NCX-4016, sildenafil, tadalafil, vardenafil, sorafenib, XL-999, CP-547632, pazopanib, ZD2171, AZD2171, ipilimumab, tremelimumab, and SC58175, which can act therapeutically and/or as an adjuvant. The amounts and concentrations of adjuvants and additives useful in the context of the present invention can readily be determined by the skilled artisan without undue experimentation. Additional adjuvants include colony-stimulating factors, such as Granulocyte Macrophage Colony Stimulating Factor (GM-CSF, sargramostim).

[00327] In some embodiments, an immunogenic composition according to the present disclosure can comprise more than one different adjuvant. Furthermore, the invention encompasses a pharmaceutical composition comprising any adjuvant substance including any of the above or combinations thereof. In some embodiments, the immunogenic composition comprises neoantigen therapeutics (e.g., peptides, polynucleotides, TCR, CAR, cells containing TCR or CAR, dendritic cell containing polypeptide, dendritic cell containing polynucleotide, antibody, etc.) and the adjuvant can be administered separately in any appropriate sequence.

[00328] Lipidation can be classified into several different types, such as N-myristoylation, palmitoylation, GPI-anchor addition, prenylation, and several additional types of modifications. N-myristoylation is the covalent attachment of myristate, a C14 saturated acid, to a glycine residue. Palmitoylation is thioester linkage of long-chain fatty acids (C16) to cysteine residues. GPI-anchor addition is glycosyl-phosphatidylinositol (GPI) linkage

via amide bond. Prenylation is the thioether linkage of an isoprenoid lipid (e.g. farnesyl (C-15), geranylgeranyl (C-20)) to cysteine residues. Additional types of modifications can include attachment of S-diacylglycerol by a sulfur atom of cysteines, O-octanoyl conjugation via serine or threonine residues, S-archaeol conjugation to cysteine residues, and cholesterol attachment.

[00329] Fatty acids for generating a lipidated peptides can include C2 to C30 saturated, monounsaturated, or polyunsaturated fatty acyl groups. Exemplary fatty acids can include palmitoyl, myristoyl, stearoyl and decanoyl groups. In some instances, a lipid moiety that has adjuvant property is attached to a polypeptide of interest to elicit or enhance immunogenicity in the absence of an extrinsic adjuvant. A lipidated peptide or lipopeptide can be referred to as a self-adjuvant lipopeptide. Any of the fatty acids described above and elsewhere herein can elicit or enhance immunogenicity of a polypeptide of interest. A fatty acid that can elicit or enhance immunogenicity can include palmitoyl, myristoyl, stearoyl, lauroyl, octanoyl, and decanoyl groups.

[00330] Polypeptides such as naked peptides or lipidated peptides can be incorporated into a liposome. Sometimes, lipidated peptides can be incorporated into a liposome. For example, the lipid portion of the lipidated peptide can spontaneously integrate into the lipid bilayer of a liposome. Thus, a lipopeptide can be presented on the “surface” of a liposome.

[00331] Liposome can also be used to deliver nucleic acids into a cell. The nucleic acid of interest comprises one or more sequences encoding a T cell receptor. Liposomes may be used to deliver a DNA or an RNA. Liposomes may be used to deliver a nucleic acid incorporated in a vector. The nucleic acid may be 50-200,000 nucleotides long, or may be 100-500,000 nucleotides long, or may be 20-500,000 nucleotides long. Exemplary liposomes suitable for incorporation in the formulations include, and are not limited to, multilamellar vesicles (MLV), oligolamellar vesicles (OLV), unilamellar vesicles (UV), small unilamellar vesicles (SUV), medium-sized unilamellar vesicles (MUV), large unilamellar vesicles (LUV), giant unilamellar vesicles (GUV), multivesicular vesicles (MVV), single or oligolamellar vesicles made by reverse-phase evaporation method (REV), multilamellar vesicles made by the reverse-phase evaporation method (MLV-REV), stable plurilamellar vesicles (SPLV), frozen and thawed MLV (FATMLV), vesicles prepared by extrusion methods (VET), vesicles prepared by French press (FPV), vesicles prepared by fusion (FUV), dehydration-rehydration vesicles (DRV), and bubblesomes (BSV).

[00332] Depending on the method of preparation, liposomes can be unilamellar or multilamellar, and can vary in size with diameters ranging from about 0.02 μm to greater than about 10 μm . Liposomes can adsorb many types of cells and then release an incorporated agent (e.g., a peptide described herein). In some cases, the liposomes fuse with the target cell, whereby the contents of the liposome then empty into the target cell. A liposome can be endocytosed by cells that are phagocytic. Endocytosis can be followed by intralysosomal degradation of liposomal lipids and release of the encapsulated agents.

[00333] The liposomes provided herein can also comprise carrier lipids. In some embodiments, the carrier lipids are phospholipids. Carrier lipids capable of forming liposomes include, but are not limited to dipalmitoylphosphatidylcholine (DPPC), phosphatidylcholine (PC; lecithin), phosphatidic acid (PA),

phosphatidylglycerol (PG), phosphatidylethanolamine (PE), phosphatidylserine (PS). Other suitable phospholipids further include distearoylphosphatidylcholine (DSPC), dimyristoylphosphatidylcholine (DMPC), dipalmitoylphosphatidylglycerol (DPPG), distearoylphosphatidylglycerol (DSPG), dimyristoylphosphatidylglycerol (DMPG), dipalmitoylphosphatidic acid (DPPA); dimyristoylphosphatidic acid (DMPA), distearoylphosphatidic acid (DSPA), dipalmitoylphosphatidylserine (DPPS), dimyristoylphosphatidylserine (DMPS), distearoylphosphatidylserine (DSPS), dipalmitoylphosphatidylethanolamine (DPPE), dimyristoylphosphatidylethanolamine (DMPE), distearoylphosphatidylethanolamine (DSPE) and the like, or combinations thereof. In some embodiments, the liposomes further comprise a sterol (e.g., cholesterol) which modulates liposome formation. The carrier lipids can be any known non-phosphate polar lipids.

[00334] A pharmaceutical composition can be encapsulated within liposomes using well-known technology. Biodegradable microspheres can also be employed as carriers for the pharmaceutical compositions of this invention.

[00335] The pharmaceutical composition can be administered in liposomes or microspheres (or microparticles). Methods for preparing liposomes and microspheres for administration to a patient are well known to those of skill in the art. Essentially, material is dissolved in an aqueous solution, the appropriate phospholipids and lipids added, along with surfactants if required, and the material dialyzed or sonicated, as necessary.

[00336] Microspheres formed of polymers or proteins are well known to those skilled in the art, and can be tailored for passage through the gastrointestinal tract directly into the blood stream. Alternatively, the compound can be incorporated and the microspheres, or composite of microspheres, implanted for slow release over a period of time ranging from days to months.

[00337] Cell-based immunogenic pharmaceutical compositions can also be administered to a subject. For example, an antigen presenting cell (APC) based immunogenic pharmaceutical composition can be formulated using any of the well-known techniques, carriers, and excipients as suitable and as understood in the art. APCs include monocytes, monocyte-derived cells, macrophages, and dendritic cells. Sometimes, an APC based immunogenic pharmaceutical composition can be a dendritic cell-based immunogenic pharmaceutical composition.

[00338] A dendritic cell-based immunogenic pharmaceutical composition can be prepared by any methods well known in the art. In some cases, dendritic cell-based immunogenic pharmaceutical compositions can be prepared through an ex vivo or in vivo method. The ex vivo method can comprise the use of autologous DCs pulsed ex vivo with the polypeptides described herein, to activate or load the DCs prior to administration into the patient. The in vivo method can comprise targeting specific DC receptors using antibodies coupled with the polypeptides described herein. The DC-based immunogenic pharmaceutical composition can further comprise DC activators such as TLR3, TLR-7-8, and CD40 agonists. The DC-based immunogenic pharmaceutical composition can further comprise adjuvants, and a pharmaceutically acceptable carrier.

[00339] An adjuvant can be used to enhance the immune response (humoral and/or cellular) elicited in a patient receiving the immunogenic pharmaceutical composition. Sometimes, adjuvants can elicit a Th1-type response. Other times, adjuvants can elicit a Th2-type response. A Th1-type response can be characterized by the production of cytokines such as IFN- γ as opposed to a Th2-type response which can be characterized by the production of cytokines such as IL-4, IL-5 and IL-10.

[00340] In some aspects, lipid-based adjuvants, such as MPLA and MDP, can be used with the immunogenic pharmaceutical compositions disclosed herein. Monophosphoryl lipid A (MPLA), for example, is an adjuvant that causes increased presentation of liposomal antigen to specific T Lymphocytes. In addition, a muramyl dipeptide (MDP) can also be used as a suitable adjuvant in conjunction with the immunogenic pharmaceutical formulations described herein.

[00341] Adjuvant can also comprise stimulatory molecules such as cytokines. Non-limiting examples of cytokines include: CCL20, α -interferon (IFN α), β -interferon (IFN β), γ -interferon (IFN γ), platelet derived growth factor (PDGF), TNF α , GM-CSF, epidermal growth factor (EGF), cutaneous T cell-attracting chemokine (CTACK), epithelial thymus-expressed chemokine (TECK), mucosae-associated epithelial chemokine (MEC), IL-12, IL-15, IL-28, MHC, CD80, CD86, IL-1, IL-2, IL-4, IL-5, IL-6, IL-10, IL-18, MCP-1, MIP-1a, MIP-1-, IL-8, L-selectin, P-selectin, E-selectin, CD34, GlyCAM-1, MadCAM-1, LFA-1, VLA-1, Mac-1, p150.95, PECAM, ICAM-1, ICAM-2, ICAM-3, CD2, LFA-3, M-CSF, G-CSF, mutant forms of IL-18, CD40, CD40L, vascular growth factor, fibroblast growth factor, IL-7, nerve growth factor, vascular endothelial growth factor, Fas, TNF receptor, Fit, Apo-1, p55, WSL-1, DR3, TRAMP, Apo-3, AIR, LARD, NGRF, DR4, DRS, KILLER, TRAIL-R2, TRICK2, DR6, Caspase ICE, Fos, c-jun, Sp-1, Ap-1, Ap-2, p38, p65Rel, MyD88, IRAK, TRAF6, I κ B, Inactive NIK, SAP K, SAP-I, JNK, interferon response genes, NF κ B, Bax, TRAIL, TRAIL_{rec}, TRAIL_{rec}DRC5, TRAIL-R3, TRAIL-R4, RANK, RANK LIGAND, Ox40, Ox40 LIGAND, NKG2D, MICA, MICB, NKG2A, NKG2B, NKG2C, NKG2E, NKG2F, TAPI, and TAP2.

[00342] Additional adjuvants include: MCP-1, MIP-1a, MIP-1p, IL-8, RANTES, L-selectin, P-selectin, E-selectin, CD34, GlyCAM-1, MadCAM-1, LFA-1, VLA-1, Mac-1, p150.95, PECAM, ICAM-1, ICAM-2, ICAM-3, CD2, LFA-3, M-CSF, G-CSF, IL-4, mutant forms of IL-18, CD40, CD40L, vascular growth factor, fibroblast growth factor, IL-7, IL-22, nerve growth factor, vascular endothelial growth factor, Fas, TNF receptor, Fit, Apo-1, p55, WSL-1, DR3, TRAMP, Apo-3, AIR, LARD, NGRF, DR4, DR5, KILLER, TRAIL-R2, TRICK2, DR6, Caspase ICE, Fos, c-jun, Sp-1, Ap-1, Ap-2, p38, p65Rel, MyD88, IRAK, TRAF6, I κ B, Inactive NIK, SAP K, SAP-1, JNK, interferon response genes, NF κ B, Bax, TRAIL, TRAIL_{rec}, TRAIL_{rec}DRC5, TRAIL-R3, TRAIL-R4, RANK, RANK LIGAND, Ox40, Ox40 LIGAND, NKG2D, MICA, MICB, NKG2A, NKG2B, NKG2C, NKG2E, NKG2F, TAP1, TAP2 and functional fragments thereof.

[00343] In some aspects, an adjuvant can be a modulator of a toll like receptor. Examples of modulators of toll-like receptors include TLR9 agonists and are not limited to small molecule modulators of toll-like receptors such as Imiquimod. Sometimes, an adjuvant is selected from bacteria toxoids, polyoxypropylene-polyoxyethylene block polymers, aluminum salts, liposomes, CpG polymers, oil-in-water emulsions, or a

combination thereof. Sometimes, an adjuvant is an oil-in-water emulsion. The oil-in-water emulsion can include at least one oil and at least one surfactant, with the oil(s) and surfactant(s) being biodegradable (metabolizable) and biocompatible. The oil droplets in the emulsion can be less than 5 μm in diameter, and can even have a sub-micron diameter, with these small sizes being achieved with a microfluidiser to provide stable emulsions. Droplets with a size less than 220 nm can be subjected to filter sterilization.

[00344] In some instances, an immunogenic pharmaceutical composition can include carriers and excipients (including but not limited to buffers, carbohydrates, mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, bacteriostats, chelating agents, suspending agents, thickening agents and/or preservatives), water, oils including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like, saline solutions, aqueous dextrose and glycerol solutions, flavoring agents, coloring agents, and other acceptable additives, adjuvants, or binders, other pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions, such as pH buffering agents, tonicity adjusting agents, emulsifying agents, wetting agents and the like. Examples of excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the like. In another instances, the pharmaceutical preparation is substantially free of preservatives. In other instances, the pharmaceutical preparation can contain at least one preservative. It will be recognized that, while any suitable carrier known to those of ordinary skill in the art can be employed to administer the pharmaceutical compositions described herein, the type of carrier will vary depending on the mode of administration.

[00345] An immunogenic pharmaceutical composition can include preservatives such as thiomersal or 2-phenoxyethanol. In some instances, the immunogenic pharmaceutical composition is substantially free from (e.g., $<10 \mu\text{g/mL}$) mercurial material e.g. thiomersal-free. α -Tocopherol succinate may be used as an alternative to mercurial compounds.

[00346] For controlling the tonicity, a physiological salt such as sodium salt can be included in the immunogenic pharmaceutical composition. Other salts can include potassium chloride, potassium dihydrogen phosphate, disodium phosphate, and/or magnesium chloride, or the like.

[00347] An immunogenic pharmaceutical composition can have an osmolality of between 200 mOsm/kg and 400 mOsm/kg, between 240-360 mOsm/kg, or within the range of 290-310 mOsm/kg.

[00348] An immunogenic pharmaceutical composition can comprise one or more buffers, such as a Tris buffer; a borate buffer; a succinate buffer; a histidine buffer (particularly with an aluminum hydroxide adjuvant); or a citrate buffer. Buffers, in some cases, are included in the 5-20 or 10-50 mM range.

[00349] The pH of the immunogenic pharmaceutical composition can be between about 5.0 and about 8.5, between about 6.0 and about 8.0, between about 6.5 and about 7.5, or between about 7.0 and about 7.8.

[00350] An immunogenic pharmaceutical composition can be sterile. The immunogenic pharmaceutical composition can be non-pyrogenic e.g. containing <1 EU (endotoxin unit, a standard measure) per dose, and can be <0.1 EU per dose. The composition can be gluten free.

[00351] An immunogenic pharmaceutical composition can include detergent e.g. a polyoxyethylene sorbitan ester surfactant (known as ‘Tweens’), or an octoxynol (such as octoxynol-9 (Triton X-100) or t-octylphenoxypolyethoxyethanol). The detergent can be present only at trace amounts. The immunogenic pharmaceutical composition can include less than 1 mg/mL of each of octoxynol-10 and polysorbate 80. Other residual components in trace amounts can be antibiotics (e.g. neomycin, kanamycin, polymyxin B).

[00352] An immunogenic pharmaceutical composition can be formulated as a sterile solution or suspension, in suitable vehicles, well known in the art. The pharmaceutical compositions can be sterilized by conventional, well-known sterilization techniques, or can be sterile filtered. The resulting aqueous solutions can be packaged for use as is, or lyophilized, the lyophilized preparation being combined with a sterile solution prior to administration.

[00353] Pharmaceutical compositions comprising, for example, an active agent such as immune cells disclosed herein, in combination with one or more adjuvants can be formulated to comprise certain molar ratios. For example, molar ratios of about 99:1 to about 1:99 of an active agent such as an immune cell described herein, in combination with one or more adjuvants can be used. In some instances, the range of molar ratios of an active agent such as an immune cell described herein, in combination with one or more adjuvants can be selected from about 80:20 to about 20:80; about 75:25 to about 25:75, about 70:30 to about 30:70, about 66:33 to about 33:66, about 60:40 to about 40:60; about 50:50; and about 90:10 to about 10:90. The molar ratio of an active agent such as an immune cell described herein, in combination with one or more adjuvants can be about 1:9, and in some cases can be about 1:1. The active agent such as an immune cell described herein, in combination with one or more adjuvants can be formulated together, in the same dosage unit e.g., in one vial, suppository, tablet, capsule, an aerosol spray; or each agent, form, and/or compound can be formulated in separate units, e.g., two vials, suppositories, tablets, two capsules, a tablet and a vial, an aerosol spray, and the like.

[00354] In some instances, an immunogenic pharmaceutical composition can be administered with an additional agent. The choice of the additional agent can depend, at least in part, on the condition being treated. The additional agent can include, for example, a checkpoint inhibitor agent such as an anti-PD1, anti-CTLA4, anti-PD-L1, anti CD40, or anti-TIM3 agent (e.g., an anti-PD1, anti-CTLA4, anti-PD-L1, anti CD40, or anti-TIM3 antibody); or any agents having a therapeutic effect for a pathogen infection (e.g. viral infection), including, e.g., drugs used to treat inflammatory conditions such as an NSAID, e.g., ibuprofen, naproxen, acetaminophen, ketoprofen, or aspirin. For example, the checkpoint inhibitor can be a PD-1/PD- L1 antagonist selected from the group consisting of: nivolumab (ONO-4538/BMS-936558, MDX1 106, OPDIVO), pembrolizumab (MK-3475, KEYTRUDA), pidilizumab (CT-011), and MPDL3280A (ROCHE). As another example, formulations can additionally contain one or more supplements, such as vitamin C, E or other anti-oxidants.

[00355] A pharmaceutical composition comprising an active agent such as an immune cell described herein, in combination with one or more adjuvants can be formulated in conventional manner using one or more physiologically acceptable carriers, comprising excipients, diluents, and/or auxiliaries, e.g., which facilitate

processing of the active agents into preparations that can be administered. Proper formulation can depend at least in part upon the route of administration chosen. The agent(s) described herein can be delivered to a patient using a number of routes or modes of administration, including oral, buccal, topical, rectal, transdermal, transmucosal, subcutaneous, intravenous, and intramuscular applications, as well as by inhalation.

[00356] The active agents can be formulated for parenteral administration (e.g., by injection, for example bolus injection or continuous infusion) and can be presented in unit dose form in ampoules, pre-filled syringes, small volume infusion or in multi-dose containers with an added preservative. The compositions can take such forms as suspensions, solutions, or emulsions in oily or aqueous vehicles, for example solutions in aqueous polyethylene glycol.

[00357] For injectable formulations, the vehicle can be chosen from those known in art to be suitable, including aqueous solutions or oil suspensions, or emulsions, with sesame oil, corn oil, cottonseed oil, or peanut oil, as well as elixirs, mannitol, dextrose, or a sterile aqueous solution, and similar pharmaceutical vehicles. The formulation can also comprise polymer compositions which are biocompatible, biodegradable, such as poly(lactic-co-glycolic)acid. These materials can be made into micro or nanospheres, loaded with drug and further coated or derivatized to provide superior sustained release performance. Vehicles suitable for periocular or intraocular injection include, for example, suspensions of therapeutic agent in injection grade water, liposomes and vehicles suitable for lipophilic substances. Other vehicles for periocular or intraocular injection are well known in the art.

[00358] In some instances, pharmaceutical composition is formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous administration to human beings. Typically, compositions for intravenous administration are solutions in sterile isotonic aqueous buffer. Where necessary, the composition can also include a solubilizing agent and a local anesthetic such as lidocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachette indicating the quantity of active agent. Where the composition is to be administered by infusion, it can be dispensed with an infusion bottle containing sterile pharmaceutical grade water or saline. Where the composition is administered by injection, an ampoule of sterile water for injection or saline can be provided so that the ingredients can be mixed prior to administration.

[00359] When administration is by injection, the active agent can be formulated in aqueous solutions, specifically in physiologically compatible buffers such as Hanks solution, Ringer's solution, or physiological saline buffer. The solution can contain formulatory agents such as suspending, stabilizing and/or dispersing agents. In another embodiment, the pharmaceutical composition does not comprise an adjuvant or any other substance added to enhance the immune response.

[00360] In addition to the formulations described previously, the active agents can also be formulated as a depot preparation. Such long acting formulations can be administered by implantation or transcutaneous delivery (for example subcutaneously or intramuscularly), intramuscular injection or use of a transdermal patch.

Thus, for example, the agents can be formulated with suitable polymeric or hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

[00361] In some cases, pharmaceutical compositions comprising one or more agents exert local and regional effects when administered topically or injected at or near particular sites of infection. Direct topical application, e.g., of a viscous liquid, solution, suspension, dimethylsulfoxide (DMSO)-based solutions, liposomal formulations, gel, jelly, cream, lotion, ointment, suppository, foam, or aerosol spray, can be used for local administration, to produce for example local and/or regional effects. Pharmaceutically appropriate vehicles for such formulation include, for example, lower aliphatic alcohols, polyglycols (e.g., glycerol or polyethylene glycol), esters of fatty acids, oils, fats, silicones, and the like. Such preparations can also include preservatives (e.g., p-hydroxybenzoic acid esters) and/or antioxidants (e.g., ascorbic acid and tocopherol). See also *Dermatological Formulations: Percutaneous absorption*, Barry (Ed.), Marcel Dekker Incl, 1983. In another embodiment, local/topical formulations comprising a transporter, carrier, or ion channel inhibitor are used to treat epidermal or mucosal viral infections.

[00362] Pharmaceutical compositions can contain adjuvants such as hydrophilic or lipophilic gelling agents, hydrophilic or lipophilic active agents, preserving agents, antioxidants, solvents, fragrances, fillers, sunscreens, odor-absorbers and dyestuffs. The amounts of these various adjuvants are those conventionally used in the fields considered and, for example, are from about 0.01% to about 20% of the total weight of the composition. Depending on their nature, these adjuvants can be introduced into the fatty phase, into the aqueous phase and/or into the lipid vesicles.

XII. Methods of Treatment

[00363] Provided herein are method of using any of the nucleic acid disclosed above, the vector containing any of the nucleic acid sequence disclosed above, the protein encoded by any of the nucleic acid disclosed above, or the host cell disclosed above, for manufacture of a medicament for treating an immune disease or cancer.

[00364] Also provided herein are methods of treating a subject with a disease, disorder or condition. A method of treatment can comprise administering a pharmaceutical composition disclosed herein to a subject with a disease, disorder or condition. The present disclosure provides methods of treatment comprising an immunogenic therapy. Methods of treatment for a disease (such as cancer or a viral infection) are provided. A method can comprise administering to a subject an effective amount of a pharmaceutical composition comprising an immunogenic antigen specific T cells. In some embodiments, the antigen comprises a tumor antigen.

[00365] In some embodiments, the method of treating a subject with a disease or condition comprises administering to the subject the pharmaceutical composition disclosed herein. In some embodiments, the method is a method of preventing resistance to a cancer therapy, wherein the method comprises administering to a subject in need thereof the pharmaceutical composition disclosed herein. In some embodiments, the method

is a method of inducing an immune response, wherein the method comprises administering to a subject in need thereof the pharmaceutical composition disclosed herein. In some embodiments, the immune response is a humoral response. In some embodiments, the immune response is a cytotoxic T cell response.

[00366] In some embodiments, the subject has cancer, wherein the cancer is selected from the group consisting of melanoma, ovarian cancer, lung cancer, prostate cancer, breast cancer, colorectal cancer, endometrial cancer, and chronic lymphocytic leukemia (CLL).

[00367] In some embodiments, the subject has a breast cancer that is resistant to anti-estrogen therapy. In some embodiments, the breast cancer expresses an estrogen receptor with a mutation. In some embodiments, the subject has a CLL that is resistant to ibrutinib therapy. In some embodiments, the CLL expresses a Bruton tyrosine kinase with a mutation, such as a C481S mutation. In some embodiments, the subject has a lung cancer that is resistant to a tyrosine kinase inhibitor. In some embodiments, the lung cancer expresses an epidermal growth factor receptor (EGFR) with a mutation, such as a T790M, L792F, or C797S mutation.

[00368] In some embodiments, the method further comprises administering at least one additional therapeutic agent or modality. In some embodiments, the at least one additional therapeutic agent or modality is surgery, a checkpoint inhibitor, an antibody or fragment thereof, a chemotherapeutic agent, radiation, a vaccine, a small molecule, a T cell, a vector, and APC, a polynucleotide, an oncolytic virus or any combination thereof. In some embodiments, the at least one additional therapeutic agent is an anti-PD-1 agent and anti-PD-L1 agent, an anti-CTLA-4 agent, or an anti-CD40 agent. In some embodiments, the additional therapeutic agent is administered before, simultaneously, or after administering the pharmaceutical composition disclosed herein.

[00369] In some other aspects, provided here is use of a pharmaceutical composition for the manufacture of a medicament for use in therapy. In some embodiments, a method of treatment comprises administering to a subject an effective amount of T cells specifically recognizing an immunogenic neoantigen peptide. In some embodiments, a method of treatment comprises administering to a subject an effective amount of a TCR that specifically recognizes an immunogenic neoantigen peptide, such as a TCR expressed in a T cell.

[00370] In some embodiments, the cancer is selected from the group consisting of carcinoma, lymphoma, blastoma, sarcoma, leukemia, squamous cell cancer, lung cancer (including small cell lung cancer, non-small cell lung cancer, adenocarcinoma of the lung, and squamous carcinoma of the lung), cancer of the peritoneum, hepatocellular cancer, gastric or stomach cancer (including gastrointestinal cancer), pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, breast cancer, colon cancer, melanoma, endometrial or uterine carcinoma, salivary gland carcinoma, kidney or renal cancer, liver cancer, prostate cancer, vulval cancer, thyroid cancer, hepatic carcinoma, head and neck cancer, colorectal cancer, rectal cancer, soft-tissue sarcoma, Kaposi's sarcoma, B-cell lymphoma (including low grade/follicular non-Hodgkin's lymphoma (NHL), small lymphocytic (SL) NHL, intermediate grade/follicular NHL, intermediate grade diffuse NHL, high grade immunoblastic NHL, high grade lymphoblastic NHL, high grade small non-cleaved cell NHL, bulky disease NHL, mantle cell lymphoma, AIDS-related lymphoma, and Waldenstrom's macroglobulinemia), chronic lymphocytic leukemia (CLL), acute lymphoblastic leukemia

(ALL), myeloma, Hairy cell leukemia, chronic myeloblasts leukemia, and post-transplant lymphoproliferative disorder (PTLD), abnormal vascular proliferation associated with phakomatoses, edema, Meigs' syndrome, and combinations thereof.

[00371] The methods of the disclosure can be used to treat any type of cancer known in the art. Non-limiting examples of cancers to be treated by the methods of the present disclosure can include melanoma (e.g., metastatic malignant melanoma), renal cancer (e.g., clear cell carcinoma), prostate cancer (e.g., hormone refractory prostate adenocarcinoma), pancreatic adenocarcinoma, breast cancer, colon cancer, lung cancer (e.g., non-small cell lung cancer), esophageal cancer, squamous cell carcinoma of the head and neck, liver cancer, ovarian cancer, cervical cancer, thyroid cancer, glioblastoma, glioma, leukemia, lymphoma, and other neoplastic malignancies.

[00372] Additionally, the disease or condition provided herein includes refractory or recurrent malignancies whose growth may be inhibited using the methods of treatment of the present disclosure. In some embodiments, a cancer to be treated by the methods of treatment of the present disclosure is selected from the group consisting of carcinoma, squamous carcinoma, adenocarcinoma, sarcomata, endometrial cancer, breast cancer, ovarian cancer, cervical cancer, fallopian tube cancer, primary peritoneal cancer, colon cancer, colorectal cancer, squamous cell carcinoma of the anogenital region, melanoma, renal cell carcinoma, lung cancer, non-small cell lung cancer, squamous cell carcinoma of the lung, stomach cancer, bladder cancer, gall bladder cancer, liver cancer, thyroid cancer, laryngeal cancer, salivary gland cancer, esophageal cancer, head and neck cancer, glioblastoma, glioma, squamous cell carcinoma of the head and neck, prostate cancer, pancreatic cancer, mesothelioma, sarcoma, hematological cancer, leukemia, lymphoma, neuroma, and combinations thereof. In some embodiments, a cancer to be treated by the methods of the present disclosure include, for example, carcinoma, squamous carcinoma (for example, cervical canal, eyelid, tunica conjunctiva, vagina, lung, oral cavity, skin, urinary bladder, tongue, larynx, and gullet), and adenocarcinoma (for example, prostate, small intestine, endometrium, cervical canal, large intestine, lung, pancreas, gullet, rectum, uterus, stomach, mammary gland, and ovary). In some embodiments, a cancer to be treated by the methods of the present disclosure further include sarcomata (for example, myogenic sarcoma), leukosis, neuroma, melanoma, and lymphoma. In some embodiments, a cancer to be treated by the methods of the present disclosure is breast cancer. In some embodiments, a cancer to be treated by the methods of treatment of the present disclosure is triple negative breast cancer (TNBC). In some embodiments, a cancer to be treated by the methods of treatment of the present disclosure is ovarian cancer. In some embodiments, a cancer to be treated by the methods of treatment of the present disclosure is colorectal cancer.

[00373] In some embodiments, a patient or population of patients to be treated with a pharmaceutical composition of the present disclosure have a solid tumor. In some embodiments, a solid tumor is a melanoma, renal cell carcinoma, lung cancer, bladder cancer, breast cancer, cervical cancer, colon cancer, gall bladder cancer, laryngeal cancer, liver cancer, thyroid cancer, stomach cancer, salivary gland cancer, prostate cancer, pancreatic cancer, or Merkel cell carcinoma. In some embodiments, a patient or population of patients to be treated with a pharmaceutical composition of the present disclosure have a hematological cancer. In some embodiments, the patient has a hematological cancer such as Diffuse large B cell lymphoma (“DLBCL”), Hodgkin’s lymphoma (“HL”), Non-Hodgkin’s lymphoma (“NHL”), Follicular lymphoma (“FL”), acute myeloid leukemia (“AML”), or Multiple myeloma (“MM”). In some embodiments, a patient or population of patients to be treated having the cancer selected from the group consisting of ovarian cancer, lung cancer and melanoma.

[00374] Specific examples of cancers that can be prevented and/or treated in accordance with present disclosure include, but are not limited to, the following: renal cancer, kidney cancer, glioblastoma multiforme, metastatic breast cancer; breast carcinoma; breast sarcoma; neurofibroma; neurofibromatosis; pediatric tumors; neuroblastoma; malignant melanoma; carcinomas of the epidermis; leukemias such as but not limited to, acute leukemia, acute lymphocytic leukemia, acute myelocytic leukemias such as myeloblastic, promyelocytic, myelomonocytic, monocytic, erythroleukemia leukemias and myelodysplastic syndrome, chronic leukemias such as but not limited to, chronic myelocytic (granulocytic) leukemia, chronic lymphocytic leukemia, hairy cell leukemia; polycythemia vera; lymphomas such as but not limited to Hodgkin’s disease, non-Hodgkin’s disease; multiple myelomas such as but not limited to smoldering multiple myeloma, nonsecretory myeloma, osteosclerotic myeloma, plasma cell leukemia, solitary plasmacytoma and extramedullary plasmacytoma; Waldenstrom’s macroglobulinemia; monoclonal gammopathy of undetermined significance; benign monoclonal gammopathy; heavy chain disease; bone cancer and connective tissue sarcomas such as but not limited to bone sarcoma, myeloma bone disease, multiple myeloma, cholesteatoma-induced bone osteosarcoma, Paget’s disease of bone, osteosarcoma, chondrosarcoma, Ewing’s sarcoma, malignant giant cell tumor, fibrosarcoma of bone, chordoma, periosteal sarcoma, soft-tissue sarcomas, angiosarcoma (hemangiosarcoma), fibrosarcoma, Kaposi’s sarcoma, leiomyosarcoma, liposarcoma, lymphangio sarcoma, neurilemmoma, rhabdomyosarcoma, and synovial sarcoma; brain tumors such as but not limited to, glioma, astrocytoma, brain stem glioma, ependymoma, oligodendroglioma, nonglial tumor, acoustic neurinoma, craniopharyngioma, medulloblastoma, meningioma, pineocytoma, pineoblastoma, and primary brain lymphoma; breast cancer including but not limited to adenocarcinoma, lobular (small cell) carcinoma, intraductal carcinoma, medullary breast cancer, mucinous breast cancer, tubular breast cancer, papillary breast cancer, Paget’s disease (including juvenile Paget’s disease) and inflammatory breast cancer; adrenal cancer such as but not limited to pheochromocytoma and adrenocortical carcinoma; thyroid cancer such as but not limited to papillary or follicular thyroid cancer, medullary thyroid cancer and anaplastic thyroid cancer; pancreatic cancer such as but not limited

to, insulinoma, gastrinoma, glucagonoma, vipoma, somatostatin-secreting tumor, and carcinoid or islet cell tumor; pituitary cancers such as but limited to Cushing's disease, prolactin-secreting tumor, acromegaly, and diabetes insipidus; eye cancers such as but not limited to ocular melanoma such as iris melanoma, choroidal melanoma, and ciliary body melanoma, and retinoblastoma; vaginal cancers such as squamous cell carcinoma, adenocarcinoma, and melanoma; vulvar cancer such as squamous cell carcinoma, melanoma, adenocarcinoma, basal cell carcinoma, sarcoma, and Paget's disease; cervical cancers such as but not limited to, squamous cell carcinoma, and adenocarcinoma; uterine cancers such as but not limited to endometrial carcinoma and uterine sarcoma; ovarian cancers such as but not limited to, ovarian epithelial carcinoma, borderline tumor, germ cell tumor, and stromal tumor; cervical carcinoma; esophageal cancers such as but not limited to, squamous cancer, adenocarcinoma, adenoid cystic carcinoma, mucoepidermoid carcinoma, adenosquamous carcinoma, sarcoma, melanoma, plasmacytoma, verrucous carcinoma, and oat cell (small cell) carcinoma; stomach cancers such as but not limited to, adenocarcinoma, fungating (polypoid), ulcerating, superficial spreading, diffusely spreading, malignant lymphoma, liposarcoma, fibrosarcoma, and carcinosarcoma; colon cancers; colorectal cancer, KRAS mutated colorectal cancer; colon carcinoma; rectal cancers; liver cancers such as but not limited to hepatocellular carcinoma and hepatoblastoma, gallbladder cancers such as adenocarcinoma; cholangiocarcinomas such as but not limited to papillary, nodular, and diffuse; lung cancers such as KRAS-mutated non-small cell lung cancer, non-small cell lung cancer, squamous cell carcinoma (epidermoid carcinoma), adenocarcinoma, large-cell carcinoma and small-cell lung cancer; lung carcinoma; testicular cancers such as but not limited to germinal tumor, seminoma, anaplastic, classic (typical), spermatocytic, nonseminoma, embryonal carcinoma, teratoma carcinoma, choriocarcinoma (yolk-sac tumor), prostate cancers such as but not limited to, androgen-independent prostate cancer, androgen-dependent prostate cancer, adenocarcinoma, leiomyosarcoma, and rhabdomyosarcoma; penile cancers; oral cancers such as but not limited to squamous cell carcinoma; basal cancers; salivary gland cancers such as but not limited to adenocarcinoma, mucoepidermoid carcinoma, and adenoidcystic carcinoma; pharynx cancers such as but not limited to squamous cell cancer, and verrucous; skin cancers such as but not limited to, basal cell carcinoma, squamous cell carcinoma and melanoma, superficial spreading melanoma, nodular melanoma, lentigo malignant melanoma, acral lentiginous melanoma; kidney cancers such as but not limited to renal cell cancer, adenocarcinoma, hypernephroma, fibrosarcoma, transitional cell cancer (renal pelvis and/or uterus); renal carcinoma; Wilms' tumor; bladder cancers such as but not limited to transitional cell carcinoma, squamous cell cancer, adenocarcinoma, carcinosarcoma. In addition, cancers include myxosarcoma, osteogenic sarcoma, endotheliosarcoma, lymphangioendotheliosarcoma, mesothelioma, synovium, hemangioblastoma, epithelial carcinoma, cystadenocarcinoma, bronchogenic carcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma and papillary adenocarcinomas.

[00375] Cancers include, but are not limited to, B cell cancer, *e.g.*, multiple myeloma, Waldenström's macroglobulinemia, the heavy chain diseases, such as, for example, alpha chain disease, gamma chain disease, and mu chain disease, benign monoclonal gammopathy, and immunocytic amyloidosis, melanomas, breast

cancer, lung cancer, bronchus cancer, colorectal cancer, prostate cancer (*e.g.*, metastatic, hormone refractory prostate cancer), pancreatic cancer, stomach cancer, ovarian cancer, urinary bladder cancer, brain or central nervous system cancer, peripheral nervous system cancer, esophageal cancer, cervical cancer, uterine or endometrial cancer, cancer of the oral cavity or pharynx, liver cancer, kidney cancer, testicular cancer, biliary tract cancer, small bowel or appendix cancer, salivary gland cancer, thyroid gland cancer, adrenal gland cancer, osteosarcoma, chondrosarcoma, cancer of hematological tissues, and the like. Other non-limiting examples of types of cancers applicable to the methods encompassed by the present disclosure include human sarcomas and carcinomas, *e.g.*, fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, colorectal cancer, pancreatic cancer, breast cancer, ovarian cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, liver cancer, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, cervical cancer, bone cancer, brain tumor, testicular cancer, lung carcinoma, small cell lung carcinoma, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, melanoma, neuroblastoma, retinoblastoma; leukemias, *e.g.*, acute lymphocytic leukemia and acute myelocytic leukemia (myeloblastic, promyelocytic, myelomonocytic, monocytic and erythroleukemia); chronic leukemia (chronic myelocytic (granulocytic) leukemia and chronic lymphocytic leukemia); and polycythemia vera, lymphoma (Hodgkin's disease and non-Hodgkin's disease), multiple myeloma, Waldenstrom's macroglobulinemia, and heavy chain disease. In some embodiments, the cancer whose phenotype is determined by the method of the present disclosure is an epithelial cancer such as, but not limited to, bladder cancer, breast cancer, cervical cancer, colon cancer, gynecologic cancers, renal cancer, laryngeal cancer, lung cancer, oral cancer, head and neck cancer, ovarian cancer, pancreatic cancer, prostate cancer, or skin cancer. In other embodiments, the cancer is breast cancer, prostate cancer, lung cancer, or colon cancer. In still other embodiments, the epithelial cancer is non-small-cell lung cancer, nonpapillary renal cell carcinoma, cervical carcinoma, ovarian carcinoma (*e.g.*, serous ovarian carcinoma), or breast carcinoma. The epithelial cancers may be characterized in various other ways including, but not limited to, serous, endometrioid, mucinous, clear cell, brenner, or undifferentiated. In some embodiments, the present disclosure is used in the treatment, diagnosis, and/or prognosis of lymphoma or its subtypes, including, but not limited to, mantle cell lymphoma. Lymphoproliferative disorders are also considered to be proliferative diseases.

[00376] In some embodiments, the subject has a breast cancer that is resistant to anti-estrogen therapy, is an MSI breast cancer, is a metastatic breast cancer, is a Her2 negative breast cancer, is a Her2 positive breast cancer, is an ER negative breast cancer, is an ER positive breast cancer or any combination thereof.

[00377] In some embodiments, the breast cancer expresses an estrogen receptor with a mutation.

[00378] In some embodiments, the cancer is recurrent or metastatic breast cancer. In some embodiments, a cancer to be treated by the methods of treatment of the present disclosure is triple negative breast cancer (TNBC).

[00379] The pharmaceutical compositions provided herein may be used alone or in combination with conventional therapeutic regimens such as surgery, irradiation, chemotherapy and/or bone marrow transplantation (autologous, syngeneic, allogeneic or unrelated).

[00380] In some embodiments, at least one or more chemotherapeutic agents may be administered in addition to the pharmaceutical composition comprising an immunogenic therapy. In some embodiments, the one or more chemotherapeutic agents may belong to different classes of chemotherapeutic agents.

[00381] In practicing the methods of treatment or use provided herein, therapeutically-effective amounts of the pharmaceutical compositions can be administered to a subject having a disease or condition. A therapeutically-effective amount can vary widely depending on the severity of the disease, the age and relative health of the subject, the potency of the compounds used, and other factors.

[00382] Subjects can be, for example, mammal, humans, pregnant women, elderly adults, adults, adolescents, pre-adolescents, children, toddlers, infants, newborn, or neonates. A subject can be a patient. In some cases, a subject can be a human. In some cases, a subject can be a child (i.e. a young human being below the age of puberty). In some cases, a subject can be an infant. In some cases, the subject can be a formula-fed infant. In some cases, a subject can be an individual enrolled in a clinical study. In some cases, a subject can be a laboratory animal, for example, a mammal, or a rodent. In some cases, the subject can be a mouse. In some cases, the subject can be an obese or overweight subject.

[00383] In some embodiments, the subject has previously been treated with one or more different cancer treatment modalities. In some embodiments, the subject has previously been treated with one or more of radiotherapy, chemotherapy, or immunotherapy. In some embodiments, the subject has been treated with one, two, three, four, or five lines of prior therapy. In some embodiments, the prior therapy is a cytotoxic therapy.

[00384] In some embodiments, the disease or condition that can be treated with the methods disclosed herein is abnormal growth of cells. In some embodiments, the disease or condition that can be treated with the methods disclosed herein is cancer. In some embodiments, the cancer is a malignant cancer. In some embodiments, the cancer is a benign cancer. In some embodiments, the cancer is an invasive cancer. In some embodiments, the cancer is a solid tumor. In some embodiments, the cancer is a liquid cancer.

[00385] The methods of the disclosure can be used to treat any type of cancer known in the art. Non-limiting examples of cancers to be treated by the methods of the present disclosure include melanoma (e.g., metastatic malignant melanoma), renal cancer (e.g., clear cell carcinoma), prostate cancer (e.g., hormone refractory prostate adenocarcinoma), pancreatic adenocarcinoma, breast cancer, colon cancer, lung cancer (e.g., non-small cell lung cancer), esophageal cancer, squamous cell carcinoma of the head and neck, liver cancer, ovarian cancer, cervical cancer, thyroid cancer, glioblastoma, glioma, leukemia, lymphoma, and other neoplastic malignancies.

[00386] Additionally, the disease or condition provided herein includes refractory or recurrent malignancies whose growth may be inhibited using the methods of treatment of the present disclosure. In some embodiments, a cancer to be treated by the methods of treatment of the present disclosure is selected from the group consisting of carcinoma, squamous carcinoma, adenocarcinoma, sarcomata, endometrial cancer, breast cancer, ovarian cancer, cervical cancer, fallopian tube cancer, primary peritoneal cancer, colon cancer, colorectal cancer, squamous cell carcinoma of the anogenital region, melanoma, renal cell carcinoma, lung cancer, non-small cell lung cancer, squamous cell carcinoma of the lung, stomach cancer, bladder cancer, gall bladder cancer, liver cancer, thyroid cancer, laryngeal cancer, salivary gland cancer, esophageal cancer, head and neck cancer, glioblastoma, glioma, squamous cell carcinoma of the head and neck, prostate cancer, pancreatic cancer, mesothelioma, sarcoma, hematological cancer, leukemia, lymphoma, neuroma, and combinations thereof. In some embodiments, a cancer to be treated by the methods of the present disclosure include, for example, carcinoma, squamous carcinoma (for example, cervical canal, eyelid, tunica conjunctiva, vagina, lung, oral cavity, skin, urinary bladder, tongue, larynx, and gullet), and adenocarcinoma (for example, prostate, small intestine, endometrium, cervical canal, large intestine, lung, pancreas, gullet, rectum, uterus, stomach, mammary gland, and ovary). In some embodiments, a cancer to be treated by the methods of the present disclosure further include sarcomata (for example, myogenic sarcoma), leukosis, neuroma, melanoma, and lymphoma. In some embodiments, a cancer to be treated by the methods of the present disclosure is breast cancer. In some embodiments, a cancer to be treated by the methods of treatment of the present disclosure is triple negative breast cancer (TNBC). In some embodiments, a cancer to be treated by the methods of treatment of the present disclosure is ovarian cancer. In some embodiments, a cancer to be treated by the methods of treatment of the present disclosure is colorectal cancer.

[00387] In some embodiments, a patient or population of patients to be treated with a pharmaceutical composition of the present disclosure have a solid tumor. In some embodiments, a solid tumor is a melanoma, renal cell carcinoma, lung cancer, bladder cancer, breast cancer, cervical cancer, colon cancer, gall bladder cancer, laryngeal cancer, liver cancer, thyroid cancer, stomach cancer, salivary gland cancer, prostate cancer, pancreatic cancer, or Merkel cell carcinoma. In some embodiments, a patient or population of patients to be treated with a pharmaceutical composition of the present disclosure have a hematological cancer. In some embodiments, the patient has a hematological cancer such as Diffuse large B cell lymphoma (“DLBCL”), Hodgkin’s lymphoma (“HL”), Non-Hodgkin’s lymphoma (“NHL”), Follicular lymphoma (“FL”), acute myeloid leukemia (“AML”), or Multiple myeloma (“MM”). In some embodiments, a patient or population of patients to be treated having the cancer selected from the group consisting of ovarian cancer, lung cancer and melanoma.

[00388] Specific examples of cancers that can be prevented and/or treated in accordance with present disclosure include, but are not limited to, the following: renal cancer, kidney cancer, glioblastoma multiforme, metastatic breast cancer; breast carcinoma; breast sarcoma; neurofibroma; neurofibromatosis; pediatric tumors; neuroblastoma; malignant melanoma; carcinomas of the epidermis; leukemias such as but not limited to, acute

leukemia, acute lymphocytic leukemia, acute myelocytic leukemias such as myeloblastic, promyelocytic, myelomonocytic, monocytic, erythroleukemia leukemias and myelodysplastic syndrome, chronic leukemias such as but not limited to, chronic myelocytic (granulocytic) leukemia, chronic lymphocytic leukemia, hairy cell leukemia; polycythemia vera; lymphomas such as but not limited to Hodgkin's disease, non-Hodgkin's disease; multiple myelomas such as but not limited to smoldering multiple myeloma, nonsecretory myeloma, osteosclerotic myeloma, plasma cell leukemia, solitary plasmacytoma and extramedullary plasmacytoma; Waldenstrom's macroglobulinemia; monoclonal gammopathy of undetermined significance; benign monoclonal gammopathy; heavy chain disease; bone cancer and connective tissue sarcomas such as but not limited to bone sarcoma, myeloma bone disease, multiple myeloma, cholesteatoma-induced bone osteosarcoma, Paget's disease of bone, osteosarcoma, chondrosarcoma, Ewing's sarcoma, malignant giant cell tumor, fibrosarcoma of bone, chordoma, periosteal sarcoma, soft-tissue sarcomas, angiosarcoma (hemangiosarcoma), fibrosarcoma, Kaposi's sarcoma, leiomyosarcoma, liposarcoma, lymphangio sarcoma, neurilemmoma, rhabdomyosarcoma, and synovial sarcoma; brain tumors such as but not limited to, glioma, astrocytoma, brain stem glioma, ependymoma, oligodendroglioma, nonglial tumor, acoustic neurinoma, craniopharyngioma, medulloblastoma, meningioma, pineocytoma, pineoblastoma, and primary brain lymphoma; breast cancer including but not limited to adenocarcinoma, lobular (small cell) carcinoma, intraductal carcinoma, medullary breast cancer, mucinous breast cancer, tubular breast cancer, papillary breast cancer, Paget's disease (including juvenile Paget's disease) and inflammatory breast cancer; adrenal cancer such as but not limited to pheochromocytom and adrenocortical carcinoma; thyroid cancer such as but not limited to papillary or follicular thyroid cancer, medullary thyroid cancer and anaplastic thyroid cancer; pancreatic cancer such as but not limited to, insulinoma, gastrinoma, glucagonoma, vipoma, somatostatin-secreting tumor, and carcinoid or islet cell tumor; pituitary cancers such as but limited to Cushing's disease, prolactin-secreting tumor, acromegaly, and diabetes insipidus; eye cancers such as but not limited to ocular melanoma such as iris melanoma, choroidal melanoma, and ciliary body melanoma, and retinoblastoma; vaginal cancers such as squamous cell carcinoma, adenocarcinoma, and melanoma; vulvar cancer such as squamous cell carcinoma, melanoma, adenocarcinoma, basal cell carcinoma, sarcoma, and Paget's disease; cervical cancers such as but not limited to, squamous cell carcinoma, and adenocarcinoma; uterine cancers such as but not limited to endometrial carcinoma and uterine sarcoma; ovarian cancers such as but not limited to, ovarian epithelial carcinoma, borderline tumor, germ cell tumor, and stromal tumor; cervical carcinoma; esophageal cancers such as but not limited to, squamous cancer, adenocarcinoma, adenoid cystic carcinoma, mucoepidermoid carcinoma, adenosquamous carcinoma, sarcoma, melanoma, plasmacytoma, verrucous carcinoma, and oat cell (small cell) carcinoma; stomach cancers such as but not limited to, adenocarcinoma, fungating (polypoid), ulcerating, superficial spreading, diffusely spreading, malignant lymphoma, liposarcoma, fibrosarcoma, and carcinosarcoma; colon cancers; colorectal cancer, RAS mutated colorectal cancer; colon carcinoma; rectal cancers; liver cancers such as but not limited to hepatocellular carcinoma and hepatoblastoma, gallbladder cancers such as adenocarcinoma; cholangiocarcinomas such as but not limited to papillary, nodular, and diffuse; lung cancers such as RAS-

mutated non-small cell lung cancer, non-small cell lung cancer, squamous cell carcinoma (epidermoid carcinoma), adenocarcinoma, large-cell carcinoma and small-cell lung cancer; lung carcinoma; testicular cancers such as but not limited to germinal tumor, seminoma, anaplastic, classic (typical), spermatocytic, nonseminoma, embryonal carcinoma, teratoma carcinoma, choriocarcinoma (yolk-sac tumor), prostate cancers such as but not limited to, androgen-independent prostate cancer, androgen-dependent prostate cancer, adenocarcinoma, leiomyosarcoma, and rhabdomyosarcoma; penal cancers; oral cancers such as but not limited to squamous cell carcinoma; basal cancers; salivary gland cancers such as but not limited to adenocarcinoma, mucoepidermoid carcinoma, and adenoidecystic carcinoma; pharynx cancers such as but not limited to squamous cell cancer, and verrucous; skin cancers such as but not limited to, basal cell carcinoma, squamous cell carcinoma and melanoma, superficial spreading melanoma, nodular melanoma, lentigo malignant melanoma, acral lentiginous melanoma; kidney cancers such as but not limited to renal cell cancer, adenocarcinoma, hypernephroma, fibrosarcoma, transitional cell cancer (renal pelvis and/or uterer); renal carcinoma; Wilms' tumor; bladder cancers such as but not limited to transitional cell carcinoma, squamous cell cancer, adenocarcinoma, carcinosarcoma. In addition, cancers include myxosarcoma, osteogenic sarcoma, endotheliosarcoma, lymphangioendotheliosarcoma, mesothelioma, synovioma, hemangioblastoma, epithelial carcinoma, cystadenocarcinoma, bronchogenic carcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma and papillary adenocarcinomas.

[00389] In some embodiments, a subject with a mutation in a RAS gene is treated for cancer by administering a pharmaceutical composition comprising a TCR that recognizes a RAS mutant epitope in complex with an MHC protein encoded by the HLA allele of the subject, the TCR having a TCR alpha chain variable region and a TCR beta chain variable region having an amino acid sequence disclosed herein. In some embodiments, the pharmaceutical composition comprises a nucleic acid sequence encoding the TCR. In some embodiments, the nucleic acid is a DNA or an RNA. In some embodiments, the nucleic acid is a messenger RNA encoding the TCR having a TCR alpha chain variable region and a TCR beta chain variable region having an amino acid sequence disclosed herein. In some embodiments, the pharmaceutical composition comprises a vector that comprises a nucleic acid sequence encoding the TCR and is capable of driving the expression of the TCR, wherein the TCR recognizes a RAS mutant epitope in complex with an MHC protein encoded by the HLA allele of the subject, and wherein the TCR having a TCR alpha chain variable region and a TCR beta chain variable region having an amino acid sequence disclosed herein. In some embodiments, the pharmaceutical composition comprises a cell that comprises a nucleic acid sequence encoding the TCR that recognizes a RAS mutant epitope in complex with an MHC protein encoded by the HLA allele of the subject, the TCR having a TCR alpha chain variable region and a TCR beta chain variable region having an amino acid sequence disclosed herein. In some embodiments, the subject having a cancer is administered a pharmaceutical composition comprising a TCR that recognizes a RAS mutant epitope in complex with an MHC protein encoded by the HLA allele of the subject, the TCR having a TCR alpha chain variable region and a TCR beta chain variable region having an amino acid sequence disclosed herein, wherein the cancer is selected from adenocarcinoma of the biliary tract, transitional

cell carcinoma of the bladder, breast carcinoma, cervical adenocarcinoma, colon adenocarcinoma, colon adenoma, neuroblastoma (autonomic ganglia), acute myeloid leukemia, chronic myeloid leukemia, chronic myelomonocytic leukemia, juvenile myelomonocytic leukemia, acute lymphoblastic leukemia, Burkitt's lymphoma, Hodgkin's lymphoma, plasma cell myeloma, hepatocellular carcinoma, large cell carcinoma, non-small cell carcinoma, ductal carcinoma, endocrine tumor, prostate adenocarcinoma, basal cell carcinoma, squamous cell carcinoma, malignant melanoma, angiosarcoma, leiomyosarcoma, liposarcoma, rhabdomyosarcoma, myxoma, malignant fibrous histiocytoma, pleomorphic sarcoma, germinoma, seminoma, anaplastic carcinoma, follicular carcinoma, papillary carcinoma and Hurthle cell carcinoma.

[00390] In some embodiments, a subject with a mutation in a GATA3 gene is treated for cancer by administering a pharmaceutical composition comprising a TCR that recognizes a GATA3 mutant epitope in complex with an MHC protein encoded by the HLA allele of the subject, the TCR having a TCR alpha chain variable region and a TCR beta chain variable region having an amino acid sequence disclosed herein. In some embodiments, the subject with a mutation in a GATA3 gene is treated for breast cancer.

[00391] In some embodiments, a subject with a mutation in EGFR gene is treated for cancer by administering a pharmaceutical composition comprising a TCR that recognizes a EGFR mutant epitope in complex with an MHC protein encoded by the HLA allele of the subject, the TCR having a TCR alpha chain variable region and a TCR beta chain variable region having an amino acid sequence disclosed herein. In some embodiments, a subject with a mutation in TMPRSS2:ERG gene is treated for cancer by administering a pharmaceutical composition comprising a TCR that recognizes a TMPRSS2:ERG mutant epitope in complex with an MHC protein encoded by the HLA allele of the subject, the TCR having a TCR alpha chain variable region and a TCR beta chain variable region having an amino acid sequence disclosed herein.

[00392] In some embodiments, a subject with a mutation in BTK gene is treated for cancer by administering a pharmaceutical composition comprising a TCR that recognizes a BTK mutant epitope in complex with an MHC protein encoded by the HLA allele of the subject, the TCR having a TCR alpha chain variable region and a TCR beta chain variable region having an amino acid sequence disclosed herein.

[00393] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

EXAMPLES

Example 1: Workflow for antigen-specific T cell identification and validation

[00394] In this example, an exemplary workflow to generate and use antigen peptide specific TCRs is described. **FIG. 1** demonstrates a graphical representation of the workflow. **FIG. 2** details an exemplary timeline for the workflow process, starting with obtaining and culturing PBMCs from a subject, the PBMCs are then stabilized in overnight culture, and incubated in the presence of peptides and cytokines; the monocyte- and DC-derived antigen presenting cells (APCs) help induce T cells in response to the peptide antigens presented by the APCs; between 10 days to 2 weeks, antigen specific T cells expand and are sorted for antigen specificity and activation (for example, CD8⁺ marker expression indicating generation of cytotoxic T lymphocytes). The activated antigen responsive T cells contain antigen specific TCRs.

[00395] Briefly, Mutated peptides containing mutant target epitopes (e.g., mutant TMPRSS2:ERG, RAS, BTK and GATA3 peptides) were synthesized using a peptide synthesizer. The synthesized peptides were used to load APCs to stimulate T cells from a sample of healthy donor peripheral blood mononuclear cells (PBMCs). PBMCs from patients harboring neoantigens of interest can also be used to obtain neoantigen-specific T cells. After incubation with the peptide loaded APCs, T cell populations were analyzed by flow cytometry. Antigen-specific T cells were isolated using flow cytometry (**FIGs. 1, 2, 4A, 5, 6, 8F, 8G, 9, 10A, 10B, 11, 13, 15, 16A and 16B**). Single cell TCR sequencing was performed for the isolated antigen-specific T cells using 10x Genomics Single Cell V(D)J system to profile the sequences of isolated antigen-specific TCRs. Sequencing reads were analyzed using the Cell RangerTM analysis pipeline, and candidate sequences of TCRs were selected for further analysis and functional assays (**FIGs. 1, 6A, 10A, 10B, 11, 13, 15 and 16A and 16B**).

[00396] For analysis of TCR functionality, vectors or mRNA encoding TMPRSS2:ERG, RAS, BTK or GATA3 peptides containing target mutant epitopes were transduced into HEK293T or A375 cells to produce antigen expressing cell lines. Jurkat cells, TCR β deficient Jurkat cells or PBMCs from healthy donors were transduced with nucleic acids (**FIG. 3A**) encoding candidate TCRs in a lentiviral vector. An exemplary vector is shown in **FIG. 3B**. **FIGs. 4B, 6A and 6B, 10C-10F, 11 and 13** show functional assays for TCR-expressing vector transduced cells. TMPRSS2:ERG, RAS, BTK and GATA3 antigen expressing cell lines were cocultured with TCR transduced Jurkat cells, TCR β deficient Jurkat cells or PBMCs from healthy donors for antigen recognition assays to analyze the functionality of candidate TCRs (**FIGs. 7A-7B, 8A-8E, 10A-10F, 12B and 14**).

Example 2: Obtaining antigen specific T cells

[00397] In vitro T cell inductions were used to expand antigen specific T cells. The healthy human donor PBMCs were seeded in each well of 24 well plate in AIM V media (Invitrogen). Mutant peptides (TMPRSS2:ERG, RAS, BTK or GATA3), TNF- α , IL-1 β , PGE1, and IL-7 were added into wells after 24 hours incubation. The culture media was exchanged every 2 days with fresh media. The antigen specific T cells were evaluated and isolated at day 10 to 20 (**FIG. 2**).

Example 3: HLA-multimer staining and sorting

[00398] Neoantigen specific T cells were detected by combining HLA-multimer staining with 2 different fluorochrome conjugated recombinant HLA (HLA-A02.01, HLA-A03.01, or HLA-A11.01) multimer with

neoantigen peptides. Anti-CD8, anti-CD4, anti-CD19, anti-CD16, anti-CD14, anti-CD56 and antibodies and Live/Dead IR dye (Invitrogen) were used for cell surface staining. CD8⁺ T cells were identified as CD8⁺CD4⁺CD19⁺CD16⁺CD14⁺CD56⁺IR⁻ (FIGs. 1, 2, 4A, 5, 6A, 8F, 8G, 9, 10A, 10B, 11, 13, 15, 16A and 16B). For sorting, up to 5×10⁶ cells were incubated with 1-20 µg multimer in 100 µL PBS + 0.5% human serum. Antibodies and Live/Dead IR dye were used to stain the cells for an additional 30 min. After staining, cells were washed twice and diluted in PBS + 0.5% human serum. Live/Dead IR dye-negative cells were gated and CD8⁺/multimer⁺ T cells were sorted on a FACSAria cell sorter (BD Biosciences).

Example 4: Deep sequencing of antigen-specific TCRs

[00399] Antigen-specific T cells were sorted into a mixture of PBS and 2% FBS (Hyclone Defined), and 10x Genomics V(D)J kit was used to genetically barcode the RNAs from single T cells. RNA libraries were prepared according to the manufacturer's protocols. The resulting libraries were sequenced using ILLUMINA's MiSeq platform. 10x Genomics analysis software was then used to analyze the sequencing data to obtain paired TCR alpha and beta sequences. Dominant clones were identified based on the frequency of cells with a common TCR alpha and/or TCR beta (FIGs. 1, 6, 8F, 8G, 10A, 10B, 11, 13, 15 and 16A).

Example 5: Antigen-specific TCR gene synthesis and cloning

[00400] FIG. 3A represents a graphical diagram of an exemplary vector design, incorporating a TCR alpha chain and a TCR beta chain construct; wherein the TCR alpha- and beta- chain constructs comprise nucleic acid sequences encoding a variable (V), a diversity ((D), only in beta chain construct) a joining (J) and a constant (C) region for each of a TCR alpha (α) chain and a TCR beta (β) chain as shown in the diagram, in a vector with an upstream regulatory element comprising elements necessary for expression of the incorporated nucleic acid sequence, including, for example, a promoter (example EF1a region as shown in the diagram), further incorporating F2A and P2A proteolytic cleavage sites and a sequence encoding for Puromycin resistance (Puro) for Puromycin mediated selection. The lentiviral vectors were constructed from pCDH-EF1-T2A-Puro (SBI system bioscience). Antigen-specific TCR lentiviral vectors were generated by inserting a TCR beta variable region, followed by a TCR beta mouse constant region, furin cleavage site, SGSG linker, F2A site, a TCR alpha variable region, a TCR alpha constant region, a T2A site, and a puromycin resistance gene (FIGs. 3A and 3B).

Example 6: Transfection and transduction

[00401] Lentivirus encoding antigen-specific TCRs was prepared by transient transfection of 293T cells. The cells were seeded on a 10 cm plate at 7×10⁶ cells 16 hours before transfection with 7 µg of lentiviral vector, 7 µg of packaging plasmid mix (pPAX and pMD2.G), 28 µL of Fugene (Promega) and 1 mL of Opti-MEM (Gibco). The culture media was replaced a day after transfection. 72 hours after transfection, the supernatant was harvested concentrated 10-fold.

[00402] Jurkat cells or PBMCs were transduced with concentrated lentivirus encoding TCR sequences. Jurkat cells were washed and resuspended in RPMI-1640 containing polybrene and 10% FBS. 5×10⁵ CD8-Jurkat cells in 100 µL of media were plated per well in 96-well plate and 25 µL of concentrated lentivirus was added. The cells were centrifuged at 2400 rotation per minute (rpm) for 1 hour and incubated in a CO₂ incubator. The cells

were transduced again with fresh media with polybrene and FBS and 25 μ L of concentrated lentivirus. The media was replaced with RPMI-1640 containing 10% FBS and Pen/Strep 24 hours after the second transduction. Puromycin treatment (1 μ g/ml) started at day 4 after transduction.

Example 7: TCR transduced Jurkat binding to HLA-peptide

[00403] To evaluate TCR transduction, transduced Jurkat cells were stained with fluorochrome conjugated multimer (HLA-neoantigen), anti-CD8 antibody, anti-mTCR constant region antibody, and Live/Dead IR dye. mTCR and multimer positive cells were measured by flow cytometry (FIGs. 4B, 6A, 6B, 10A-10F, 11 and 13).

Example 8: Peptide loading of target cells

[00404] For exogenous peptide pulsing, 1×10^6 T2, 293T or A375 cells were incubated at 37 °C and 5% CO₂ for 2 h with 10 pg/mL human β_2 -microglobulin (Calbiochem) and titrating amounts, ranging from 1×10^{-5} M to 1×10^{-12} M of the RAS or GATA3 peptides, T2 cells pulsed with 10^{-5} M influenza peptide GIL (influenza matrix protein₅₈₋₆₆ GILGFVTL, Metabion) served as negative control. After washing, peptide-loaded T2 cells were used in IL-2 release assays (FIGs. 6B, 7, 8, 12E and 14).

Example 9: Neoantigen expressing target cells

[00405] For endogenous antigen expressing target cells, 1×10^6 HEK293 or A375 cells were transduced with lentivirus vectors encoding TMPRSS2::ERG, BTK, GATA3 or KRAS mutated peptides. The transduced target cells were selected by puromycin (1 μ g/ml) in culture media (DMEM with 10% FBS).

Example 10: IL-2 Release Assay

[00406] For investigation of specificity, T cell clones (2.5×10^5 cells in 50 μ L) can be incubated with HEK293T, HLA-A03.01 transduced A375 or HLA-A11.01 transduced A375 cell lines (5×10^4 cells in 50 μ L) and TMPRSS2::ERG, BTK, GATA3 or KRAS mutated peptide neoantigens. The following figures demonstrate IL2 release assay results in case of the respective TCRs as depicted within the figures: FIGs. 6B, 7A, 7B, 8E, 10C, 12A, 12B and 14). Culture supernatants were harvested after 24 h co-culture and assessed IL-2 concentration by a standard MSD using V-PLEX Human IL-2 assays (Meso Scale Discovery).

Example 11: IFN- γ Release Assay

[00407] For investigation of specificity, T cell clones (2×10^3 cells in 100 μ L) were incubated with cell lines expressing TMPRSS2::ERG, BTK, GATA3 or KRAS mutated peptide neoantigens. Culture supernatants were harvested after 24 h co-culture and assessed by a standard ELISA using the OptEIA™ Human IFN- γ Set (BD Biosciences Pharmingen).

Example 12: Cytotoxicity Assay

[00408] Cytotoxic activity of T cell clones can be analyzed in a standard 4 h ⁵¹chromium release assay. Briefly, 1×10^6 target cells can be labeled with 100 μ Ci Na₂ ⁵¹CrO₄ (ICN Biochemicals) for 1-1.5 h. ⁵¹Cr-labeled target cells can be cultured with T cells in RPMI 1640 with 12% FCS. For determination of functional avidity 1×10^4 T cells can be added to 1×10^3 peptide-pulsed T2 cells loaded with titrated amounts of TMPRSS2::ERG, BTK, GATA3 or KRAS mutated peptide neoantigens, giving a constant E:T of 10:1.

[00409] After 4 h co-culture at 37° C, 50 μ L of supernatant can be collected and radioactivity can be measured in a gamma counter. The percentage of specific lysis can be calculated as: $100 \times (\text{experimental release} - \text{spontaneous release}) / (\text{maximum release} - \text{spontaneous release})$. Spontaneous release can be assessed by incubating target cells in the absence of effector cells. For the calculation of percent relative lysis, the maximum percent specific lysis can be set to the reference value of 100% and corresponding values can be calculated corresponding to this reference. To determine half-maximum lysis, percent relative lysis can be plotted against peptide concentration. The peptide concentration at which the curve crossed 50% relative lysis can be taken as the value of half-maximum lysis.

Example 13: Cell Killing Assay

[00410] A RAS-neoantigen specific recombinant TCR was transduced into PBMCs and their ability to kill a cancer cell line was analyzed (**FIGs. 8A, 8B**). The recombinant TCR expressing cells killed showed more than a 30% higher killing of cancer cell lines compared to control. A modified recombinant TCR (rTCR) with mouse constant regions was expressed from a SFFV promoter and a 30% neoantigen specific TCR transduction yield in PBMCs from a healthy donor was achieved. The SW620 cell line was used as target cell which naturally expresses the KRAS G12V mutation. HLA-A11:01 was introduced into the SW620 cell line by lentiviral transductions. The rTCR transduced PBMCs were co-cultured with two different SW620 cell lines with or without expression of HLA-A11:01 for 6 hours. Supernatant and cells were then harvested to analyze cytokine secretion and apoptosis.

[00411] After 6 hour co-culture, significantly higher levels of IFN γ , IL-2, and TNF α were detected for the groups of HLA-A11:01 transduced SW620 cell line (Ras^{mut} cell line + HLA-A11:01) compared to non-transduced SW620 (Ras^{mut} cell line). This shows that the rTCR PBMC can specifically recognize a RAS peptide containing a G12V mutation on HLA-A11:01 of a cell line close to real tumor model. Also, a significantly higher percent of Caspase-3 (apoptosis marker) positive cells was observed in HLA-A11:01 transduced SW620 cell lines compared to control. Thus, the rTCR transduced PBMCs can not only secrete cytokine (IFN γ , IL-2, and TNF α) but also functionally kill target cells specifically.

[00412] In some examples, cytotoxicity activity is assessed by co-culturing T cells expressing a TCR specific to a mutant RAS peptide on a specific HLA, with mutant RAS peptide-transduced target cancer cells expressing the corresponding HLA, and by determining the relative growth of the target cells, along with measuring the apoptotic marker Annexin V in the target cancer cells specifically (**FIGs. 8C, 8D, 10D, 10E**). Target cancer cells are engineered to express the mutant peptide along with the proper MHC-I allele. Mock-transduced target cells (i.e. not expressing the mutant peptide) are used as a negative control. The cells are also transduced to stably express GFP allowing the tracking of target cell growth. PBMCs from healthy donors, used as effector cells, are transduced to express a TCR specific to a mutant RAS peptide. Mock-transduced cells are used as a negative control. The target cells are cocultured with different amount of effector cells for 72h in media containing Annexin V-detection reagent. The GFP signal and Annexin-V signal are measured over time with an InCyte S3 apparatus. Annexin V signal originating from effector cells is filtered out by size exclusion.

Target cell growth and death is expressed as GFP and Annexin-V area (mm²) over time, respectively. FIG. 8C demonstrate high degree of inverse correlation of the TCR levels as determined by the TCR/CD8+: target ratio with the growth of the target cells (upper panel). Similarly, higher TCR levels correlated with higher Annexin V positive target cells, indicating higher number of apoptotic target cells. This indicates high degree of specificity and efficiency in target cell destruction with RAS TCR4.

[00413] In some examples, cytotoxic activity is assessed before TCR cloning. T cells induced against a mutant RAS peptide on a specific HLA are co-cultured with mutant target cancer cells expressing the corresponding HLA loaded with a range of concentrations of the RAS mutant peptides (**FIGs. 8F, 8G**). The relative growth and the apoptotic marker Annexin V in the target cancer cells specifically are both measured. The target cells are also transduced to stably express GFP allowing the tracking of target cell growth. The GFP signal and Annexin-V signal are measured over time with an IncuCyte S3 apparatus. Annexin V signal originating from effector cells is filtered out by size exclusion. Target cell growth and death is expressed as GFP and Annexin-V area (mm²) over time, respectively. For T cells demonstrating cytotoxicity at low peptide concentrations compared to no peptide and/or wild-type peptide, TCR sequencing can be performed as above. Regarding the data shown in experiments shown in FIG. 8F and 8G, (figures on the upper right corner), the cytotoxicity of the T cells showed good dose responsiveness to the peptides as indicated by lower GFP-expressing cells with the higher dose of peptides over the indicated time. The inverse correlation depicts that with higher amounts of peptides for stimulating the TCR on the T cells, higher suppression of target cell growth was observed, as demonstrated by lower GFP-positive cells. This demonstrates that the T cells exhibit high TCR specificity and effectivity in limiting target cell progression.

Example 14: Summary of recombinant TCRs developed

[00414] This example provides the details of the TCRs developed. Table 1 provides a synopsis of the TCRs described herein and Table 2 provides the specific amino acid and coding sequences.

Table 1.

TCR name	Gene	Mutation	Allele	TCRbeta CDR3	TCR binding to peptide-MHC	Method of determining TCR binding to peptide-MHC	
						Multimer Hit	IL-2 by Jurkat and/or PBMC
RAS TCR-1	KRAS	G12V, G12D, G12C	A02:01	SARDRGLVSLPSVEAFF	-	-	-
RAS TCR-2	KRAS	G12V, G12D, G12C	A02:01	ASYLSGSIYNEQFF	-	-	-
RAS TCR-3	KRAS	G12V	A11:01	ASSYSTERGTIY	Yes	Yes	Yes
RAS TCR-4	KRAS	G12V	A11:01	ASSLADIYEQY	Yes	Yes	Yes
RAS TCR-5	KRAS	G12V	A03:01	CASSARNDEAFF	Yes	Yes	Yes
RAS TCR-6	KRAS	G12V	A03:01	CASSLGDSEQYF	Yes	Yes	IL-2 by Jurkat

RAS TCR-7	KRAS	G12C	A03:01	CASSQRSNTGELFF	Yes	Yes	Yes
RAS TCR-8	KRAS	G12V	A11:01	CASGGRDSTDQYF	Yes	Yes	IL-2 by Jurkat
RAS TCR-10	KRAS	G12C	A11:01	ASSTSFWEVNTEAF	Yes	-	IL-2 by Jurkat
RAS TCR-11	KRAS	G12C	A11:01	ASSKRGWPYEQY	Yes	-	IL-2 by Jurkat
RAS TCR-12	KRAS	G12C	A11:01	ASSLADIYEQY	-	-	-
RAS TCR-13	KRAS	G12D	A03:01	ASSSTDRIEAF	-	-	-
RAS TCR-14	KRAS	G12D	A03:01	ASTTFKTGRAIEKLF	-	-	-
RAS TCR-15	KRAS	G12D	A03:01	ASSSRGHSQTAEF	-	-	-
RAS TCR-16	KRAS	G12D	A03:01	ASSSRGHSQTAEF	-	-	-
RAS TCR-17	KRAS	G12D	A03:01	ATYKVGDEQF	-	-	-
RAS TCR-18	KRAS	G12D	A11:01	ASSDWLAGAKDEQY	-	-	-
RAS TCR-19	KRAS	G12V	A03:01	ASSLVASNEQF	-	-	-
RAS TCR-20	KRAS	G12V	A11:01	ASSLGLLLYNEQF	Yes	-	IL-2 by Jurkat
RAS TCR-21	KRAS	G12V	A11:01	ASSLGDSYEQYF	-	-	-
RAS TCR-26	KRAS	G12V	A11:01	ASSEWGSTGELF	-	-	-
RAS-TCR-27	KRAS	G12V	A11:01	ASSEWGSTGELF	-	-	-
RAS-TCR-28	KRAS	G12V	A11:01	ASSEYTMGTQY	-	-	-
GATA3 TCR-1	GATA3	neoORF (CSNH)	A02:01	ASSLDFVLGAGSYSYNEQF	Yes	Yes	IL-2 by Jurkat
GATA3 TCR-2	GATA3	neoORF (CSNH)	B07:02	ASSQSGQGPYEQY	-	-	-
GATA3 TCR-3	GATA3	neoORF (CSNH)	B08:01	ASSRTAMNTEAF	Yes	-	IL-2 by Jurkat
TMPRSS2::ERG TCR-1	TMPRSS2::ERG	Fusion	A02:01	ASSQADSPLH	Yes	Yes	IL-2 by Jurkat and PBMC
BTK TCR-1	BTK	C481S	A02:01	ASSFGPDEKLFF	Yes	Yes	IL-2 by Jurkat
BTK TCR-2	BTK	C481S	A02:01	ASSPGANEKLF	Yes	Yes	IL-2 by Jurkat
EGFR TCR-1	EGFR	T790M	A02:01	ASGGGLGLFETQY	-	-	-
EGFR TCR-2	EGFR	T790M	A02:01	SARRREGEIEQY	-	-	-
EGFR TCR-3	EGFR	T790M	A02:01	ASSLAYLTGRVEAF	-	-	-
EGFR TCR-4	EGFR	T790M	A02:01	SAQGSSGRIEQF	-	-	-
EGFR TCR-5	EGFR	T790M	A02:01	SALPGFSYEQY	-	-	-

[00415] While preferred embodiments of the present invention have been shown and described herein, it will be apparent to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

[00416] Table 2. SEQUENCES

Name	SEQ ID NO	Sequence
RAS TCR-1 alpha chain CDR1	1	SIFNT
RAS TCR-1 alpha chain CDR2	2	LYKAGEL
RAS TCR-1 alpha chain CDR3	3	CAGRNFGEKLTFF
RAS TCR-1 beta chain CDR1	4	DFQATT
RAS TCR-1 beta chain CDR2	5	SNEGSKA
RAS TCR-1 beta chain CDR3	6	SARDRGLVSLPSVEAFF
RAS TCR-1 alpha chain variable domain	7	ATGCTCCTTGAACATTTATTAATAATCTTGTGGATGCAGCTGACATGGGTCACTGGTCAACAGCTGAA TCAGAGTCCTCAATCTATGTTTATCCAGGAAGGAGAAGATGTCTCCATGAACTGCCTTCTTCAAGCA TATTTAACACCTGGCTATGGTACAAGCAGGACCCCTGGGGAAGGTCTGTCTCTTGATAGCCTTATAT AAGGCTGGTGAATTGACCTCAAATGGAAGACTGACTGCTCAGTTTGGTATAACAGAAAGGACAGCTT CCTGAATATCTCAGCATCCATACCTAGTGATGTAGGCATCTACTTCTGTGCTGGGAGAACTTTGGAA ATGAGAAATTAACCTTTGGGACTGGAACAAGACTCACCATCATACCC
	8	ATGCTCCTTGAACATTTATTAATAATCTTGTGGATGCAGCTGACATGGGTCACTGGTCAACAGCTGAA TCAGAGTCCTCAATCTATGTTTATCCAGGAAGGAGAAGATGTCTCCATGAACTGCCTTCTTCAAGCA TATTTAACACCTGGCTATGGTACAAGCAGGACCCCTGGGGAAGGTCTGTCTCTTGATAGCCTTATAT AAGGCTGGTGAATTGACCTCAAATGGAAGACTGACTGCTCAGTTTGGTATAACAGAAAGGACAGCTT CCTGAATATCTCAGCATCCATACCTAGTGATGTAGGCATCTACTTCTGTGCTGGGAGAACTTTGGAA ATGAGAAATTAACCTTTGGGACTGGAACAAGACTCACCATCATACCC
	9	MLLEHLLIILWMQLTWVSGQQLNQSPQSMFIQEGEDVSMNCTSSSIFNTWLWYKQDPGEGPVLLIALY KAGELTSNGRLTAQFGITRKDSFLNISASIPSDVGIYFCAGRNFGEKLTFFGTGTRLTIIIP
RAS TCR-1 beta chain variable domain	10	ATGCTGCTGCTTCTGTGCTTCTGGGGCCAGGCTCCGGGCTTGGTGTGTCGTCTCTCAACATCCGAG CAGGGTTATCTGTAAGAGTGGAACCTCTGTGAAGATCGAGTGCCGTTCCTGGACTTTCAGGCCACAA CTATGTTTGGTATCGTCAGTTCCCGAAACAGAGTCTCATGCTGATGGCAACTTCCAATGAGGGCTCC AAGGCCACATACGAGCAAGGCGTCGAGAAGGACAAGTTTCTCATCAACCATGCAAGCCTGACCTTGT CCACTCTGACAGTGACCAAGTGGCCATCCTGAAGACAGCAGCTTCTACATCTGCAAGTCTCGCGACAGGG GGCTTGTATCGTTGCCGTCCGTAGAAAGCTTTCTTTGGACAAGGCACCAGACTCACAGTTGTACTG
	11	ATGCTGCTGCTTCTGTGCTTCTGGGGCCAGGCTCCGGGCTTGGTGTGTCGTCTCTCAACATCCGAG CAGGGTTATCTGTAAGAGTGGAACCTCTGTGAAGATCGAGTGCCGTTCCTGGACTTTCAGGCCACAA CTATGTTTGGTATCGTCAGTTCCCGAAACAGAGTCTCATGCTGATGGCAACTTCCAATGAGGGCTCC AAGGCCACATACGAGCAAGGCGTCGAGAAGGACAAGTTTCTCATCAACCATGCAAGCCTGACCTTGT CCACTCTGACAGTGACCAAGTGGCCATCCTGAAGACAGCAGCTTCTACATCTGCAAGTCTCGCGACAGGG GGCTTGTATCGTTGCCGTCCGTAGAAAGCTTTCTTTGGACAAGGCACCAGACTCACAGTTGTACTG
	12	MLLLLLLLGPGSGLGAVVVSQHPHRSVICKSGTSVKIECRSLDFQATTMFYRQFPKQSLMLMATSNEGS KATYEQGVEKDKFLINHASLTLSTLTVTSAHPEDSSFYICSARDRGLVSLPSVEAFFGQGTRLTVV
RAS TCR-1 alpha chain	13	MLLEHLLIILWMQLTWVSGQQLNQSPQSMFIQEGEDVSMNCTSSSIFNTWLWYKQDPGEGPVLLIALY KAGELTSNGRLTAQFGITRKDSFLNISASIPSDVGIYFCAGRNFGEKLTFFGTGTRLTIIIPDIQNPD PAVYQLRDSKSSDKSVCLFTDFDSQTNVSQSKSDSVYITDKTVLDMRSMDFKSN SAVAWSNKSDFACAN AFNNSIIPEDTFFPSPSSCDVKLVEKSFETDTNLFQNL SVIGFRILLKLVAGFNLLMTLRLWSS
RAS TCR-1 beta chain	14	MLLLLLLLGPGSGLGAVVVSQHPHRSVICKSGTSVKIECRSLDFQATTMFYRQFPKQSLMLMATSNEGS KATYEQGVEKDKFLINHASLTLSTLTVTSAHPEDSSFYICSARDRGLVSLPSVEAFFGQGTRLTVVLE DLNKVFPPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWVWNGKEVHSGVSTDPQLKEQPAL NDSRYCLSSRLRSATFWQNP RNHRFCQVQFYGLSENDEWTQDRAKPVTVIIVSAEAWGRADCGFTSVS YQQGVLSATILYEILLGKATLYAVLV SALVLMAMVKRKDF
RAS TCR-1/2 peptide	15	KLVVVGACGV
RAS TCR-2 alpha chain CDR1	16	VSGNPY

Name	SEQ ID NO	Sequence
RAS TCR-2 alpha chain CDR2	17	YITGDNLV
RAS TCR-2 alpha chain CDR3	18	CAVRDQSGANNLFF
RAS TCR-2 beta chain CDR1	19	SEHNR
RAS TCR-2 beta chain CDR2	20	FQNEAQ
Ras TCR-2 beta chain CDR3	21	ASYLSGSIYNEQFF
RAS TCR-2 alpha chain variable domain	22	ATGGCCTCTGCACCCATCTCGATGCTTGCGATGCTCTTCACATTGAGTGGGCTGAGAGCTCAGTCAGTGGCTCAGCCGGAAGATCAGGTCAACGTTGCTGAAGGGAATCCTCTGACTGTGAAATGCACCTATTTCAGTCTCTGGAAACCTTATCTTTTGGTATGTTCAATACCCCAACCGAGGCCTCCAGTTCCTTCTGAAATACATCACAGGGGATAACCTGGTTAAAGGCAGCTATGGCTTTGAAGCTGAATTTAACAAGAGCCAAACCTCCTTCCACCTGAAGAAACCATCTGCCCTTGTGAGCGACTCCGCTTTGTACTTCTGTGCTGTGAGAGACCAAAGTGGGGCAAACAACCTCTTCTTTGGGACTGGAACGAGACTCACCGTTATTCCC
	23	ATGGCTTCTGCGCCTATATCAATGCTTGCCATGCTGTTTACTGTCCGGTCTGAGGGCTCAAAGCGTGGCCCAACCTGAGGATCAGGTGAATGTAGCGGAGGGCAATCCGTTGACAGTTAAGTGTACATACTCCGTATCAGGCAATCCGTACTTGTTTGGTATGTGCAGTACCCCAATCGGGGGCTTCAATTCTTGCTGAAGTACATTACAGGCGATAATCTGGTAAAGGTAGTTATGGTTTTGAGGCCGAATTCAACAAATCACAAACATCATTTTCATCTTAAAGCCAAGCGCACTTGTGAGTACTCAGCGCTTTATTTCTGTGCAGTCAGAGACCAATCAGGGGCAAATAATCTGTTCTTTGGGACAGGGACTAGATTGACTGTTATACCC
	24	MASAPI SMLAMFLTLSGLRAQSVAPEDQVNVAEGNPLTVKCTYSVSGNPYLFWYVQYPNRLQLFLK YITGDNLVKGSYGFEAEFNKSQTSFHLKKPSALVSDSALYFCAVRDQSGANNLFFGTGRLTVIP
RAS TCR-2 beta chain variable domain	25	ATGGGACACAGCCTCCTCTGCTGGATGGCCCTGTGTCTCCTGGGGGCGAGTACGCGAGATACTGGAGTCTCCCAGGACCCAGACACAAGATCACAAAGAGGGGACAGAATGTAACCTTTCAGGTGTGATCCAAATTTCTGAACACACACCGCCTTATTGGTACCGACAGACCCCTGGGGCAGGGCCAGAGTTTCTGACTTACTTCAGAAATGAAGCTCAACTAGAAAAATCAAGGCTGCTCAGTGTATCGGTTCTCTGCAGAGAGGCCAAGGGATCTTTCTCCACCTTGAGATCCAGCGCACAGAGCAGGGGGACTCGGCCATGTATCTCTGTGCCAGCTACCTGAGCGGTTCCATTTACAATGAGCAGTTCTTCGGGCCAGGGACACGGCTCACCGTGCTA
	26	ATGGGCACTAGCCTCTGTGTGGATGGCACTTTGCCTTCTTGGCGCGGATCACGCCGATACAGGCGTCTCCCAAGATCCCAGACATAAAATCACAAACGGGGCCAGAACGTTACCTTTTCGCTGCGATCCGATATCAGAGCATAATCGACTGTATTGGTATAGGCCAACTCTCGGGCAAGGGCCTGAGTTCTCACTTATTTCCAAAATGAGGCGCAACTGGAAAAGAGCCGGTTGTTGAGTGTAGGTTTTCCGCGAGAGCCCAAGGGGAGGCTTCTCAACACTGGAGATACAAAGGACCGAACAGGTGATTCCGCAATGTATCTCTGTGCTAGTTATTTGAGCGGCTCCATATATAACGAACAGTTTTTCGGACCGGGCACTCGCCTGACCGTACTA
	27	MGTSLLCWMALCLLGADHDTGVSQDPRHKITKRGQNVTFRCDPIS EHNRLYWYRQTLGQGPEFLTYFQNEAQLEKSRLSDRFS AERP KGSFSTLEIQRT EQGDSAMYL CASYLSGSIYNEQFFGPGTRLTVL
RAS TCR-2 alpha chain	28	MASAPI SMLAMFLTLSGLRAQSVAPEDQVNVAEGNPLTVKCTYSVSGNPYLFWYVQYPNRLQLFLK YITGDNLVKGSYGFEAEFNKSQTSFHLKKPSALVSDSALYFCAVRDQSGANNLFFGTGRLTVIPDIQ NPDPVYQLRDSKSDKSVCLFTDFDSQTNVQSQKSDVYITDKTVLDMRSMDFKNSAVAWSNKSDF ACANAFNNSIIPEDTFFPSPSSCDVKLVEKS FETDTNLFQNL SVIGFRI LLLKVAGFNLLMTLRLWSS
RAS TCR-2 beta chain	29	MGTSLLCWMALCLLGADHDTGVSQDPRHKITKRGQNVTFRCDPIS EHNRLYWYRQTLGQGPEFLTYFQNEAQLEKSRLSDRFS AERP KGSFSTLEIQRT EQGDSAMYL CASYLSGSIYNEQFFGPGTRLTVLED LNKVFPPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWVNGKEVHSGVSTDPQPLKEQPALNDSRYCLSSRLRVSATFWQNP RNHFRCQVQFYGLSENDEWTQDRAKPTQIVISAEAWGRADCGFTSVSYQQGVLSATILYEILLGKATLYAVLVLSALVLMAMVKKRDF
RAS TCR-1/2 peptide	30	LVVVGACGV
Ras TCR-3 alpha chain CDR1	31	NSMFDY
RAS TCR-3 alpha chain CDR2	32	ISSIKDK
RAS TCR-3 alpha chain CDR3	33	AASGGGGADGLT

Name	SEQ ID NO	Sequence
RAS TCR-3 beta chain CDR1	34	MNHHY
RAS TCR-3 beta chain CDR2	35	SVGAGI
RAS TCR-3 beta chain CDR3	36	ASSYSTERGTIY
RAS TCR-3 alpha chain variable domain	37	ATGGCCATGCTCCTGGGGGCATCAGTGCTGATTCTGTGGCTTCAGCCAGACTGGGTAAACAGTCAACA GAAGAATGATGACCAAGCAAGTTAAGCAAAATTCACCATCCCTGAGCGTCCAGGAAGGAAGAAATTTCTA TTCTGAACTGTGACTATACTAACAGCATGTTTGATTATTTCTATGGTACAAAAAATACCTGCTGAA GGTCTTACATTCTGATATCTATAAGTTCCATTAAGGATAAAAATGAAGATGGAAGATTCACTGTCTT CTTAAACAAAAGTGCCAAGCACCTCTCTGTCACATGTGCCCCTCCAGCCTGGAGACTCTGCAGTGT ACTTCTGTGCAGCAAGCGGGGGAGGAGGTGTGACGGACTCACCTTTGGCAAAGGGACTCATCTAATC ATCCAGCCC
	38	ATGGCCATGCTGCTGGGCGCCAGCGTGTGATTTTATGGCTGCAGCCGACTGGGTGAACAGCCAGCA GAAGAACGACGACCAAGCAAGTGAAGCAGAACTCCCTTCTTAAAGCGTGCAAGAAGGTCGTATCAGCA TTTAAACTGCGACTACACCAACAGCATGTTGCGACTACTTTTATGGTACAGAAGTACCCGCGGAG GGCCCCACCTTTTAAATCAGCATCAGCAGCATCAAGGACAAGAACGAGGACGGTCGTTTCACCGTGTT TTTAAACAAGAGCGCCAAAGCATTTATCTTTACACATCGTGCCCTCCAGCCCGGTGATAGCGCCGTGT ACTTCTGCGCCGCCAGCGGAGGAGGAGCGCGGATGGACTGACCTTCGGCAAGGGACCCATTTAATC ATCCAGCCC
	39	MAMLLGASVLILWLQPDWVNSQQKNDQOVKQNSPSSLVQEGRISILNCDYTNMFDYFLWYKKYPAE GPTFLISISSIKDKNEDGRFTVFLNLSAKHLSLHIVPSQPGDSAVYFCAASGGGGADGLTFGKGTHLI IQP
RAS TCR-3 beta chain variable domain	40	ATGAGGTCTCAGAATGACTTCCTTGAGAGTCTGTTCCTTTCATCAATGCACAGATACAGAAGACC CCTCCGTCTGGAGCACCTGCCATGAGCATCAGCCTCCTGTGCTGTGCAGCCTTTCCTCTCTGTGGG CAGGTCCAGTGAATGCTGGTGTCACTCAGACCCCAAATTCGCGATCCTGAAGATAGGACAGAGCATG ACACTGCAGTGTACCCAGGATATGAACCATAACTACATGTACTGGTATCGACAAGACCCAGGCATGGG GCTGAAGCTGATTTATTATTAGTTGGTGTGTTATCACTGATAAAGGAGAAGTCCCGAATGGCTACA ACGTCTCCAGATCAACCACAGAGGATTTCCGCTCAGGCTGGAGTTGGCTGCTCCCTCCAGACATCT GTGTACTTCTGTGCCAGCAGTTACTCGACGGAACGCGGGACCATATATTTTGGAGAGGGAAGTTGGCT CACTGTTGTA
	41	ATGAGGAGCCAGAACGACTTTTTAGAGAGCCCCGTGCTCTGAGCAGCATGCATAGGTATAGGAGGCC TCTGAGACCCGGTGCCCCGCTATGAGCATCTCTTTACTGTGCTGTGCTGCCTTTCCTTTACTGTGGG CTGGCCCCGTAAACGCTGGCGTGACCCAGACCCCAAGTTTAGGATTTTAAAGATCGGCCAGTCCATG ACTTTACAGTGCACCAAGATATGAACCACAACTACATGTACTGGTATCGTCAAGATCCCGGCATGGG TTTAAAGCTGATTTACTACAGCTGGGAGCGGCGCATCACCAGCAAGGGCGAGGTGCCAACGGCTACA ATGTGTCTCGTAGCACCAAGGAGCTTCCCTCTGAGACTGGAGCTGGCGCCCCCTAGCCAGACAAGC GTGTACTTCTGCGCCTCTCTACAGACCGAGAGGGGACCATCTACTTCGGCGAGGGCAGCTGGCT GACCGTGGTG
	42	MRSQNDFLESFVPLSSMHRYPRLRPAPAMSSILLCCAFPLWAGFVNAGVTQTPKFRILKIGQSM TLQCTQDMNHNMYWYRQDPGMGLKLIYYSVGAGITDKGEVPNGYNVSRSTEDFPLRLELAAPSQTS VYFCASSYSTERGTIYFEGESWLTVV
RAS TCR-3 alpha chain	43	MAMLLGASVLILWLQPDWVNSQQKNDQOVKQNSPSSLVQEGRISILNCDYTNMFDYFLWYKKYPAE GPTFLISISSIKDKNEDGRFTVFLNLSAKHLSLHIVPSQPGDSAVYFCAASGGGGADGLTFGKGTHLI IQPDIQNPDPVYQLRDSKSDKSVCLFTDFDSQTNVSQSKSDVYITDKTVLDMRSMDFKSN SAVAW SNKSDFACANAFNNSSIIPEDTFFPSPSSCDVKLVKS FETDTNLNFQNL SVIGFRILLKLVAGFNLL MTLRLWSS
RAS TCR-3 beta chain	44	MRSQNDFLESFVPLSSMHRYPRLRPAPAMSSILLCCAFPLWAGFVNAGVTQTPKFRILKIGQSM TLQCTQDMNHNMYWYRQDPGMGLKLIYYSVGAGITDKGEVPNGYNVSRSTEDFPLRLELAAPSQTS VYFCASSYSTERGTIYFEGESWLTVVEDLNKVFPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVE LSWWVNGKEVHSGVSTDPQLKEQPALNDSRYCLSSRLRVSATFWQNPRNHFRCQVQFYGLSENDEWT QDRAKPVTOIVSAEAWGRADCGFTSVSYQQGVLSATILYEILLGKATLYAVLV SALVLMAMVKRKDF
RAS TCR-3 peptide	45	VVGAVGVGK
	46	VVGAVGVGK
RAS TCR-4 alpha chain CDR1	47	TSINN

Name	SEQ ID NO	Sequence
RAS TCR-4 alpha chain CDR2	48	IRSNERE
RAS TCR-4 alpha chain CDR3	49	ATDRQSSGDKLT
RAS TCR-4 beta chain CDR1	50	SGHAT
RAS TCR-4 beta chain CDR2	51	FQNNGV
RAS TCR-4 beta chain CDR3	52	ASSLADIYEQY
RAS TCR-4 alpha chain variable domain	53	ATGGAAACTCTCCTGGGAGTGTCTTTGGTGATTCTATGGCTTCAACTGGCTAGGGTGAACAGTCAACA GGGAGAAGAGGATCCTCAGGCCTTGAGCATCCAGGAGGGTGAAAATGCCACCATGAACTGCAGTTACA AACTAGTATAAACAATTTACAGTGGTATAGACAAAATTCAGGTAGAGGCCTTGTCCACCTAATTTTA ATACGTTCAAATGAAAGAGAGAAACACAGTGGAAGATTAAGAGTCACGCTTGACACTTCCAAGAAAAG CAGTTCCTTGTGATCAGCGCTTCCCGGGCAGCAGACACTGCTTCTTACTTCTGTGCTACGGACCGTC AAAGCAGCGGAGACAAGCTGACTTTTGGGACCGGGACTCGTTTAGCAGTTAGGCC
	54	ATGGAGACTTTACTGGGCGTGTCTTTAGTGATTTTATGGCTGCAGCTGGCTCGTGTGAATAGCCAGCA AGGTGAAGAGGACCCCAAGCTTTAAGCATCCAAGAAGGCGAGAACGCCACCATGAACTGCTCCTACA AGACCAGCATCAACAATTTACAGTGGTATCGTCAGAACAGCGGTCGTGGTTTGTGATTTAATTTTA ATTCTAGCAACGAGAGAGGAGAGACAGCGGTCGTCTGAGGGTGACTTTAGACAGCAGCAAGAAGAG CAGCTCTTACTGATCAGCGCTCTAGGGCCGCTGACACCGCTAGCTACTTCTGCGCCACCGACAGAC AGAGCAGCGGCGACAAGCTGACCTTCGGCACCAGGACCAAGACTGGCCGTGAGACCC
	55	METLLGVSLVILWLQRLARVNSQQGEEDFQALS IQEGENATMNC SYKTS INNLQWYRQNSGRGLVHLIL IRSNEREKHSRGLRVTLDTSKKSSLLI TASRAADTASYFCATDRQSSGDKLTFGTGTRLAVRP
RAS TCR-4 beta chain variable domain	56	ATGGGCACCAAGCTCCTCTGCTGGGCGGCCCTCTGTCTCCTGGGAGCAGAACTCACAGAAGCTGGAGT TGCCCACTCTCCAGATATAAGATTATAGAGAAAAGGCAGAGTGTGGCTTTTGGTGCAATCCTATAT CTGGCCATGCTACCTTTACTGGTACCAGCAGATCCTGGGACAGGGCCCAAAGCTTCTGATTCAGTTT CAGAATAACGGTGTAGTGGATGATTCACAGTTGCCTAAGGATCGATTTCTGCAGAGAGGCTCAAAGG AGTAGACTCCACTCTCAAGATCCAGCCTGCAAAGCTTGAGGACTCGGCCGTGTATCTCTGTGCCAGCA GCTTAGCCGACATCTACGAGCAGTACTTCGGGCCGGGCACCAAGCTCACGGTCACA
	57	ATGGGCACCAAGCTGCTGTGCTGGGCGGCTCTGTGTCTGCTGGGCGCTGAGCTGACAGAAGCTGGCGT GGCCCAAGGCCCTCGTTACAAGATCATCGAGAAGAGGCAGAGCGTGGCCTTCTGGTGCAACCCCATCA GCGGCCACGCCACTTTATACTGGTACCAGCAGATTTTAGGCCAAGGTCCCAAGCTGCTGATCCAGTTC CAGAACAACGGCGTGGTGGACGACAGCCAGCTGCCCAAGGATCGTTTCAGCGCCGAGAGGCTGAAGGG CGTGGACAGCACTTTAAAAATCCAGCCCGCTAAGCTGGAGGACAGCGCCGTGATTTATGCGCTAGCT CTTAGCCGACATCTACGAGCAGTACTTCGGCCCCGGCAGCTCGTCTGACCGTGACC
	58	MGTRLLCWAALCLLGAELTEAGVAQSPRYKII EKRSVAFWCNPI SGHATLYWYQQILGQGPKLLIQF QNNGVVDDSQLPKDRFSAERLKGVDSTLKI QPAKLEDSAVYLCASSLADIYEQYFPGTRTLTVT
RAS TCR-4 alpha chain	59	METLLGVSLVILWLQRLARVNSQQGEEDFQALS IQEGENATMNC SYKTS INNLQWYRQNSGRGLVHLIL IRSNEREKHSRGLRVTLDTSKKSSLLI TASRAADTASYFCATDRQSSGDKLTFGTGTRLAVRPDIQN PDFAVYQLRDSKSSDKSVCLFTDFDSQTNVSQSKSDVYITDKTVLDMRSMDFKNSAVAWSNKSDF CANAFNNSIIPEDTFFPSPSSCDVKLVEKSFETDTNLFQNL SVIGFRIILLKVAGFNLLMTLRLWS S
RAS TCR-4 beta chain	60	MGTRLLCWAALCLLGAELTEAGVAQSPRYKII EKRSVAFWCNPI SGHATLYWYQQILGQGPKLLIQF QNNGVVDDSQLPKDRFSAERLKGVDSTLKI QPAKLEDSAVYLCASSLADIYEQYFPGTRTLTVTEDLN KVFPPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWVNGKEVHSGVSTDPQPLKEQPALNDS RYCLSSRLRVSATFWQNPRNHFRQCQVQFYGLSENDEWTDQRAKPVTOIVSAEAWGRADCGFTSVSYQQ GVL SATILYEILLGKATLYAVLVSAVLMMVMKRKDF
RAS TCR-4 peptide	61	VVGAVGVGK
	62	VVVGAVGVGK
RAS TCR-5 alpha chain CDR1	63	TSGFNG
RAS TCR-5 alpha chain CDR2	64	NVLDGL

Name	SEQ ID NO	Sequence
RAS TCR-5 alpha chain CDR3	65	CAPGDNFNKIFYF
RAS TCR-5 beta chain CDR1	66	SGHRS
RAS TCR-5 beta chain CDR2	67	YFSETQ
RAS TCR-5 beta chain CDR3	68	CASSARNDEAFF
RAS TCR-5 alpha chain variable domain	69	ATGTGGGGAGTTTTCCTTCTTTATGTTTCCATGAAGATGGGAGGCACTACAGGACAAAACATTGACCA GCCCCTGAGATGACAGCTACGGAAGGTGCCATTGTCCAGATCAACTGCACGTACCAGACATCTGGGT TCAACGGGCTGTTCTGGTACCAGCAACATGCTGGCGAAGCACCACATTTCTGTCTTACAATGTTCTG GATGGTTTGGAGGAGAAAGGTGTTTTCTTCATTCCTTAGTCGGTCTAAAGGGTACAGTTACCTCCT TTTGAAGGAGCTCCAGATGAAAGACTCTGCCTCTTACCTCTGTGCTCCCGGGGACAACTTCAACAAAT TTACTTTGGATCTGGGACCAAACCTCAATGTAAACCA
	70	ATGTGGGGCGTGTTCCTGCTGTACGTGTCCATGAAGATGGGCGGCACCACAGGCCAGAACATCGACCA GCCAACCGAGATGACCGCCACAGAGGGCGCCATCGTGCAGATCAACTGCACCTACCAGACATCTGGCT TCAATGGCCTGTTTTGGTATCAGCAGCAGCAGGAGAGGCACCCACATTCCTGAGCTATAATGTGCTG GATGGCCTGGAGGAGAGGGGAGGTTCTCCTCTTTCTGTCTCGCAGCAAGGGCTCCTATCTGCT GCTGAAGGAGCTGCAGATGAAGGACTCGCCTCTTACCTGTGCGCCCTGGCGATAACTTTAATAAGT TCTATTTCCGGCTCTGGCACCAGCTGAATGTGAAGCCA
	71	MWGVFLLYVSMKMGTTGQNDIQPTTEMTATEGAIVQINCTYQTSGFNGLFWYQQHAGEAPTFLSYNVL DGLEEKGRFSSFLSRSGYSYLLKELQMKDSASYLCAPGDNFNKIFYFGSGTKLNVKP
RAS TCR-5 beta chain variable domain	72	ATGGGCTCCAGGCTGCTCTGTTGGGTGCTGCTTTGTCTCCTGGGAGCAGGCCAGTAAAGGCTGGAGT CACTCAAACCTCCAAGATATCTGATCAAACAGAGAGGACAGCAAGTGACACTGAGCTGCTCCCTATCT CTGGGCATAGGAGTGTATCCTGGTACCAACAGACCCAGGACAGGGCCTTCAGTTCTCTTTGAATAC TTCAGTGAGACACAGAGAAACAAAGGAACTTCCCTGGTCGATTCTCAGGGCGCCAGTTCTCTAACTC TCGCTCTGAGATGAATGTGAGCACCTTGGAGCTGGGGGACTCGGCCCTTTATCTTTGCGCCAGCAGCG CGAGAAATGATGAAGCTTCTTTGGACAAGGCACCAGACTCACAGTTGTA
	73	ATGGGCGAGCCGGCTGCTGTGCTGGGTGCTGCTGTGCCTGCTGGGAGCAGGACCAGTGAAGGCAGGCGT GACCCAGACACCTCGGTACCTGATCAGAGACCAGAGGCCAGCAGGTGACACTGAGCTGCTCCCCAATCT CCGGCCACAGATCTGTGAGCTGGTACCAGCAGACCCAGGACAGGGACTGCAGTTCTGTTTGAGTAT TTCTCCGAGACACAGAGGAACAAGGGCAATTTCCCTGGCCGGTTTTCTGGCAGACAGTTTTCCAATC TCGACGCGAGATGAATGTGAGCACCTTGGAGCTGGGCGACTCCGCCCTGTACCTGTGCGCCAGCTCCG CCAGGAACGATGAGGCCTTCTTTGGCCAGGGCACCCGGCTGACAGTGGTG
	74	MGSRLLCWVLLCLLGAGFVKAGVTQTTPRYLIKTRGQQVTLSCSPI SGHRVSWSYQQTPGQGLQFLFEY FSETQRNKGNFGRFSGRQFSNSRSEMNVTLELGDALYLCASSARNDEAFFGQGTRLTVV
RAS TCR-5 alpha chain	75	MWGVFLLYVSMKMGTTGQNDIQPTTEMTATEGAIVQINCTYQTSGFNGLFWYQQHAGEAPTFLSYNVL DGLEEKGRFSSFLSRSGYSYLLKELQMKDSASYLCAPGDNFNKIFYFGSGTKLNVKPDINPDPAVY QLRDSKSSDKSVCLFTDFDSQTNVSQSKSDSVYITDKTVLDMRSMDFKSN SAVAWSNKSDFACANAFN NSIIPEDTFFPSPSSCDVKLVEKSFETDTNLNFQNL SVIGFRILLKLVAGFNLLMTLRWSS
RAS TCR-5 beta chain	76	MGSRLLCWVLLCLLGAGFVKAGVTQTTPRYLIKTRGQQVTLSCSPI SGHRVSWSYQQTPGQGLQFLFEY FSETQRNKGNFGRFSGRQFSNSRSEMNVTLELGDALYLCASSARNDEAFFGQGTRLTVVEDLNKV FPPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWVNGKEVHSGVSTDPQPLKEQPALNDSRY CLSSRLRVSATFWQNP RNHFRQVQFYGLSENDEWTQDRAKPVTOIVSAEAWGRADCGFTSVSYQQGV LSATILYEILLKATLYAVLVLSALVLMAMVKRKDF
RAS TCR-5 peptide	77	VVGAVGVGK
	78	VVVGAVGVGK
RAS TCR-6 alpha chain CDR1	79	DRGSQS
RAS TCR-6 alpha chain CDR2	80	IYSNGD
RAS TCR-6 alpha chain CDR3	81	CAVKSRAGSYQLTF
RAS TCR-6 beta chain CDR1	82	SGHNS

Name	SEQ ID NO	Sequence
RAS TCR-6 beta chain CDR2	83	FNNNV
RAS TCR-6 beta chain CDR3	84	CASSLGDSQYF
RAS TCR-6 alpha chain variable domain	85	ATGAAATCCTTGAGAGTTTTACTAGTGATCCTGTGGCTTCAGTTGAGCTGGGTTTGGAGCCAACAGAA GGAGGTGGAGCAGAATTCTGGACCCCTCAGTGTTCCAGAGGGAGCCATTGCCTCTCTCAACTGCACTT ACAGTGACCGAGGTTCCCACTCTTCTTCTGGTACAGACAATATTCTGGGAAAAGCCCTGAGTTGATA ATGTTTCATATACTCCAATGGTGACAAAGAAGATGGAAGGTTTACAGCACAGCTCAATAAAGCCAGCCA GTATGTTTCTCTGCTCATCAGAGACTCCAGCCAGTGATTACAGCCACCTACCTCTGTGCCGTGAAGT CAAGGGCTGGGAGTTACCAACTCACTTTTGGGAAGGGGACCAACTCTCGGTCATACCA
	86	ATGAAGAGCCTGCGGGTGCTGCTGGTCATCCTGTGGCTGCAGCTGTCTGGGTGTGGTCTCAGCAGAA GGAGGTGGAGCAGAATAGCGGACCACTGTCCGTGCCAGAGGGAGCCATCGCTCCCTGAACTGCACAT ACTCTGACAGGGGCTCCCACTCTTCTTTTGGTACCGCCAGTATAGCGGCAAGTCCCCGAGCTGATC ATGTTTCATCTACTCTAATGGCGACAAGGAGGATGGCAGGTTTACCGCCAGCTGAACAAGGCTCTCA GTATGTGAGCCTGCTGATCCGCGACAGCCAGCCTAGCGATTCCGCCACATACCTGTGCGCAGTGAAGT CCCGGGCAGGCTCTTATCAGCTGACCTTTGGCAAGGGCACAAAGCTGAGCGTGATCCCA
	87	MKSLRVLLVILWLQLSWVWSQQKEVEQNSGPLSVPEGAIAISLNCTYSDRGSQSFFWYRQYSGKSPELI MFIYSNGDKEDGRFTAQLNKASQYVSLIRDSQPSDSATYLCVKS RAGSYQLTFGKGTKLSVIP
RAS TCR-6 beta chain variable domain	88	ATGGACTCCTGGACCTTCTGCTGTGTGTCCTTTGTCATCCTGGTAGCGAAGCATACAGATGCTGGAGT TATCCAGTCACCCCGCCATGAGGTGACAGAGATGGGACAAGAAGTGACTCTGAGATGTAAACCAATTT CAGGCCACAACCTCCCTTTTCTGGTACAGACAGACCATGATGCGGGGACTGGAGTTGCTCATTTACTTT AACAACAACGTTCCGATAGATGATTACGGGATGCCCAGGATCGATTCTCAGCTAAGATGCGTAAATGC ATCATTCTCCACTCTGAAGATCCAGCCCTCAGAACCAGGGACTCAGCTGTGTACTTCTGTGCCAGCA GTCTCGGGACAGCGAGCAGTACTTCGGGCCGGGCACCAGGCTCACGGTCACA
	89	ATGGACAGCTGGACCTTCTGCTGCGTGAGCCTGTGCATCCTGGTGGCCAAGCACACAGATGCAGGCGT GATCCAGTCCCCAAGGCACAGGTGACCGAGATGGGACAGGAGGTGACACTGAGGTGTAAGCCTATCT CTGGCCACAATAGCCTGTTCTGGTACAGGACAGCCATGATGCGCGGCTGGAGCTGCTGATCTACTTC AACAATAACGTGCCTATCGACGATTCCGGCATGCCAGAGGACAGATTCTCTGCAAGATGCCCAACGC CTCCTTTTCTACACTGAAGATCCAGCCAAGCGAGCCTAGGGACTCCGCCGTGACTTCTGCGCCAGCT CCCTGGCGGATAGCGAGCAGTATTTTGGCCCTGGCACCCGGCTGACCGTGACA
	90	MDSWTFCCVSLCILVAKHTDAGVIQSPRHEVTEMGQEVTLRCKPISGHNSLFWYRQTMRRGLELLIYF NNNVPIIDDSGMPEDRFSAKMPNASFSTLKIQSEPRDSAVYFCASSLGDSQYFPGTRLTLVT
RAS TCR-6 alpha chain	91	MKSLRVLLVILWLQLSWVWSQQKEVEQNSGPLSVPEGAIAISLNCTYSDRGSQSFFWYRQYSGKSPELI NPDPAVYQLRDSKSDKSVCLFTDFDSQTNVSQSKSDVYITDKTVLDMRSMDFKSN SAVAWSNKSD ACANAFNNSIIPEDTFFPSPSSCDVKLVEKS FETDTNLFQNLVIGFRI LLLKVAGFNLLMTLRLW SS
RAS TCR-6 beta chain	92	MDSWTFCCVSLCILVAKHTDAGVIQSPRHEVTEMGQEVTLRCKPISGHNSLFWYRQTMRRGLELLIYF NNNVPIIDDSGMPEDRFSAKMPNASFSTLKIQSEPRDSAVYFCASSLGDSQYFPGTRLTLVTEDLNK VFPPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWVWNGKEVHSGVSTDPQPLKEQPALNDSR YCLSSRLRVSATFWQNP RNHFRCQVQFYGLSENDEWTQDRAKPVTVI VSAEAWGRADCGFTSVSYQGG VLSATILYEIILGKATLYAVLVSAVLMMAMVKRKDF
RAS TCR-6 peptide	93	VVGAVGVGK
	94	VVVGAVGVGK
RAS TCR-7 alpha chain CDR1	95	SSYSPS
RAS TCR-7 alpha chain CDR2	96	YTSAAITLV
RAS TCR-7 alpha chain CDR3	97	CVVSGGSSNTGKLIF
RAS TCR-7 beta chain CDR1	98	SGHAT
RAS TCR-7 beta chain CDR2	99	FQNNGV
RAS TCR-7 beta chain CDR3	100	CASSQRSNTGELFF

Name	SEQ ID NO	Sequence
RAS TCR-7 alpha chain variable domain	101	ATGCTCCTGCTGCTCGTCCCAGTGCTCGAGGTGATTTTACTCTGGGAGGAACACAGAGCCAGTCGGT GACCCAGCTTGACAGCCACGTCTCTGTCTCTGAAGGAACCCCGGTGCTGCTGAGGTGCAACTACTCAT CTTCTTATTCACCATCTCTCTTCTGGTATGTGCAACACCCCAACAAAGGACTCCAGCTTCTCCTGAAG TACACATCAGCGGCCACCTGGTTAAAGGCATCAACGGTTTTGAGGTGAATTTAAGAAGAGTGAAAC CTCCTTCCACCTGACGAAACCTCAGCCCATATGAGCGACGCGGCTGAGTACTTCTGTGTTGTGAGTG GGGGAGGCTCTAGCAACACAGGCAAACTAATCTTTGGGCAAGGGACAACCTTACAAGTAAACCA
	102	ATGCTGCTGCTGCTGGTGCCCGTGCTGGAAGTGATCTTCACCTGGGAGGAACAAGGGCACAGAGCGT GACCCAGCTGGACTCCACGTGTCCTGTCTGAGGGCACACCCGTGCTGCTGAGATGCAACTACTCCT CTAGCTATAGCCCCCTCCCTGTTCTGGTACGTGCAGCACCCCTAATAAGGGCTGACGTGCTGCTGAAG TATACCTCCGCGGCCACACTGGTGAAGGGCATCAACGGCTTCGAGGCCGAGTTTAAAGAAGAGCGAGAC CTCCTTCCACCTGACAAAGCCTTCTGCCACATGAGCGATGCCGCCGAGTACTTTTGGCGTGGTGAGCG GCGGGCGCTCCTCTAATACCGGCAAGCTGATCTTCGGCCAGGGCACCACTGACAGGTGAAGCCA
	103	MLLLLVPLEVIFTLGGTRAQSVTQLDSHVSVEGTPVLLRCNYSYSSPSLFWYVQHPNKGQLQLLK YTSAAATLVKINGFEAEFFKSETSFHLTKPSAHMSDAAEYFCVVS GGSSNTGKLIFGQGTTLQVKP
RAS TCR-7 beta chain variable domain	104	ATGGGCACACAGGCTCCTCTGCTGGGCGGCCCTCTGTCTCCTGGGAGCAGAACTCACAGAAGCTGGAGT TGCCCACTCTCCAGATATAAGATTATAGAGAAAAGGCAGAGTGTTGGCTTTTGGTGCAATCCTATAT CTGGCCATGCTACCCCTTACTGGTACAGCAGATCCTGGGACAGGGCCCAAGCTTCTGATTACAGTTT CAGAATAACGGTGAGTGGATGATTCACAGTTGCCTAAGGATCGATTTTCTGCAGAGAGGCTCAAAGG AGTAGACTCCACTCTCAAGATCCAACCTGCAAAGCTTGAGGACTCGGCCGTGTATCTCTGTGCCAGCA GCCAGAGGTGGAACACCGGGGAGCTGTTTTTGGAGAAGGCTCTAGGCTGACCGTACTG
	105	ATGGGCACCCGGCTGCTGTGCTGGGCGGCCCTGTGCTGCTGGGAGCAGAGCTGACAGAGGCAGGAGT GGCCCACTCCCAACGGTACAAGATCATCGAGAAGAGACAGTCCGTGGCCTTTTGGTGCAACCCCATCT CTGGCCACGCCACCCGTGACTGGTATCAGCAGATCCTGGGACAGGGCCCTAAGCTGCTGATCCAGTTC CAGAACAATGGCGTGGTGGACGATTCTCAGCTGCCAAAGGACAGGTTTAGCGCCGAGCGCTGAAGGG CGTGGATAGCACCCCTGAAGATCCAGCCTGCCAAGCTGGAGGACAGCGCCGTGTATCTGTGCGCCAGCT CCAGCGGTCCAATACAGGCGAGCTGTTCTTGGCGAGGGCTCTAGGCTGACCGTGTG
	106	MGTRLLCWAALCLLGAELTEAGVAQSPRYKII EKRSVAFWCNPI SGHATLYWYQQILGQGP KLLIQF QNGVVDSDQLPKDRFSAERLKGVDSTLKI QPAKLEDSAVYLCASSQRSNTGELFFEGESRLTVL
RAS TCR-7 alpha chain	107	MLLLLVPLEVIFTLGGTRAQSVTQLDSHVSVEGTPVLLRCNYSYSSPSLFWYVQHPNKGQLQLLK YTSAAATLVKINGFEAEFFKSETSFHLTKPSAHMSDAAEYFCVVS GGSSNTGKLIFGQGTTLQVKPD IQNPDPVYQLRDSKSDKSVCLFTDFDSQTNVSQSKSDSVYITDKTVLDMRSMDFKSN SAVAWSNKS DFACANAFNNSIIPEDTFFPSP ESSCDVKLVEKSFETDTNLFQNL SVIGFRILLKLVAGFNLLMTLR LWSS
RAS TCR-7 beta chain	108	MGTRLLCWAALCLLGAELTEAGVAQSPRYKII EKRSVAFWCNPI SGHATLYWYQQILGQGP KLLIQF QNGVVDSDQLPKDRFSAERLKGVDSTLKI QPAKLEDSAVYLCASSQRSNTGELFFEGESRLTVLEDL NKVFPPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWVNGKEVHSGVSTDPQPLKEQ PALND SRYCLSSRLRVSATFWQNP RNHFRCQVQFYGLSENDEWTQDRAKPV TQIVSAEAWGRADCGFTSVSYQ QGVLSATILYEILLGKATLYAVLV SALVLMAMVKRKDF
RAS TCR-7 peptide	109	VVGACGVGK
	110	VVVGACGVGK
RAS TCR-8 alpha chain CDR1	111	TSINN
RAS TCR-8 alpha chain CDR2	112	IRSNERE
RAS TCR-8 alpha chain CDR3	113	CATDAGGGADGLTF
RAS TCR-8 beta chain CDR1	114	SGDLS
RAS TCR-8 beta chain CDR2	115	YNGEE
RAS TCR-8 beta chain CDR3	116	CASGGRDSTDTQYF

Name	SEQ ID NO	Sequence
RAS TCR-8 alpha chain variable domain	117	ATGGAAACTCTCCTGGGAGTGTCTTTGGTGATTCTATGGCTTCAACTGGCTAGGGTGAACAGTCAACA GGGAGAAGAGGATCCTCAGGCCCTTGAGCATCCAGGAGGGTGAATGCCACCATGAAGTGCAGTTACA AAACTAGTATAAACAATTTACAGTGGTATAGACAAAATTCAGGTAGAGGCCCTTGTCACCTAATTTTA ATACGTTCAAATGAAAGAGAGAAACACAGTGAAGATTAAAGAGTCACGCTTGACACTTCCAAGAAAAG CAGTTCCTTGTGATCAGCGCTTCCCGGGCAGCAGACACTGCTTCTTACTTGTGCTACGGACGCCG GAGGAGGTGCTGACGGACTCACCTTTGGCAAAGGGACTCATCTAATCATCCAGCCC
	118	ATGGAGACACTGCTGGGCGTGCCCTGGTTCATCCTGTGGCTGCAGCTGGCCAGGGTGAACAGCCAGCA GGGAGAGGAGGACCCCGAGGCCCTGTCTATCCAGGAGGGCGAGAAGCCACCATGAATTGCTCTTACA AGACAAGCATCAACAATCTGCAGTGGTATAGACAGAACTCCGGCAGGGGCTGGTGACCTGATCCTG ATCCGCTCCAATGAGCGGGAGAAAGCACTCTGGCCGGCTGAGAGTGACCTGGATACATCTAAGAAGTC CTCTAGCCTGCTGATCACCGCCAGCCGGGCAGCAGACACAGCCTCTACTTTTGTGCCACCGATGCCG GGGGCGGAGCAGACGGACTGACATTCGGGAAGGGGACTCACCTGATTATCCAGCCA
	119	METLLGVSLVILWLQLARVNSQQGEEDPQALS IQEENATMNC SYKTS INNLQWYRQNSGRGLVHLIL IRSNEREKHSGRRLVTLDTSKKSSLLITASRAADTASYFCATDAGGGADGLTFGKGTHLI IQP
RAS TCR-8 beta chain variable domain	120	ATGGGCTTCAGGCTCCTCTGCTGTGTGGCCTTTTGTCTCCTGGGAGCAGGCCAGTGGATTCTGGAGT CACACAAACCCCAAAGCACCTGATCAGCAACTGGACAGCGAGTGACGCTGAGATGCTCCCTAGGT CTGGAGACCTCTCTGTGTACTGGTACCAACAGAGCCTGGACCAGGGCCTCCAGTTCCTCATTAGTAT TATAATGGAGAAGAGAGAGCAAAAGGAAACATTCTTGAACGATTCTCCGCACAACAGTTCCTGACTT GCACTCTGAATAAACCTGAGCTCTCTGGAGCTGGGGGACTCAGCTTTGTATTTCTGTGCCAGCGGGG GACGGGATTCCACAGATACGAGTATTTTGGCCAGGCACCCGGCTGACAGTGCTC
	121	ATGGGCTTTCCGCTGCTGTGCTGCGTGGCTTTTTCCTGCTGGGGGCTGGGCTGTGGATAGCGGGGT CACTCAGACACCTAAACATCTGATCACCGCAACAGGACAGAGGGTGACCTGAGGTGCTCTCCTCGGA GCGGCGACCTGAGCGTGTACTGGTATCAGCAGAGCCTGGATCAGGGCCTGCAGTTCCTGATCCAGTAC TATAACGGCGAGGAGCGGCCAAGGGCAATATCCTGGAGCGGTTCTCTGCCAGCAGTTCCTCAGACCT GCACAGCGAGCTGAACCTGAGCTCCCTGGAGCTGGGGGATAGCGCCCTGTACTTCTGCGCCTCCGGCG GCAGAGACTCTACCGATACAGATATTTTGGCCCCGGCACCAGACTGACAGTGCTC
	122	MGFRLLCCVAFCLLGAGPVD SGVTQT PKHLITATGQRVTLRCS PRSGDLSVYVYQQSLDQGLQFLIQY YNGEERAKGNILERFSAQQFPDLHSELNLS SLELGDSALYFCASGGRDSTDQYFGPGTRLTVL
RAS TCR-8 alpha chain	123	METLLGVSLVILWLQLARVNSQQGEEDPQALS IQEENATMNC SYKTS INNLQWYRQNSGRGLVHLIL IRSNEREKHSGRRLVTLDTSKKSSLLITASRAADTASYFCATDAGGGADGLTFGKGTHLI IQPDIQN PDPAVYQLRDSKSSDKSVCLFTDFDSQTNVQS KSDSVYITDKTVLDMRSMDFKSN SAVAWSNKS DFA CANAFNNS IIPEDTFFPSP ESSCDVKLVEKSFETDTNLFQNL SVIGFRI LLLKVAGFNLLMTLR LWS S
RAS TCR-8 beta chain	124	MGFRLLCCVAFCLLGAGPVD SGVTQT PKHLITATGQRVTLRCS PRSGDLSVYVYQQSLDQGLQFLIQY YNGEERAKGNILERFSAQQFPDLHSELNLS SLELGDSALYFCASGGRDSTDQYFGPGTRLTVLEDLN KVFPPEVAVFEPSEAEISHTQKATLVCLATGFPPDHVELSWVWNGKEVHSGVSTDPQLKEQPALNDS RYCLSSRLRVSATFWQNPRNHFR CQVQFYGLSENDEWTQDRAKPVTVQIVSAEAWGRADCGFTSVSYQQ GVLSATILYEILGKATLYAVLV SALVLMAMVKRKDF
RAS TCR-8 peptide	125	VVGAVGVGK
	126	VVVGAVGVGK
Ras TCR-1/2 peptide	219	KLVVVGADGV
Ras TCR-1/2 peptide	220	LVVVGADGV
Ras TCR-1/2 peptide	221	KLVVVGAVGV
Ras TCR-1/2 peptide	222	LVVVGAVGV
RAS TCR-10 alpha chain CDR1	239	SVFSS
RAS TCR-10 alpha chain CDR2	240	VVTGGEV
RAS TCR-10 alpha chain CDR3	241	AGGPNTGNQFY

Name	SEQ ID NO	Sequence
RAS TCR-10 beta chain CDR1	242	SGHNT
RAS TCR-10 beta chain CDR2	243	YYREEE
RAS TCR-10 beta chain CDR3	244	ASSTSFWEVNTEAF
RAS TCR-10 alpha chain variable domains	245	ATGGTCCTGAAATTCTCCGTGTCCATTCTTTGGATTCAAGTTGGCATGGGTGAGCAGCCAGCTGCTGGA GCAGAGCCCTCAGTTTCTAAGCATCCAAGAGGGAGAAAATCTCACTGTGTACTGCAACTCCTCAAGTG TTTTTTCCAGCTTACAATGGTACAGACAGGAGCCTGGGGAAGGTCCTGTCTCCTGGTGACAGTAGTT ACGGGTGGAGAAGTGAAGAAGCTGAAGAGACTAACCTTTCAGTTTGGTGATGCAAGAAAGGACAGTTC TCTCCACATCACTGCGGCCAGCCTGGTGATACAGGCCTCTACCTCTGTGCGAGGAGGGCCGAACACCG GTAACCAAGTTCTATTTTGGGACAGGGACAAGTTTGACGGTCATTCCAAAT
	246	ATGGTGCTGAAGTTTTCCGTGTCTATCCTGTGGATTCAAGTTGGCCTGGGTGTCTACCCAGCTGCTGGA GCAGAGCCCCAGTTCTGTCCATCCAGGAGGGCGAGAACCTGACAGTGACTGCAATTCTAGCTCCG TGTTTTCTAGCCTGCAAGTGGTATAGGCAGGAGCCAGGAGAGGGACCCGTGCTGCTGGTGACCGTGGTG ACAGGCGGCGAGGTGAAGAAGCTGAAGAGACTGACCTTCCAGTTTGGCGACGCCAGGAAGGATTTCCTC TCTGCACATCACCGCAGCACAGCCTGGCGATACAGGACTGTACCTGTGCGCAGGAGGACCAAAACCG GCAATCAGTTCTATTTTGGCACCGGCACATCCCTGACAGTGATCCCTAAT
	247	MVLKFSVSIILWQLAWVSTQLLEQSPQFLSIQEGENLTVYCNSSSVFSSLQWYRQEPGEGPVLLVTVV TGGEVKKLKRITFQFGDARKDSSLHITAAQPGDTGLYLCAGGPNTGNQFYFGTGTSLTVIPN
RAS TCR-10 beta chain variable domain	248	ATGGGCCCTGGGCTCCTCTGCTGGGTGCTGCTTTGTCTCCTGGGAGCAGGCTCAGTGGAGACTGGAGT CACCCAAAGTCCACACACCTGATCAAAACGAGAGGACAGCAAGTGACTCTGAGATGCTCTTCTCAGT CTGGGCACAACACTGTGTCTGGTACCAACAGGCCCTGGGTGAGGGCCCCAGTTTATCTTTCAGTAT TATAGGAGGAGAGAAATGGCAGAGGAACTTCCCTCCTAGATTCTCAGGTCTCCAGTTCCCTAATTA TAGCTCTGAGCTGAATGTGAACGCCTTGGAGCTGGAGCACTCGGCCCTGTATCTCTGTGCCAGCAGCA CATCTTTTGGGAGGTGAACACTGAAGCTTTCTTTGGACAAGGCACAGACTCACAGTTGTA
	249	ATGGGACCAGGACTGCTGTGCTGGGTGCTGCTGTGCCTGCTGGGAGCAGGCTCCGTGGAGACCGGCGT GACACAGTCTCCACCCACCTGATCAAGACAAGAGGCCAGCAGGTGACCTGAGGTGCAGCTCCAGT CTGGCCACAACACAGTGAGCTGGTACCAGCAGGCCCTGGGACAGGACCTCAGTTTCTTTCAGTAC TATAGGAGGAGGAGAGAACGGCCGCGGCAATTTCCCCCTCGGTTTAGCGGCCCTGCAGTTCCCAAATA CTCTAGCGAGCTGAACGTGAATGCCCTGGAGCTGGACGATAGCGCCCTGTATCTGTGCGCCTCCTCTA CCTCCTTTTGGGAAGTGAATACAGAGGCCTTCTTTGGCCAGGGCACCCGCTGACAGTGCTG
	250	MGPGLLCWVLLCCLLGAGSVETGVTQSPHLLIKTRGQVTLRCSSQSGHNTVSWYQQALGQGPQFIQFY YREEENGRGNFPRFSGLQFPNYSSELNVNALELDDSAALYLCASSTSFWEVNTEAFFGQGTRLTVV
RAS TCR-10 alpha chain	251	MVLKFSVSIILWQLAWVSTQLLEQSPQFLSIQEGENLTVYCNSSSVFSSLQWYRQEPGEGPVLLVTVV TGGEVKKLKRITFQFGDARKDSSLHITAAQPGDTGLYLCAGGPNTGNQFYFGTGTSLTVIPNDIQNPE PAVYQLKDPQSQDSTLCLFTDFDSQINVPKTMESGTFITDKTVLDMKAMDSKNGAIAWSNQTSTFCQ DIFKETNATYPSSDVPDATLTKSFETDMNLNFQNLVSMGLRILLKLVAGFNLLMTLRLWSS
RAS TCR-10 beta chain	252	MGPGLLCWVLLCCLLGAGSVETGVTQSPHLLIKTRGQVTLRCSSQSGHNTVSWYQQALGQGPQFIQFY YREEENGRGNFPRFSGLQFPNYSSELNVNALELDDSAALYLCASSTSFWEVNTEAFFGQGTRLTVVKD LRNVTPPKVSLFEPKAEIANKQKATLVCLARGFFPDHVELSWVNGKEVHSGVSTDPQAYKESNYSY CLSSRLRVSATFWHNPARNHFCQVQFHGLSEEDKWPEGSPKPVTONISAEAWGRADCGITSASYHQGV LSATILYEILLGKATLYAVLVSGVLVLMAMVKKNS
TCR peptide	253	VVGACGVGK
	254	VVVGACGVGK
RAS TCR-11 alpha chain CDR1	255	TSGFNG
RAS TCR-11 alpha chain CDR2	256	NVLDGL
RAS TCR-11 alpha chain CDR3	257	AVREEVLYNQGGKLI
RAS TCR-11 beta chain CDR1	258	LNHDA

Name	SEQ ID NO	Sequence
RAS TCR-11 beta chain CDR2	259	SQIVND
RAS TCR-11 beta chain CDR3	260	ASSKRGWPYEQY
RAS TCR-11 alpha chain variable domain	261	ATGTGGGGAGTTTCTCTTTATGTTTCCATGAAGATGGGAGGCACTACAGGACAAAACATTGACCA GCCCCACTGAGATGACAGCTACGGAAGGTGCCATTGTCCAGATCAACTGCACGTACCAGACATCTGGGT TCAACGGGCTGTCTGTGTACCAGCAACATGCTGGCGAAGCACCACATTTCTGTCTTACAATGTTCTG GATGGTTTGGAGGAGAAAGGTCGTTTTTCTTCATTCTCTAGTCGGTCTAAAGGGTACAGTTACCTCCT TTTGAAGGAGCTCCAGATGAAAGACTCTGCCTCTTACCTCTGTGCTGTGAGAGAGGAGGTCTTTTATA ACCAGGGAGGAAAGCTTATCTTCGGACAGGGAACGGAGTTATCTGTGAAACCC
	262	ATGTGGGGCGTGTTCCTGCTGTACGTGAGCATGAAGATGGGCGGCACCACAGGCCAGAACATCGACCA GCCAACCGAGATGACCGCCACAGAGGGCGCCATCGTGCAGATCAACTGCACCTACCAGACAAGCGGCT TCAATGGCCTGTTTTGGTATCAGCAGCAGCAGGAGAGGCACCCACATTCCTGTCTATAATGTGCTG GACGGCCTGGAGGAGAAGGGCAGGTTCTCCTCTTTCTGAGCCGCTCCAAGGGCTACTCCTATCTGCT GCTGAAGGAGCTGCAGATGAAGGATTCTGCCAGCTACCTGTGCGCCGTGCGGGAGGAGGTGCTGTATA ATCAGGGCGGCAAGCTGATCTTTGGCCAGGGCACCAGCTGAGCGTGAAGCCT
	263	MWGVFLLYVSMKMGTTGQNIQDPTMTATEGAIVQINCTYQTSGFNGLFWYQQHAGEAPTFLSYNVL DGLEEKGRFSSFLSRSGYSYLLKELQMKDSASYLCVREEVLYNQGGKLI FGQGTLSVKP
RAS TCR-11 beta chain variable domain	264	ATGAGCAACCAGGTGCTCTGCTGTGTGCTCTTTGTCTCCTGGGAGCAAACACCGTGGATGGTGAAT CACTCAGTCCCCGAAGTACCTGTTTCAAGAAAGGAGGACAGAATGTGACCCCTGAGTTGTGAACAGAATT TGAACCAAGATGCCATGTTACTGGTACGACAGGACCCAGGGCAAGGGCTGAGATTGATCTACTACTCA CAGATAGTAAATGACTTTCAGAAAGGAGATATAGCTGAAGGGTACAGCGTCTCTCGGGAGAGAAGGA ATCCTTTCCTCTCACTGTGACATCGGCCCAAAGAACCAGAGCTTTCTATCTCTGTGCCAGTAGTA AAAGGGGATGGCCCTACGAGCAGTACTTCGGGCCGGGCACCAGGCTCACGGTCACA
	265	ATGTCCAACCAGGTGCTGTGCTGCGTGGTGTGCTGCTGCTGGGAGCAAATACCGTGGACGGAGGCAT CACACAGTCCCCCAAGTACCTGTTCCGGAAGGAGGGCCAGAACGTGACCCCTGTCTGTGAGCAGAACC TGAATCAGCAGCCATGTACTGGTATAGGCAGGACCCGGACAGGGACTGAGACTGATCTACTATAGC CAGATCGTGAACGACTTTCAGAAAGGGCGACATCGCCGAGGGCTACAGCGTGTCCCGGAGAGAAGGA GTCCTTCCCACTGACCGTGACATCTGCCAGAAGAATCCACCGCCTTTATCTGTGCGCCAGCTCCA AGAGAGGCTGGCCCTACGAGCAGTATTTCCGCCCTGGCACCAGGCTGACCGTGACA
	266	MSNQVLCVVLCLLGANTVDGGITQSPKYLFRKEGQNVTLSCQNLNHDAMYWYRQDPGQGLRLIYY QIVNDFQKGDIAEGYSVSREKKESFPLTVTSAQKNPTAFYLCASSKRGWPYEQYFGPGTRLTVT
RAS TCR-11 alpha chain	267	MWGVFLLYVSMKMGTTGQNIQDPTMTATEGAIVQINCTYQTSGFNGLFWYQQHAGEAPTFLSYNVL DGLEEKGRFSSFLSRSGYSYLLKELQMKDSASYLCVREEVLYNQGGKLI FGQGTLSVKPDIQNP EPAVYQLKDPQSQDSTLCLFTDFDSQINVPKTMESGTFITDKTVLDMKAMDSKNGAIAWSNQTSTFC QDIFKETNATYPSSDVPDATLTEKSFETDMNLNFQNLVSMGLRILLLKVAGFNLLMTLRLWSS
RAS TCR-11 beta chain	268	MSNQVLCVVLCLLGANTVDGGITQSPKYLFRKEGQNVTLSCQNLNHDAMYWYRQDPGQGLRLIYY QIVNDFQKGDIAEGYSVSREKKESFPLTVTSAQKNPTAFYLCASSKRGWPYEQYFGPGTRLTVTKDLR NVTTPKVSLEFESKAEIANKQKATLVCLARGFFPDHVELSWVNGKEVHSGVSTDPQAYKESNYSYCL SSRLRVSATFWHNP RNHFRCQVQFHGLSEEDKWPEGSFKPVTQNI SAEAWGRADCGITSASYHQGVLS ATILYEILLGKATLYAVLVSGVLVLMAMVKKNS
TCR peptide	269	VVGACGVGK
	270	VVGACGVGK
RAS TCR-12 alpha chain CDR1	271	TSINN
RAS TCR-12 alpha chain CDR2	272	IRSNERE
RAS TCR-12 alpha chain CDR3	273	ATDRQSSGDKLT
RAS TCR-12 beta chain CDR1	274	SGHAT
RAS TCR-12 beta chain CDR2	275	FQNNGV

Name	SEQ ID NO	Sequence
RAS TCR-12 beta chain CDR3	276	ASSLADIYEQY
RAS TCR-12 alpha chain variable domain	277	ATGGAAACTCTCCTGGGAGTGTCTTTGGTGATTCTATGGCTTCAACTGGCTAGGGTGAACAGTCAACA GGGAGAAGAGGATCCTCAGGCCTTGAGCATCCAGGAGGGTGAAAATGCCACCATGAACTGCAGTTACA AACTAGTATAAACAATTTACAGTGGTATAGACAAAATTCAGGTAGAGGCCTTGTCCACCTAATTTTA ATACGTTCAAATGAAAGAGAGAAACACAGTGGAAGATTAAGAGTCACGCTTGACACTTCCAAGAAAAG CAGTTCCTTGTGATCAGCGCTTCCCGGGCAGCAGACACTGCTTCTTACTTCTGTGCTACGGACCGTC AAAGCAGCGGAGACAAGCTGACTTTTGGGACCGGGACTCGTTAGCAGTTAGGCC
	278	ATGGAGACCCTGCTGGGCGTGTCCCTGGTTCATCCTGTGGCTGCAGCTGGCCAGGGTGAACAGCCAGCA GGGAGAGGAGGACCCCGAGCCCTGAGCATCCAGGAGGGCAGAACGCCACCATGAATTGCTCTTACA AGACAAGCATCAACAATCTGCAGTGGTATAGGCAGAACTCCGGCCCGGGACTGGTGCACCTGATCCTG ATCCGGAGCAATGAGAGAGAGAGCACTCCGGCCGGCTGAGAGTGACCCTGGACACATCTAAGAAGTC CTCTAGCCTGCTGATCACCCTCTCGGGCAGCAGATACAGCCAGCTACTTCTGTGCCACCGACAGAC AGTCTCTGGCGATAAGCTGACCTTTGGCACCGGCACAAGGCTGGCCGTGCCGCC
	279	METLLGVSLVILWLQRLARVNSQQGEEDPQALS IQEENATMNC SYKTS INNLQWYRQNSGRGLVHLIL IRSNEREKHSGRRLVTLDTSKSSSLITASRAADTASYFCATDRQSSGDKLTFGTGRLAVRP
RAS TCR-12 beta chain variable domain	280	ATGGGACACAGCTCCTCTGCTGGGCGGCCCTCTGTCTCCTGGGAGCAGAACTCACAGAAGCTGGAGT TGCCCACTCTCCAGATATAAGATTATAGAGAAAAGCAGAGTGTGGCTTTTGGTGCAATCCTATAT CTGGCCATGCTACCCCTTACTGGTACCAGCAGATCCTGGGACAGGGCCCAAAGCTTCTGATTAGTTT CAGAATAACGGTGTAGTGGATGATTCACAGTTGCCTAAGGATCGATTTTCTGCAGAGAGGCTCAAAGG AGTAGACTCCACTCTCAAGATCCAGCCTGCAAAGCTTGAGGACTCGGCCGTGTATCTCTGTGCCAGCA GCTTAGCCGACATCTACGAGCAGTACTTCGGGCCGGGCACAGGCTCACGGTCACA
	281	ATGGGAACAAGGCTGCTGTGCTGGGCGGCCCTGTGCCTGCTGGGAGCAGAGCTGACCGAGGCCGGCGT GGCCAGAGCCCCCGGTACAAGATCATCGAGAAGAGACAGAGCGTGGCCTTCTGGTGCAACCTATCT CCGGCCACGCCACACTGTACTGGTATCAGCAGATCCTGGGCCAGGGCCCAAAGCTGCTGATCCAGTTT CAGAACAATGGCGTGGTGACGATTCCAGCTGCCAAGGACCGGTTTCTGCCGAGAGACTGAAGGG CGTGGATTCCACCCTGAAGATCCAGCCGCCAAGCTGGAGGACTCTGCCGTGTATCTGTGCCAGCT CCCTGGCCGACATCTACGAGCAGTATTTCCGGCCTGGCACAGGCTGACCGTGACA
	282	MGTRLLCWAALCLLGAELTEAGVAQS PRYKII EKRSVAFWCNPI SGHATLYWYQQILGQGP KLLIQF QNNGVVDSDQLPKDRFSAERLKGVDSTLKI QPAKLEDSAVYLCASSLADIYEQYFPGTRLTVT
RAS TCR-12 alpha chain	283	METLLGVSLVILWLQRLARVNSQQGEEDPQALS IQEENATMNC SYKTS INNLQWYRQNSGRGLVHLIL IRSNEREKHSGRRLVTLDTSKSSSLITASRAADTASYFCATDRQSSGDKLTFGTGRLAVRPDIQN PEPAVYQLKDPQSQDSTLCLFTDFDSQINVPKTMESGTFITDKTVLDMKAMDSKSNGAIAWSNQTSFT CQDIFKETNATYFSSDVP CDATLTEKSFETDMNLFQNL SVMGLRI LLLKVAGFNLMLTLRLWSS
RAS TCR-12 beta chain	284	MGTRLLCWAALCLLGAELTEAGVAQS PRYKII EKRSVAFWCNPI SGHATLYWYQQILGQGP KLLIQF QNNGVVDSDQLPKDRFSAERLKGVDSTLKI QPAKLEDSAVYLCASSLADIYEQYFPGTRLTVT KDRLR NVT PPKVSLFEP SKAEIANKQKATLVCLARGFFPDHVELSWVNGKEVHSGVSTD PQAYKESNYSYCL SSRLRVSATFWHNPRNHFR CQVQFHGLSEEDKWPEGSFKPVTQNI SAEAWGRADCGITSAS YHQVLS ATILYEILLGKATLYAVLVSGLVLMAMVKKNS
TCR peptide	285	VVGACGVGK
	286	VVGACGVGK
RAS TCR-13 alpha chain CDR1	287	TSESDYY
RAS TCR-13 alpha chain CDR2	288	QEAYKQQN
RAS TCR-13 alpha chain CDR3	289	ALYIYGGSQGNLI
RAS TCR-13 beta chain CDR1	290	SEHNR
RAS TCR-13 beta chain CDR2	291	FQNEAQ
RAS TCR-13 beta chain CDR3	292	ASSSTDRIEAF

Name	SEQ ID NO	Sequence
RAS TCR-13 alpha chain variable domain	293	ATGGCATGCCCTGGCTTCCTGTGGGCACTTGTGATCTCCACCTGTCTTGAATTTAGCATGGCTCAGAC AGTCACTCAGTCTCAACCAGAGATGTCTGTGCAGGAGGCGAGAGACCGTGACCCTGAGCTGCACATATG ACACCACTGAGAGTGATTATTTATTTCTGGTACAAGCAGCCTCCAGCAGGCGAGATGATCTCGTT ATTGCGCAAGAAGCTTATAAGCAACAGAATGCAACAGAGAATCGTTTCTGTGAACTTCCAGAAAGC AGCCAAATCCTTCAGTCTCAAGATCTCAGACTCACAGCTGGGGGATGCCGCGATGTATTTCTGTGCTC TCTATATTTATGGAGGAAGCCAAGGAAATCTCATCTTTGGAAAAGGCATAAACTCTCTGTAAACCA
	294	ATGGCATGCCAGGCTTCCTGTGGGCACTGGTCATCAGCATGTCTGGAGTTTCTATGGCCGAGAC CGTGACACAGTCTCAGCCTGAGATGAGCGTGCAGGAGGCCGAGACCGTGACACTGAGCTGCACCTACG ACACATCTGAGAGCGATTACTATCTGTTCTGGTATAAGCAGCCACCCTCCAGACAGATGATCCTGGTC ATCAGGCAGGAGGCCCTACAAGCAGCAGAACGCCACCGAGAATCGGTTCTCCGTGAACTTTCAGAAGGC CGCCAAGTCTTTCTCTGAAGATCAGCGACTCCAGCTGGGCGATGCCGCGATGATTTCTGTGCC TGTACATCTATGGCGGCTCTCAGGGCAATCTGATCTTTGGCAAGGGCACCAAGCTGAGCGTGAAGCCT
	295	MACPGFLWALVISTCLEFSMAQTVTQSQPEMSVQEAETVTLSTYDTSSESDYYLFWYKQPPSRQMLLV IRQEAAYKQONATENRFSVNFQKAAKSFSLKISDSQLGDAAMYFCALYIYGGSQGNLIFGKGTKLSVKP
RAS TCR-13 beta chain variable domain	296	ATGGGCACCGACCTCCTGTGCTGGATGGCCCTGTGTCTCCTGGGGGAGATCAGCAGATATCGGAGT CTCCCAGGACCCAGACACAAGATCACAAGAGGGGACAGAATGTAACCTTTCAGGTGTGATCCAATTT CTGAACACAACCGCCTTATTGTTACCGACAGACCTGGGGCAGGGCCAGAGTTTCTGACTTACTTC CAGAATGAAGCTCAACTAGAAAAATCAAGGCTGCTCAGTGTATCGGTTCTCTGCAGAGAGGCCTAAGGG ATCTTTTCTCCACCTTGAGATCCAGCGCACAGAGCAGGGGGACTCGGCCATGTATCTCTGTGCCAGCA GCTCCACCGACAGGATTGAAGCTTTCTTTGGACAAGGCACCGAGCTCACAGTTGTA
	297	ATGGGCACCTCCTGTGTGCTGGATGGCACTGTGCCTGCTGGGAGCAGACCACGCAGATACAGGCGT GTCTCAGGACCCACGCCACAAGATCACAAGCGGGGCCAGAACGTGACATTCAGATGCGATCCCATCT CCGAGCACAAATAGGCTGTACTGTTATAGGCAGACCTGGGACAGGGACAGAGTTCTGCATACACTT CAGAACGAGGCCAGCTGGAGAAGAGCCGGCTGCTGTCCGACAGATTCTCTGCCGAGAGGCCCAAGGG CTCTTTTAGCACCTTGAGATCCAGAGAACAGAGCAGGGCGACAGCGCCATGTATCTGTGCCAGCT CCTCTACCGATAGGATCGAGGCCCTCTTTGGCCAGGGCACCCGCTGACAGTGGTG
	298	MGTSLLCWMALCLLGADHDTGVSQDPRHKITKRGQNVTFRCDPISSEHNRLYWYRQTLGQGPFLTYF QNEAQLEKSRLLSDRFSERPKGSFSTLEIQRTQGD SAMYLCASSSTDRIEAFQGGTRLTVV
RAS TCR-13 alpha chain	299	MACPGFLWALVISTCLEFSMAQTVTQSQPEMSVQEAETVTLSTYDTSSESDYYLFWYKQPPSRQMLLV IRQEAAYKQONATENRFSVNFQKAAKSFSLKISDSQLGDAAMYFCALYIYGGSQGNLIFGKGTKLSVKP DIQNPEPAVYQLKDPQSQDSTLCLFTDFDSQINVPKTMESGTFITDKTVLDMKAMDSKSNIAIWSNQ TSFTCQDIFKETNATYPSSDVPDCATLTEKSFETDMNLNLFQNL SVMGLRIILLKVAGFNLLMTLRLWS S
RAS TCR-13 beta chain	300	MGTSLLCWMALCLLGADHDTGVSQDPRHKITKRGQNVTFRCDPISSEHNRLYWYRQTLGQGPFLTYF QNEAQLEKSRLLSDRFSERPKGSFSTLEIQRTQGD SAMYLCASSSTDRIEAFQGGTRLTVVVKDLR NVTPPKVSLFEPKAEIANKQKATLVCLARGFFPDHVELSWVNGKEVHSGVSTDPQAYKESNYSCL SSRLRVSATFWHNP RNHFRCQVQFHGLSEEDKWPEGSPKPVTONISAEAWGRADCGITSASYHQGVLS ATILYEILLGKATLYAVLVSGVLVLMAMVKKNS
TCR Peptides	301	VVGADGVGK
	302	VVGADGVGK
RAS TCR-14 alpha chain CDR1	303	VSNAYN
RAS TCR-14 alpha chain CDR2	304	GSKP
RAS TCR-14 alpha chain CDR3	305	ATYNFNKFY
RAS TCR-14 beta chain CDR1	306	SGHTS
RAS TCR-14 beta chain CDR2	307	YDEGEE
RAS TCR-14 beta chain CDR3	308	ASTTFKTGRAIEKLF

Name	SEQ ID NO	Sequence
RAS TCR-14 alpha chain variable domain	309	ATGGCTTTGCAGAGCACTCTGGGGCGGTGTGGCTAGGGCTTCTCCTCAACTCTCTCTGGAAGGTTGC AGAAAGCAAGGACCAAGTGTTCAGCCTTCCACAGTGGCATCTTCAGAGGGAGCTGTGGTGGAAATCT TCTGTAATCACTCTGTGTCCAATGCTTACAACCTTCTCTGGTACCTTCACTTCCCGGGATGTGCACCA AGACTCCTTGTAAAGGCTCAAAGCCTTCTCAGCAGGGACGATACAACATGACCTATGAACGGTTCTC TTCATCGCTGCTCATCCTCCAGGTGCCGGAGGCAGATGCTGCTGTTTACTACTGTGCTACGTACAACCT TCAACAAATTTTACTTTGGATCTGGGACCAAACTCAATGTAAACCA
	310	ATGGCCCTGCAGTCTACACTGGGAGCCGTGTGGCTGGGACTGCTGCTGAACCTCTCTGTGGAAGGTGGC CGAGAGCAAGGACCAGGTGTTCAGCCTAGCACCGTGGCCTCCTCTGAGGGAGCAGTGGTGGAGATCT TTTGCAATCACTCCGTGTCTAACGCCACAATTTCTTTGGTATCTGCACCTTCCAGGATGTGCACCA AGGCTGCTGGTGAAGGGCAGCAAGCCATCCCAGCAGGGCCGGTACAACATGACCTATGAGAGATTGAG CTCCTCTCTGCTGATCCTGCAGGTGAGAGAGGCCGATGCCGCCGTGTACTATTGTGCCACCTACAACCT TTAATAAGTTCTATTTTGGCTCCGGCACAAAGCTGAATGTGAAGCCT
	311	MALQSTLGAVWLGLLLNSLWKVAESKDQVFQPSSTVASSEGAVVEIFCNHVSNSAYNFFWYLFHFGCAP RLLVKGSKPSQQGRYNTYERFSSSLILQVREADAAVYYCATYNFNKFFYFGSGTKLVNPK
RAS TCR-14 beta chain variable domain	312	ATGGGACCAAGGCTCCTCTTCTGGGCACTGCTTGTCTCCTCGGAACAGGCCAGTGGAGGCTGGAGT CACACAAAGTCCACACACCTGATCAAAACGAGAGGACAGCAAGCGACTCTGAGATGCTCTCCTATCT CTGGGCACACCAAGTGTGTACTGCTACCAACAGGCCCTGGGTCTGGGCCTCCAGTTCTCTCTTGGTAT GACGAGGGTGAAGAGAGAAACAGAGGAACTTCCCTCCTAGATTTTCAGGTCGCCAGTTCCCTAATTA TAGCTCTGAGCTGAATGTGAACGCCCTTGGAGCTGGAGGACTCGGCCCTGTATCTCTGTGCCAGCACCA CTTTTAAGACGGGACGGGCAATTGAAAACTGTTTTTGGCAGTGGAAACCCAGCTCTCTGTCTTG
	313	ATGGGACCAAGGCTGCTGTTCTGGGCACTGCTGTGCCTGCTGGGAACCGGACCTGTGGAGGCCGGCGT GACCCAGTCTCCAACACACCTGATCAAGACCAGGGGACAGCAGGCCACACTGAGGTGTAGCCCCATCT CCGGCCACACAAGCGTGTACTGCTATCAGCAGGCCCTGGGACTGGGACTGCAGTTCTCTGTGTGGTAC GACGAGGGCGAGGAGAGGAACCGCGGCAATTTCCACCTCGGTTCCAGCGGCCGGCAGTTTCCCAACTA CAGCTCCGAGCTGAACGTGAATGCCCTGGAGCTGGAGGACAGCGCCCTGTATCTGTGCGCCTCCACCA CATTCAAGACCGGCAGGGCCATCGAGAAGCTGTTCTTTGGCTCTGGCACCCAGCTGAGCGTGCTG
	314	MGPRLLFWALLCLLGTGPVEAGVTQSPHLLIKTRGQATLRCSPISGHTSVYVYQQALGLGLQFLWY DEGEERNRGNFPPRFSGRQFPNYSSELNVNALELEDALYLCASTTFKTRGAIKLEFFGSGTQLSVL
RAS TCR-14 alpha chain	315	MALQSTLGAVWLGLLLNSLWKVAESKDQVFQPSSTVASSEGAVVEIFCNHVSNSAYNFFWYLFHFGCAP RLLVKGSKPSQQGRYNTYERFSSSLILQVREADAAVYYCATYNFNKFFYFGSGTKLVNPKDIQNPEP AVYQLKDPQRSQDSTLCLFTDFDSQINVPKTMESGTFITDKTVLDMKAMDSKNGAIAWSNQTSTFCQD IFKETNATYPSSDVPDCLTEKS FETDMNLNFQNLVSMGLRILLKLVAGFNLMLTLRLWSS
RAS TCR-14 beta chain	316	MGPRLLFWALLCLLGTGPVEAGVTQSPHLLIKTRGQATLRCSPISGHTSVYVYQQALGLGLQFLWY DEGEERNRGNFPPRFSGRQFPNYSSELNVNALELEDALYLCASTTFKTRGAIKLEFFGSGTQLSVLK DLRNVTPPKVSLFEPKAEIANKQKATLVCLARGFFPDHVELSWVNGKEVHSGVSTDPQAYKESNYS YCLSSRLRVSATFWHNPNNHFRQVQFHGLSEEDKWPEGS PKPVTQNI SAEAWGRADCGITSASYHQG VLSATILYEIILGKATLYAVLVSGLVLMAMVKKKNS
TCR peptide	317	VVGADGVGK
	318	VVVGADGVGK
RAS TCR-15 alpha chain CDR1	319	TSGFNG
RAS TCR-15 alpha chain CDR2	320	NVL DGL
RAS TCR-15 alpha chain CDR3	321	AVRDRGGSYIPT
RAS TCR-15 beta chain CDR1	322	MNHEY
RAS TCR-15 beta chain CDR2	323	SMNVEV
RAS TCR-15 beta chain CDR3	324	ASSSRGHSGTEAF

Name	SEQ ID NO	Sequence
RAS TCR-15 alpha chain variable domain	325	ATGTGGGGAGTTTTCCTTCTTTATGTTTCCATGAAGATGGGAGGCACTACAGGACAAAACATTGACCA GCCCCTGAGATGACAGCTACGGAAGGTGCCATTGTCCAGATCAACTGCACGTACCAGACATCTGGGT TCAACGGGCTGTTCTGGTACCAGCAACATGCTGGCGAAGCACCCACATTTCTGTCTTACAATGTTCTG GATGGTTTGGAGGAGAAAGGTCGTTTTTCTTCATTCCTTAGTCGGTCTAAAGGGTACAGTTACCTCCT TTTGAAGGAGCTCCAGATGAAGACTCTGCCTCTTACCTCTGTGCTGTGAGAGATCGAGGAGGAAGCT ACATACCTACATTTGGAAGAGGAACCAAGCCTTATTGTTTCATCCG
	326	ATGTGGGGCGTGTTCCTGCTGACGTGTCTATGAAGATGGGCGGCACCAAGGCCAGAACATCGACCA GCCTACCGAGATGACCGCCACAGAGGGCGCCATCGTGCAGATCAACTGCACCTACCAGACATCTGGCT TCAATGGCCTGTTTTGGTATCAGCAGCACGCCGGCAGGCCCAACATTCTGTCTATAATGTGCTG GATGGCCTGGAGGAGAAGGGCAGGTTCTCTAGCTTTCTGTCCCGCTCTAAGGGCTACAGCTATCTGCT GCTGAAGGAGCTGCAGATGAAGGACAGCGCCTCCTACCTGTGCGCGCTGCGGGATAGAGGAGGCTCCT ATATCCCTACCTTTGGCCGGGCACATCTCTGATCGTGACCCCA
	327	MWGVFLLYVSMKMGTTGQNIQDPTMTATEGAIVQINCTYQTSGFNGLFWYQQHAGEAPTFLSYNVL DGLEEKGRFSSFLSRSGYSYLLKELQMKDSASYLCAVRDRGGSYIPTFGRGTS LIVHP
RAS TCR-15 beta chain variable domain	328	ATGGGCCCCAGCTCCTTGGCTATGTTGCTCTTTGCCTTCTAGGAGCAGGCCGCCCTGGAAGCCCAAGT GACCCAGAACCCAAGATACCTCATCAGTACTGGAAAGAAGTTAACAGTGACTTGTCTCAGAATA TGAACCATGAGTATATGTCTGCTATCGACAAGACCCAGGGCTGGGCTTAAGGCAGATCTACTATTCA ATGAATGTTGAGGTGACTGATAAGGGAGATGTTCTCTGAAGGGTACAAAGTCTCTCGAAAAGAGAAGAG GAATTTCCCCCTGATCCTGGAGTCGCCCAGCCCCAACCCAGACCTCTCTGTACTTCTGTGCCAGCAGTT CCAGGGGGCATTCCGGGCACTGAAGCTTTCTTTGGACAAGGCACCAAGCTCAGACTCACAGTTGTA
	329	ATGGGACCACAGCTGCTGGGATACGTGCTGTGCTGCTGCTGGGAGCAGGACCCTGGAGGCACAGGT GACCCAGAACCCACGGTATCTGATCACCGTGACAGGCAAGAAGCTGACCGTGACATGTTCTCAGAACA TGAATCACGAGTACATGAGCTGTTATAGGCAGGACCCCTGGACTGGGACTGAGACAGATCTACTATAGC ATGAATGTGGAGGTGACCGACAAGGGCGATGTGCCCAGGGCTACAAGGTGTCCAGGAAGGAGAAGCG CAACTTCCCTCTGATCCTGGAGTCCTCATCTCCCAATCAGACCAGCCTGTATTTTTGCGCCAGCTCCT CTAGGGGACACTCCGGAACAGAGGCCTTCTTTGGCCAGGGCACCAGGCTGACAGTGGTG
	330	MGPQLLGYVVLCLLGAGPLEAQVTQNPRLITVTGKKLTVTCQNMNHEYMSWYRQDPGLGLRQIYY MNVEVTDKGDVPEGYKVS RKEKRN FPLI LESPSPNQTS LYFCASSSRGHS GTEAFFGQGT RLTVV
RAS TCR-15 alpha chain	331	MWGVFLLYVSMKMGTTGQNIQDPTMTATEGAIVQINCTYQTSGFNGLFWYQQHAGEAPTFLSYNVL DGLEEKGRFSSFLSRSGYSYLLKELQMKDSASYLCAVRDRGGSYIPTFGRGTS LIVHPDIQNPEPA VYQLKDRSQDSTLCLFTDFDSQINVPKTMESGTFITDKTVLDMKAMDSKNGAIAWSNQTSFTCQDI FKETNATYPSSDVPCDATLTEKSFETDMNLNFQNLVSMGLRI LLLKVAGFNLLMTLRLWSS
RAS TCR-15 beta chain	332	MGPQLLGYVVLCLLGAGPLEAQVTQNPRLITVTGKKLTVTCQNMNHEYMSWYRQDPGLGLRQIYY MNVEVTDKGDVPEGYKVS RKEKRN FPLI LESPSPNQTS LYFCASSSRGHS GTEAFFGQGT RLTVVVDL RNVTPPKVSLFEPKAEIANKQKATLVCLARGFFPDHVELSWWVNGKEVHSGVSTDPQAYKESNYSYC LSRRLRVSATFWHNP RNHFRCQVQFHGLSEEDKWPEGSPKPV TQNI SAEAWGRADCGITSASYHQGV SATILYEILLGKATLYAVLVSLVLMAMVKKKNS
TCR Peptides	333	VVGADGVGK
	334	VVVGADGVGK
RAS TCR-16 alpha chain CDR1	335	TSINN
RAS TCR-16 alpha chain CDR2	336	IRSNERE
RAS TCR-16 alpha chain CDR3	337	AGLYSSASKII
RAS TCR-16 beta chain CDR1	338	MNHEY
RAS TCR-16 beta chain CDR2	339	SMNVEV
RAS TCR-16 beta chain CDR3	340	ASSSRGHS GTEAF

Name	SEQ ID NO	Sequence
RAS TCR-16 alpha chain variable domain	341	ATGGAAACTCTCCTGGGAGTGTCTTTGGTGATTCTATGGCTTCAACTGGCTAGGGTGAACAGTCAACA GGGAGAAGAGGATCCTCAGGCCTTGAGCATCCAGGAGGGTGAAAATGCCACCATGAACTGCAGTTACA AAACTAGTATAAACAATTTACAGTGGTATAGACAAAATTCAGGTAGAGGCCTTGTCACCTAATTTTA ATACGTTCAAATGAAAGAGAGAAACACAGTGAAGATTAAGAGTCACGCTTGACACTTCCAAGAAAAG CAGTTCCTTGTGATCACGGCTTCCCGGGCAGCAGACACTGCTTCTTACTTCTGTGCTGGGCTGTACA GCAGTGCTTCCAAGATAATCTTTGGATCAGGACCAGACTCAGCATCCGGCCA
	342	ATGGAGACACTGCTGGGCGTGTCCCTGGTCATCCTGTGGCTGCAGCTGGCCAGAGTGAACAGCCAGCA GGGAGAGGAGGACCTCAGGCCTTGAGCATCCAGGAGGGCGAGAACGCCACCATGAATTGCTCTTACA AGACAAGCATCAACAATCTGCAGTGGTATAGGCAGAACTCCGGCCGCGGACTGGTGCACCTGATCCTG ATCAGGTCTAATGAGCGCGAGAAGCAGCGGCCGGCTGAGAGTGACCCTGGACACAAGCAAGAAGTC TAGCTCCCTGCTGATCACCGCCTCCAGAGCAGCAGATACAGCCTCTTACTTCTGTGCCGGCTGTATT CTAGCGCCTCCAAGATCATCTTTGGCAGCGGCACCCGGCTGTCCATCAGACCC
	343	METLLGVSLVILWLQLARVNSQQGEEDFQALSIQEGENATMNC SYKTSINN LQWYRQNSGRGLVHLIL IRSNEREKHSGRRLRVTLDTSKKSSSLITASRAADTASYFCAGLYSSASKIIFGSGTRLIRP
RAS TCR-16 beta chain variable domain	344	ATGGGCCCCAGCTCCTTGGCTATGTGGTCTTTCCTTTCAGGAGCAGGCCCCCTGGAAGCCCAAGT GACCCAGAACCCAGATACCTCATCAGTACTGGAAAGAAGTTAACAGTGACTTGTCTCAGAATA TGAACCATGAGTATATGTCTTGGTATCGACAAGACCCAGGGCTGGGCTTAAGGCAGATCTACTATTCA ATGAATGTTGAGGTGACTGATAAGGGAGATGTTCTTGAAGGGTACAAAGTCTCTCGAAAAGAGAAGAG GAATTTCCCTGATCCTGGAGTCGCCCAGCCCCAACCCAGACCTCTCTGTACTTCTGTGCCAGCAGTT CCAGGGGGCATTCCGGGCACTGAAGCTTTCTTTGGACAAGGCACCCAGACTCACAGTTGTA
	345	ATGGGCCCCAGCTGCTGGGCTACGTGGTGTGTGCCTGCTGGGAGCAGGACCCTGGAGGCACAGGT GACCCAGAACCCAGGTATCTGATCACCGTGACAGGCAAGAAGCTGACCGTGACATGTAGCCAGAACA TGAATCACGAGTACATGTCTTGGTATAGGCAGGACCCCGGACTGGGACTGAGACAGATCTACTATTCC ATGAATGTGGAGGTGACCGACAAGGGCGATGTGCCTGAGGGCTACAAGGTGTCTAGGAAGGAGAAGCG CAACTTCCCACTGATCCTGGAGTCCCATCTCCCAATCAGACCTCCCTGTATTTTTGCGCCAGCTCCT CTAGGGGCCACTCTGGCACAGAGGCCTTCTTTGGCCAGGGCACCAGGCTGACAGTGGTG
	346	MGFQLLGYVVLCLLGAGPLEAQVTQNPRLITVTGKKLTVTCSQNMNHEYMSWYRQDPGLGLRQIYY MNVEVTDKGDVPEGYKVS RKEKRN FPLILESPSNQTSLYFCASSSRGHS GTEAFFGQGT RLTVV
RAS TCR-16 alpha chain	347	METLLGVSLVILWLQLARVNSQQGEEDFQALSIQEGENATMNC SYKTSINN LQWYRQNSGRGLVHLIL IRSNEREKHSGRRLRVTLDTSKKSSSLITASRAADTASYFCAGLYSSASKIIFGSGTRLIRPDIQNP EPAVYQLKDP RSQDSTLCLFTDFDSQINVPKTMESGTFITDKTVLDMKAMDSKSN GAIAWSNQTSFTC QDIFKETNATYPSSDVPCDATLTEKSFETDMNLNFQNL SVMGLRI LLLKVAGFNLLMTLR LWS
RAS TCR-16 beta chain	348	MGFQLLGYVVLCLLGAGPLEAQVTQNPRLITVTGKKLTVTCSQNMNHEYMSWYRQDPGLGLRQIYY MNVEVTDKGDVPEGYKVS RKEKRN FPLILESPSNQTSLYFCASSSRGHS GTEAFFGQGT RLTVVVDL RNVTPPKVSLFEP SKAEIANKQKATLVCLARGFFPDHVELSWWVNGKEVHSGVSTDPQAYKESNYSYC LSRRLVSATFWHNPRNHFRQVQFHGLSEEDKWPEGSPKPV TQNI SAEAWGRADCGITSASYHQGV L SATILYEILLGKATLYAVLVSLVLMAMVKKKNS
TCR Peptides	349	VVGADGVGK
	350	VVVGADGVGK
RAS TCR-17 alpha chain CDR1	351	NIATNDY
RAS TCR-17 alpha chain CDR2	352	GYKTK
RAS TCR-17 alpha chain CDR3	353	LANTGGFKTI
RAS TCR-17 beta chain CDR1	354	SGHVS
RAS TCR-17 beta chain CDR2	355	FQNEAQ
RAS TCR-17 beta chain CDR3	356	ATYKVGDEQF

Name	SEQ ID NO	Sequence
RAS TCR-17 alpha chain variable domains	357	ATGAGGCAAGTGGCGAGAGTGATCGTGTTCTTGACCCTGAGTACTTTGAGCCTTGCTAAGACCACCCA GCCCATCTCCATGGACTCATATGAAGGACAAGAAGTGAACATAACCTGTAGCCACAACAACATTGCTA CAAATGATTATATCACGTGGTACCAACAGTTTCCCAGCCAAGGACCACGATTATTATTCAAGGATAC AAGACAAAAGTTACAAACGAAGTGGCCTCCCTGTTTATCCCTGCCGACAGAAAAGTCCAGCACTCTGAG CCTGCCCCGGGTTTCCCTGAGCGACACTGCTGTGTACTACTGCCTCGCTAATACTGGAGGCTTCAAAA CTATCTTTGGAGCAGGAACAAGACTATTTGTTAAAGCA
	358	ATGAGGCAGGTGGCACGCTGATCGTGTTCTTGACCCTGAGCAGACTGTCCCTGGCCAAGACCACACA GCCTATCTCTATGGACAGCTACGAGGGCCAGGAGGTGAACATCACCTGCTCTCACAACAATATCGCCA CCAATGATTACATCACATGGTATCAGCAGTTCCCCAGCCAGGGCCCTCGGTTTATCATCCAGGGCTAT AAGACCAAGGTGACAAACGAGGTGGCCAGCCTGTTTCATCCCTGCCGACAGGAAGTCTAGCACCCCTGTC CCTGCCACGCGTGAGCCTGTCCGATACAGCCGTGTACTATTGTCTGGCCAATACCGGCGGCTTCAAGA CAATCTTTGGCGCCGGCACCAGACTGTTTGTGAAGGCC
	359	MRQVARVIVFLTLSTLSLAKTTQPI SMDSYEGQEVNITCSHNNIATNDYITWYQQFSPGPRFIIQGY KTKVTNEVASLFI PADRKSSLSLPRVLSLSDTAVYYCLANTGGFKTIFGAGTRLFVKA
RAS TCR-17 beta chain variable domains	360	ATGGGACACAGGCTCCTGCTGGGTGGTCTGGGTTTCTTAGGGACAGATCACACAGGTGCTGGAGT CTCCCAGTCCCCTAGGTACAAAGTCGCAAAGAGAGGACAGGATGTAGCTCTCAGGTGTGATCCAATTT CGGGTCATGTATCCCTTTTTTGGTACCAACAGGCCCTGGGGCAGGGGCCAGAGTTTCTGACTTATTTT CAGAATGAAGCTCAACTAGACAAATCGGGGCTGCCAGTGATCGCTTCTTTGCAGAAAGGCCTGAGGG ATCCGTCTCCACTCTGAAGATCCAGCGCACACAGCAGGAGGACTCCGCCGTGTATCTCTGTGCCACCT ATAAGGTCGGGGATGAGCAGTTCTTCGGGCCAGGGACACGGCTCACCGTGCTA
	361	ATGGGAACCAAGCTGCTGTGCTGGGTGGTGTGGGCTTCTGGGAACCGACACACAGGAGCAGGCGT GTCCCAGTCTCCAAGGTACAAGGTGGCAAAGAGGGGACAGGACGTGGCCCTGAGATGTGATCCTATCT CCGGCCACGTGTCTCTGTTTTGGTACCAGCAGGCCCTGGGACAGGGACCTGAGTTCTGACCTATTTT CAGAACGAGGCACAGCTGGACAAGAGCGGACTGCCATCCGATCGGTTCTTTGCAGAGAGACCAGAGGG CAGCGTGTCCACCCTGAAGATCCAGAGGACACAGCAGGAGGACTCCGCCGTGTACCTGTGCCACAT ATAAAGTGGGCGATGAGCAGTTCTTTGGGCCAGGCACCCGGCTGACAGTGCTG
	362	MGTRLLCWVVLGFLGTDHTGAGVSQSPRYKVAKRQDVALRCDPISGHVSLFWYQQALQGQPEFLTYF QNEAQLDKSGLPSDRFFAERPEGSVSTLKIQTQQEDSAVYLCATYKVGDEQFFGPGTRTLTVL
RAS TCR-17 alpha chain	363	MRQVARVIVFLTLSTLSLAKTTQPI SMDSYEGQEVNITCSHNNIATNDYITWYQQFSPGPRFIIQGY KTKVTNEVASLFI PADRKSSLSLPRVLSLSDTAVYYCLANTGGFKTIFGAGTRLFVKADIQNPPEAVY QLKDPQSQDSTLCLFDFDSQINVPKTMESGTFITDKTVLDMKAMDSKSNAGIAWSNQTSTFCQDIFK ETNATYPSSDVPCDATLTEKSFETDMNLNFQNLVSMGLRI LLLKVAGFNLLMTLRWSS
RAS TCR-17 beta chain	364	MGTRLLCWVVLGFLGTDHTGAGVSQSPRYKVAKRQDVALRCDPISGHVSLFWYQQALQGQPEFLTYF QNEAQLDKSGLPSDRFFAERPEGSVSTLKIQTQQEDSAVYLCATYKVGDEQFFGPGTRTLTVLKDRLN VTFPKVSLFEPKAEIANKQKATLVCLARGFFPDHVELSWWVNGKEVHSGVSTDPQAYKESNYSYCLS SRLRVSAFWHNPRNHFRQVQFHGLSEEDKWPEGS PKPVTQNI SAEAWGRADCGITSASYHQGVLSA TILYEI LLGKATLYAVLVSGLVLMAMVKKKNS
TCR Peptides	365	VVGADGVGK
	366	VVVGADGVGK
RAS TCR-18 alpha chain CDR1	367	DSASNY
RAS TCR-18 alpha chain CDR2	368	IRSNVGE
RAS TCR-18 alpha chain CDR3	369	AETGFQKL
RAS TCR-18 beta chain CDR1	370	MDHEN
RAS TCR-18 beta chain CDR2	371	SYDVKM
RAS TCR-18 beta chain CDR3	372	ASSDWLAGAKDEQY

Name	SEQ ID NO	Sequence
RAS TCR-18 alpha chain variable domains	373	ATGACATCCATTCGAGCTGTATTTATATTCTGTGGCTGCAGCTGGACTTGGTGAATGGAGAGAATGT GGAGCAGCATCCTTCAACCCGTGAGTGTCAGGAGGGAGACAGCGCTGTTATCAAGTGTACTTATTTCAG ACAGTGCCTCAAACCTACTTCCCTTGGTATAAGCAAGAACTTGGAAAAAGACCTCAGCTTATTATAGAC ATTCTGTTCAAATGTGGCGGAAAAAGAACCAACGAATTGCTGTTACATTGAACAAGACAGCCAAACA TTTCTCCCTGCACATCACAGAGACCCAACTGAAGACTCGGCTGTCTACTTCTGTGCAGAAACAGGCT TTCAGAACTTGTATTTGGAAGTGGCACCCGACTTCTGGTCAGTCCA
	374	ATGACATCTATCCGCGCCGTGTTCATCTTTCTGTGGCTGCAGCTGGACCTGGTGAACGGCGAGAATGT GGAGCAGCACCCCAAGCACCCCTGTCCGTGCAGGAGGGCGACAGCGCCGTGATCAAGTGCACATACTCTG ATAGCGCTCCAACCTACTTTCCCTGGTATAAGCAGGAGCTGGGCAAGCGGCTCAGCTGATCATCGAC ATCAGATCCAACGTGGGCGAGAAGAAGGATCAGCGGATCGCCGTGACCCTGAATAAGACAGCCAAGCA CTTCAGCTGCACATCACCGAGACACAGCCCGAGGATTCCGCGCTGATATTTTGTGCCGAGACCGGCT TCCAGAAGCTGGTGTTTGGCACCGGCACAAGACTGCTGGTGTCCCCCT
	375	MTSIRAVFIFLWLQLDLVNGENVEQHPSTLSVQEGDSAVIKCTYSDSASNYFPWYKQELGKRPLIID IRSNVGEKKDQRIAVTLNKTAKHFSLHITETQPEDSAVYFCAETGFQKLVFGTGTRLLVSP
RAS TCR-18 beta chain variable domains	376	ATGGGAATCAGGCTCCTGTGTGTGGCCTTTTGTTCCTGGCTGTAGGCTCGTAGATGTGAAAGT AACCCAGAGCTCGAGATATCTAGTCAAAAGGACGGGAGAGAAAGTTTTTCTGGAATGTGTCCAGGATA TGGACCATGAAATATGTTCTGGTATCGACAAGACCCAGGTCTGGGGCTACGGCTGATCTATTTCTCA TATGATGTTAAATGAAAGAAAAAGGAGATATTCCTGAGGGGTACAGTGTCTCTAGAGAGAAGAAGGA GCGCTTCTCCCTGATTCTGGAGTCCGCCAGCACCAACCAGACATCTATGTACCTCTGTGCCAGCAGTG ACTGGCTAGCGGGAGCGAAGGACGAGCAGTACTTCGGGCCGGGCACCAGGCTCACGGTCACA
	377	ATGGGCATCCGGCTGCTGTGCAGAGTGGCCTTCTGTTCCTGGCCGTGGGCTGGTGGACGTGAAGGT GACCCAGAGCTCCCGGTACCTGGTGAAGAGAACAGGCGAGAAGGTGTTCTGGAGTGCGTGCAGGACA TGGATCACGAGAACATGTTTTGGTATAGGCAGGACCCCGGACTGGGACTGAGACTGATCTACTTTCAGC TATGACGTGAAGATGAAGGAGAAGGGCGACATCCCAGAGGGCTACAGCGTGTCCAGGGAGAAGAAGGA GCGGTTTCAGCCTGATCTCTGGAGTCTGCCAGCACCAATCAGACAAGCATGTACCTGTGCGCCTCTAGCG ACTGGCTGGCCGGAGCAAAGGATGAGCAGTATTTCCGGCCAGGCACCAGGCTGACCGTGACA
	378	MGIRLLCRVAFCLAVGLVDVKVTQSSRYLVKRTGEKVFLECVQDMDHENMFWRQDPGLGLRLIYFS YDVKMKEKGDIPGYSVSREKKERFSLILEASTNQTSMYLCASSDWLAGAKDEQYFGPGTRLTVT
RAS TCR-18 alpha chain	379	MTSIRAVFIFLWLQLDLVNGENVEQHPSTLSVQEGDSAVIKCTYSDSASNYFPWYKQELGKRPLIID IRSNVGEKKDQRIAVTLNKTAKHFSLHITETQPEDSAVYFCAETGFQKLVFGTGTRLLVSPDIQNPEP AVYQLKDRSQDSTLCLFTDFDSQINVPKTMESGTFITDKTVLDMKAMDSKNGAIAWSNQTSTFCQD IFKETNATYPSSDVPCDATTLEKS FETDMNLNFQNLVSMGLRILLKLVAGFNLLMTLRLWSS
RAS TCR-18 beta chain	380	MGIRLLCRVAFCLAVGLVDVKVTQSSRYLVKRTGEKVFLECVQDMDHENMFWRQDPGLGLRLIYFS YDVKMKEKGDIPGYSVSREKKERFSLILEASTNQTSMYLCASSDWLAGAKDEQYFGPGTRLTVTKD LRNVTPPKVSLFEPKAEIANKQKATLVCLARGFFPDHVELSWWVNGKEVHSGVSTDPQAYKESNYSY CLSSRLRVSATFWHNPRNHFRCQVQFHGLSEEDKWPEGSPKPVTONISAEAWGRADCGITSSAYHQGV LSATILYEILLGKATLYAVLVSGLVLMAMVKKKNS
TCR peptides	381	VVGADGVGK
	382	VVVGADGVGK
RAS TCR-19 alpha chain CDR1	383	TSINN
RAS TCR-19 alpha chain CDR2	384	IRSNERE
RAS TCR-19 alpha chain CDR3	385	ATDPLDYKLS
RAS TCR-19 beta chain CDR1	386	MNHEY
RAS TCR-19 beta chain CDR2	387	SMNVEV
RAS TCR-19 beta chain CDR3	388	ASSLVASNEQF

Name	SEQ ID NO	Sequence
RAS TCR-19 alpha chain variable domains	389	ATGGAAACTCTCTGGGAGTGTCTTTGGTGATTCTATGGCTTCAACTGGCTAGGGTGAACAGTCAACA GGGAGAAGAGGATCCTCAGGCCTTGAGCATCCAGGAGGGTGAAAATGCCACCATGAACTGCAGTTACA AACTAGTATAAACAATTTACAGTGGTATAGACAAAATTCAGGTAGAGGCCTTGTCACCTAATTTTA ATACGTTCAAATGAAAGAGAGAAACACAGTGAAGATTAAGAGTCACGCTTGACACTTCCAAGAAAAG CAGTTCCTTGTGATCACGGCTTCCCGGGCAGCAGACACTGCTTCTACTTCTGTGCTACGGACCCCT TAGACTACAAGCTCAGCTTTGGAGCCGGAACACAGTAAGTGAAGAGCA
	390	ATGGAGACCCTGCTGGGCGTGTCTGTGTCATCTGTGGCTGCAGCTGGCCAGAGTGAACCTCAGCA GGGAGAGGAGGACCCTCAGGCCTTGAGCATCCAGGAGGGCGAGAACGCCACCATGAATTGCTCTTACA AGACAAGCATCAACAATCTGCAGTGGTATCGGCAGAACTCCGGCAGAGGCCTGGTGACCTGATCCTG ATCAGGAGCAATGAGCGCGAGAAGCACTCCGGCCGGCTGAGAGTGACCTGGACACATCTAAGAAGTC CTCTAGCCTGCTGATCACCGCCTCTAGGGCAGCAGATACAGCCAGCTACTTCTGTGCCACCGACCAC TGGATTATAAGCTGTCTTTGGCGCCGGCACCACAGTGACCGTGCGCGCC
	391	METLLGVSLVILWLQRLARVNSQQGEEDFQALSIQEGENATMNC SYKTS INNLQWYRQNSGRGLVHLIL IRSNEREKHSGRRLVTLDTSKKSSSLITASRAADTASYFCATDPLDYKLSFGAGTTVTVRA
RAS TCR-19 beta chain variable domains	392	ATGGGCCCCAGCTCCTTGGCTATGTGGTCTCTTGGCTTCTAGGAGCAGGCCAGCTGGAAGCCCAAGT GACCCAGAACCAAGATACCTCATCAGTGACTGGAAAGAAGTTAACAGTGACTTGTCTCAGAATA TGAACCATGAGTATATGTCTTGGTATCGACAAGACCCAGGGCTGGGCTTAAGGCAGATCTACTATTCA ATGAATGTTGAGGTGACTGATAAGGGAGATGTTCTTGAAGGGTACAAAGTCTCTCGAAAAGAGAAGAG GAATTTCCCGCTGATCCTGGAGTCGCCCCAGCCCCAACCCAGACCTCTCTGTACTTCTGTGCCAGCAGTT TGGTGGCTAGCAATGAGCAGTTCTTCGGGCCAGGGACACGGCTCACCGTGCTA
	393	ATGGGCCCCACAGCTGCTGGGCTACGTGCTGTGTGCTGCTGGGAGCAGGACCCTGGAGGCACAGGT GACCCAGAATCCCGGTATCTGATCACCGTGACAGGCAAGAAGCTGACCGTGACATGTTCCCGAACA TGAATCACGAGTACATGTCTTGGTATAGGCAGGACCCCGGACTGGGACTGAGGCAGATCTACTATTCT ATGAACGTGGAGGTGACAGACAAGGGCGATGTGCTGAGGGCTACAAGGTGAGCAGGAAGGAGAAGCG CAACTTCCCACTGATCCTGGAGTCCCATCTCCCAATCAGACCAGCCTGTATTTTTGCGCCAGCTCCC TGGTGGCCTCCAACGAGCAGTTCTTTGGCCCTGGCACCCGGCTGACAGTGCTG
	394	MGPQLLYVVLCLLGAGPLEAQVTQNPRLITVTGKKLTVTCSQNMNHEYMSWYRQDPGLGLRQIYY MNVEVTDKGDVPEGYKVS RKEKRN FPLI LESPSPNQTSLYFCASSLVASNEQFFGPGTRLTVL
RAS TCR-19 alpha chain	395	METLLGVSLVILWLQRLARVNSQQGEEDFQALSIQEGENATMNC SYKTS INNLQWYRQNSGRGLVHLIL IRSNEREKHSGRRLVTLDTSKKSSSLITASRAADTASYFCATDPLDYKLSFGAGTTVTVRADIQNPE PAVYQLKDP RSQDSTLCFTDFDSQINVPKTMESGTFITDKTVLDMKAMDSKSNIAWSNQTSTFCQ DIFKETNATYPSSDVP CDATLEKSFETDMNLNFQNL SVMGLRILLLKVAGFNLLMTLR LWSS
RAS TCR-19 beta chain	396	MGPQLLYVVLCLLGAGPLEAQVTQNPRLITVTGKKLTVTCSQNMNHEYMSWYRQDPGLGLRQIYY MNVEVTDKGDVPEGYKVS RKEKRN FPLI LESPSPNQTSLYFCASSLVASNEQFFGPGTRLTVLKDLRN VTFPKVSLFEP SKAEIANKQKATLVLCIARGFPPDHVELSWWVNGKEVHSGVSTDPQAYKESNYSYCLS SRLRVSATFWHNP RNHFRCQVQFHGLSEEDKWPEGS PKPVTONI SAEAWGRADCGITSASYHQGVLSA TILYEI LLGKATLYAVLVSGLVLMAMVKKKNS
TCR Peptides	397	VVGAVGVGK
	398	VVVGAVGVGK
RAS TCR-20 alpha chain CDR1	399	TSESDY
RAS TCR-20 alpha chain CDR2	400	QEAYKQQN
RAS TCR-20 alpha chain CDR3	401	ACQGGSEKLV
RAS TCR-20 beta chain CDR1	402	SGHNT
RAS TCR-20 beta chain CDR2	403	YYREEE
RAS TCR-20 beta chain CDR3	404	ASSLGLLLYNEQF

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RAS TCR-20 alpha chain variable domains	405	ATGGCATGCCCTGGCTTCCTGTGGGCACTTGTGATCTCCACCTGTCTTGAATTTAGCATGGCTCAGAC AGTCACTCAGTCTCAACCAGAGATGTCTGTGCAGGAGGCAGAGACCGTGACCCTGAGCTGCACATATG ACACCACTGAGAGTGATTATTTATTTCTGGTACAAGCAGCCTCCAGCAGGCAGATGATTTCTCGTT ATTGCGCAAGAAGCTTATAAGCAACAGAATGCAACAGAGAATCGTTTCTCTGTGAACCTCCAGAAAGC AGCCAAATCCTTCAGTCTCAAGATCTCAGACTCACAGCTGGGGGATGCCGCATGTATTTCTGTGCTT GTCAGGGCGGATCTGAAAAGCTGGTCTTTGGAAAGGGAACGAACTGACAGTAAACCCA
	406	ATGGCATGCCAGGCTTCCTGTGGGCACTGGTTCATCAGCACCTGTCTGGAGTTTCTATGGCCAGAC CGTGACACAGAGCCAGCCAGAGATGTCCGTGCAGGAGGCAGAGACCGTGACACTGTCTGTACCTACG ACACAAGCGAGTCCGATTACTATCTGTTCTGGTATAAGCAGCCTCCATCTCGCCAGATGATCCTGGTC ATCCGGCAGGAGGCCCTACAAGCAGCAGAACGCCACCGAGAATCGGTTCTCTGTGAATTTTCAGAAAGC CGCCAAGTCTTTAGCCTGAAGATCTCCGACTCTCAGCTGGGCGATGCCGCCATGTATTTCTGCGCAT GTCAGGGAGGCAGCGAGAAGCTGGTGTGTTGGCAAGGGCACCAAGCTGACAGTGAACCCCT
	407	MACPGFLWALVISTCLEFSMAQTVTQSQPEMSVQEAETVTLSCITYDTSSESDYLLFWYKQPPSRQMI LVIRQEAAYKQONATENRFSVNFQKAAKSFSLKISDSQLGDAAMYFCACQGGSEKLVFGKGTCLTVNP
RAS TCR-20 beta chain variable domains	408	ATGGGCCCTGGGCTCCTGTGGGTGCTGCTTTGTCTCCTGGGAGCAGGTCTAGTGGAGACTGGAGT CACCACAAAGTCCACACACCTGATCAAAACGAGAGGACAGCAAGTGACTCTGAGATGCTCTTCTCAGT CTGGGCACAACACTGTGTCTGTGTACCAACAGGCCCTGGGTGAGGGGCCAGTTTATCTTTTCAGTAT TATAGGAGGAGAAGAGAATGGCAGAGGAACTTCCCTCCTAGATTCTCAGGTCTCCAGTTCCTAATTA TAGCTCTGAGCTGAATGTGAACGCCCTGGAGCTGGACGACTCGGCCCTGTATCTCTGTGCCAGCAGCT TGGGACTCCTCCTCTACAATGAGCAGTTCTTCGGGCCAGGGACACGGCTCACCGTGCTA
	409	ATGGGACCAGGACTGCTGTGCTGGGTGCTGTGTGCTGCTGGGAGCAGGCAGCGTGGAGACCGGCGT GACACAGTCCCCTACCCACCTGATCAAGACAAGAGGCCAGCAGGTGACCCCTGAGGTGCAGCTCCCAGT CTGGCCACAATACAGTGAGCTGTTACCAAGCAGGCCCTGGGACAGGGACCTCAGTTCTCTTCAGTAC TATAGGAGGAGGAGAAACGGCCGCGGCAATTTCCCCCTCGGTTTAGCGGCTGCAGTTCCCAAATA TTCTAGCGAGCTGAACGTGAATGCCCTGGAGCTGGACGATTCCGCCCTGTACCTGTGCGCCTCCTCTC TGGGCCCTGCTGCTGTATAACGAGCAGTTCTTTGGCCCCGGCACCAGACTGACAGTCTG
	410	MGFGLLCWVLLCLLGAGSVETGVTQSPHLLIKTRGQVTLRCSSQSGHNTVSWYQQALGQGPQFI FYQY YREEENGRGNFPPRFSGLQFPNYSSELNVNALELDDSAALYLCASSLGLLLYNEQFFGPGTRLTLV
RAS TCR-20 alpha chain	411	MACPGFLWALVISTCLEFSMAQTVTQSQPEMSVQEAETVTLSCITYDTSSESDYLLFWYKQPPSRQMI LVIRQEAAYKQONATENRFSVNFQKAAKSFSLKISDSQLGDAAMYFCACQGGSEKLVFGKGTCLTVNPDIQ NPPEAVYQLKDRSQDSTLCFLTFDQSQINVPKTMESGTFITDKTVLDMKAMDSKNGAIAWSNQTSF TCQDIFKETNATYPSSDVPCDALTLEKSFETDMNLNFQNLVSMGLRIILLKLVAGFNLLMTLRLWSS
RAS TCR-20 beta chain	412	MGFGLLCWVLLCLLGAGSVETGVTQSPHLLIKTRGQVTLRCSSQSGHNTVSWYQQALGQGPQFI FYQY YREEENGRGNFPPRFSGLQFPNYSSELNVNALELDDSAALYLCASSLGLLLYNEQFFGPGTRLTLVLDL RNVTPPKVSLFEPKAEIANKQKATLVCLARGFFPDHVELSWVNGKEVHSGVSTDPQAYKESNYSYC LSRRLVRSATFWHNP RNHFRCQVQFHGLSEEDKWPEGSPKPVTONISAEAWGRADCGITSASYHQGV LSATILYEILLGKATLYAVLVSLVLMAMVKKKNS
TCR Peptides	413	VVGAVGVGK
	414	VVVGAVGVGK
RAS TCR-21 alpha chain CDR1	415	TSINN
RAS TCR-21 alpha chain CDR2	416	IRSNERE
RAS TCR-21 alpha chain CDR3	417	ATDAQTGANNLF
RAS TCR-21 beta chain CDR1	418	SGHAT
RAS TCR-21 beta chain CDR2	419	FQNNGV
RAS TCR-21 beta chain CDR3	420	ASSLGDSYEQYF

Name	SEQ ID NO	Sequence
RAS TCR-21 alpha chain variable domains	421	ATGGAAACTCTCCTGGGAGTGTCTTTGGTGATTCTATGGCTTCAACTGGCTAGGGTGAACAGTCAACA GGGAGAAGAGGATCCTCAGGCCTTGAGCATCCAGGAGGGTGAAAATGCCACCATGAACTGCAGTTACA AACTAGTATAAACAATTTACAGTGGTATAGACAAAATTCAGGTAGAGGCCCTGTCCACCTAATTTTA ATACGTTCAAATGAAAGAGAGAAACACAGTGAAGATTAAGAGTCACGCTTGACACTTCCAAGAAAAG CAGTTCCTTGTGATCACGGCTTCCCGGGCAGCAGACACTGCTTCTTACTTCTGTGCTACGGACGCTC AACTGGGGCAAACAACCTCTTCTTTGGGACTGGAACGAGACTCACCGTTATTCCC
	422	ATGGAGACACTGTGGGCGTGTCTCTGGTCATCCTGTGGCTGCAGCTGGCCAGAGTGAATAGCCAGCA GGGAGAGGAGGACCCCGAGGCCTGTCCATCCAGGAGGGCGAGAACGCCACCATGAATTGCAGCTACA AGACATCCATCAACAATCTGCAGTGGTATCGGCAGAACTCTGGCAGAGGCCCTGGTGCACCTGATCCTG ATCCGGTCCAATGAGAGAGAGAAGCACTCTGGCCGGCTGAGAGTGACCCTGGATACATCCAAGAAGTC CTCTAGCCTGCTGATCACCGCCAGCCGGGCAGCAGACACAGCCTCCTATTTTGTGCCACCGATGCCC AGACAGGCGCCAACAATCTGTTCTTTGGCACCGGCACAAGACTGACCGTGATCCCT
	423	METLLGVSLVILWLQRLARVNSQQGEEDFQALSIQEGENATMNC SYKTSINN LQWYRQNSGRGLVHLIL IRSNEREKHSGRRLRVTLDTSKKSSSLITASRAADTASYFCATDAQTGANNLFFGTGTRLTVIP
RAS TCR-21 beta chain variable domains	424	ATGGGACACAGGCTCCTCTGCTGGGCGGCCCTCTGTCTCCTGGGAGCAGAACTCACAGAAGCTGGAGT TGCCCACTCTCCAGATATAAGATTATAGAGAAAAGGCAGAGTGTGGCTTTTTGGTGCAATCCTATAT CTGGCCATGCTACCCCTTACTGCTACAGCAGATCCTGGGACAGGGCCCAAAGCTTCTGATTCAGTTT CAGAATAACGGTGTAGTGGATGATTCACAGTTGCCTAAGGATCGATTTTCTGCAGAGAGGCTCAAAGG AGTAGACTCCACTCTCAAGATCCAGCCTGCAAAGCTTGAGGACTCGGCCGTGTATCTCTGTGCCAGCA GCTTA
	425	ATGGGCACACAGGCTGTGTGCTGGGCGGCCCTGTGCCTGCTGGGAGCAGAGCTGACAGAGGCAGGAGT GGCCCAAGAGCCCAAGGTACAAGATCATCGAGAAGCGCCAGTCCGTGGCCTTCTGGTGCAACCCCTATCT CTGGCCACGCCACCCCTGTACTGCTATCAGCAGATCCTGGGCCAGGGCCCAAAGCTGCTGATCCAGTTC CAGAACAATGGCGTGGTGGACGATTCTCAGCTGCCCAGGACAGGTTTAGCGCCGAGCGCTGAAGGG CGTGGATTCTACCCCTGAAGATCCAGCCAGCAAAGCTGGAGGACAGCGCCGTGTACCTGTGCCAGCT CCCTG
	426	MGTRLLCWAALCLLGAELTEAGVAQSPRYKII EKRSVAFWCNPI SGHATLYWYQQILGQGP KLLIQF QNGVVDSDSQLPKDRFSAERLKGVDSTLKI QPAKLEDSAVYLCASSL
RAS TCR-21 alpha chain	427	METLLGVSLVILWLQRLARVNSQQGEEDFQALSIQEGENATMNC SYKTSINN LQWYRQNSGRGLVHLIL IRSNEREKHSGRRLRVTLDTSKKSSSLITASRAADTASYFCATDAQTGANNLFFGTGTRLTVIPDIQN PEPAVYQLKDP RSQDSTLCLETFDSDQINVPKTMESGTFITDKTVLDMKAMDSKSNGAIAWSNQTSFT CQDI FKETNATYPSSDVPCDATLTEKSFETDMNLNFQNL SVMGLRI LLLKVAGFNLMTLRLWSS
RAS TCR-21 beta chain	428	MGTRLLCWAALCLLGAELTEAGVAQSPRYKII EKRSVAFWCNPI SGHATLYWYQQILGQGP KLLIQF QNGVVDSDSQLPKDRFSAERLKGVDSTLKI QPAKLEDSAVYLCASSLKDRLNVT PPKVSLFEP SKAEI ANKQKATLVCLARGFFPDHVELSWWVNGKEVHSGVSTDPQAYKESNYSYCLSSRLRV SATFWHNP RNH FRCQVQFHGLSEEDKWPEGS PKPVTQNI SAEAWGRADCGITSASYHQGVLSATILYEILLGKATLYAV LVSGLVLMAMVKKKNS
TCR Peptides	429	VVGAVGVGK
	430	VVVGAVGVGK
RAS TCR-26 alpha chain CDR1	532	NSMFDY
RAS TCR-26 alpha chain CDR2	533	ISSIKDK
RAS TCR-26 alpha chain CDR3	534	AANAGGTSYGKLT
RAS TCR-26 beta chain CDR1	535	SNHLY
RAS TCR-26 beta chain CDR2	536	FYNNEI
RAS TCR-26 beta chain CDR3	537	ASSEWGSTGELF

Name	SEQ ID NO	Sequence
RAS TCR-26 alpha chain variable domain	538	atggccatgctcctgggggcatcagtgctgattctgtggcttcagccagactgggtaaacagtcaaca gaagaatgatgaccagcaagttaagcaaaattcaccatccctgagcgtccaggaaggaagaatttcta ttctgaactgtgactatactaacagcatgtttgattatctctatggtaaaaaataccctgctgaa ggctctacattcctgatactataagttccattaaggataaaaaatgaagatggaagattcactgtctt cttaaacaaaagtgccagcactctctctgcacattgtgccctcccagcctggagactctgcagtg acttctgtgcagcaaatgctgggtggtactagctatggaaagctgacatttggacaaggaccatcttg actgtccatccaa
	539	MAMLLGASVLILWLQPDWVNSQQKNDDQVQKQNSPSSLVQEGRISILNCDYTNMFDYFLWYKKYPAE GPTFLISISSIKDNEDGRFTVFLNKS AKHLSLHIVPSQPGDSAVYFCAANAGGTSYGKLTFGQGTIL TVHP
RAS TCR-26 beta chain variable domain	540	atggatacctggctcgtatgctgggcaatttttagtctcttgaagcaggactcacagaacctgaagt caccagactcccagccatcaggtcacacagatgggacaggaagtgatcttgcgctgtgtccccatct ctaatacacttatacttctatttggtacagacaaatcttggggcagaaagtcgagtttctggtttccttt tataataatgaaatctcagagaagtcgaaatattcgatgatcaattctcagttgaaaggcctgatgg atcaaatcttactctgaagatccggtccacaaagctggaggactcagccatgtacttctgtgccagca gtgaatggggaagcaccggggagctgttttttggagaaggctctaggtgaccgtactgg
	541	MDTWLVCWAI FSLKAGLTEPEVTQT PSHQVTQMGEVILRCVPI SNHLYFYWYRQILGQKVEFLVSF YNNEISEKSEIFDDQFSVERPDGNSFTLKI RSTKLEDSAMYFCASSEWGSGTGELFFGEGSRLTVL
RAS TCR-26 alpha chain	542	MAMLLGASVLILWLQPDWVNSQQKNDDQVQKQNSPSSLVQEGRISILNCDYTNMFDYFLWYKKYPAE GPTFLISISSIKDNEDGRFTVFLNKS AKHLSLHIVPSQPGDSAVYFCAANAGGTSYGKLTFGQGTIL TVHPDIQNPEPAVYQLKDP RSQDSTLC LFTDFDSQINVPKTMESGTFITDKTVLDMKAMD SKSNGAIA WSNQTSFTCQDIFKETNATYPS SDVPCDATLTEKS FETDMNLNFQNL SVMGLRILLKLVAGFNLLMTL RLWSS
RAS TCR-26 beta chain	543	MDTWLVCWAI FSLKAGLTEPEVTQT PSHQVTQMGEVILRCVPI SNHLYFYWYRQILGQKVEFLVSF YNNEISEKSEIFDDQFSVERPDGNSFTLKI RSTKLEDSAMYFCASSEWGSGTGELFFGEGSRLTVL KDL RNVTPPKVSLFEP SKAEIANKQKATLVCLARGFFPDHVELSWVNGKEVHSGVSTDPQAYKESNYSYC LSRRLRSATFWHNP RNHFRCQVQ FHLSEEDKWPEGSPKPVQTQNI SAEAWGRADCGITSASYHQGV L SATILYEILLGKATLYAVLVSLVLMAMVKKNS
RAS TCR-26 peptide	544	VVGAVGVGK
RAS TCR-27 alpha chain CDR1	545	TTSDR
RAS TCR-27 alpha chain CDR2	546	LLSNGAV
RAS TCR-27 alpha chain CDR3	547	AVDIIGGKST
RAS TCR-27 beta chain CDR1	548	SNHLY
RAS TCR-27 beta chain CDR2	549	FYNNEI
RAS TCR-27 beta chain CDR3	550	ASSEWGSGTGELF
RAS TCR-27 alpha chain variable domain	551	atgaagaagctactagcaatgattctgtggcttcaactagaccgggttaagtggagagctgaaagtgga acaaaaccctctgttctctgagcatgcaggagggaactataccatctactgcaattattcaacca cttcagacagactgtatttggtacaggcaggatcctgggaaaagtctggaatctctgtttgtgttgcta tcaaatggagcagtgaaagcaggaggacgattaatggcctcacttgataccaaagccgctctcagcac cctccacatcacagctgccgtgcagtgacctctctgccacctaacttctgtgccgtggacatcatcgag gcaaatcaaccttggggatgggactacgctcactgtgaagccaa
	552	MKKLLAMILWLQLDRLSGELKVEQNPLFLSMQEGKNYTIYCNYSTTSDRLYWRQDPGKSLESFLVLL SNGAVKQEGRLMASLDTKARLSTLHI TAAVHDL SATYFCAVDI IGGKSTFGDGTTLTVKP
RAS TCR-27 beta chain variable domain	553	atggatacctggctcgtatgctgggcaatttttagtctcttgaagcaggactcacagaacctgaagt caccagactcccagccatcaggtcacacagatgggacaggaagtgatcttgcgctgtgtccccatct ctaatacacttatacttctatttggtacagacaaatcttggggcagaaagtcgagtttctggtttccttt tataataatgaaatctcagagaagtcgaaatattcgatgatcaattctcagttgaaaggcctgatgg atcaaatcttactctgaagatccggtccacaaagctggaggactcagccatgtacttctgtgccagca gtgaatggggaagcaccggggagctgttttttggagaaggctctaggtgaccgtactgg

Name	SEQ ID NO	Sequence
	554	MDTWLVCWAI F S L L K A G L T E P E V T Q T P S H Q V T Q M G Q E V I L R C V P I S N H L Y F Y W Y R Q I L G Q K V E F L V S F Y N N E I S E K S E I F D D Q F S V E R P D G S N F T L K I R S T K L E D S A M Y F C A S E W G S T G E L F F G E G S R L T V L
RAS TCR-27 alpha chain	555	MK K L L A M I L W L Q L D R L S G E L K V E Q N P L F L S M Q E G K N Y T I Y C N Y S T T S D R L Y W Y R Q D P G K S L E S L F V L L S N G A V K Q E G R L M A S L D T K A R L S T L H I T A A V H D L S A T Y F C A V D I I G G K S T F G D G T T L T V K P D I Q N P E P A V Y Q L K D P R S Q D S T L C L F T D F D S Q I N V P K T M E S G T F I T D K T V L D M K A M D S K S N G A I A W S N Q T S F T C Q D I F K E T N A T Y P S S D V P C D A T L T E K S F E T D M N L N F Q N L S V M G L R I L L L K V A G F N L L M T L R L W S S
RAS TCR-27 beta chain	556	MDTWLVCWAI F S L L K A G L T E P E V T Q T P S H Q V T Q M G Q E V I L R C V P I S N H L Y F Y W Y R Q I L G Q K V E F L V S F Y N N E I S E K S E I F D D Q F S V E R P D G S N F T L K I R S T K L E D S A M Y F C A S E W G S T G E L F F G E G S R L T V L K D L R N V T P P K V S L F E P S K A E I A N K Q K A T L V C L A R G F F P D H V E L S W W V N G K E V H S G V S T D P Q A Y K E S N Y S Y C L S S R L R V S A T F W H N P R N H F R C Q V Q F H G L S E E D K W P E G S P K P V T Q N I S A E A W G R A D C G I T S A S Y H Q G V L S A T I L Y E I L L G K A T L Y A V L V S G L V L M A M V K K K N S
RAS TCR-27 peptide	557	VVGAVGVGK
RAS TCR-28 alpha chain CDR1	558	NSMFDY
RAS TCR-28 alpha chain CDR2	559	ISSIKDK
RAS TCR-28 alpha chain CDR3	560	AASAVGQ E Y G N K L V
RAS TCR-28 beta chain CDR1	561	SEHNR
RAS TCR-28 beta chain CDR2	562	FQNEAQ
RAS TCR-28 beta chain CDR3	563	ASSEYTMGTQY
RAS TCR-28 alpha chain variable domain	564	atggccatgctcctgggggcatcagtgctgattctgtggcttcagccagactgggtaaacagtcaaca gaagaatgatgaccagcaagttaagcaaaaattcaccatccctgagcggtccaggaaggaagaatttcta ttctgaactgtgactataactaacagcatggttgattatctctatggtacaaaaataaccctgctgaa ggtcctacattcctgatactataagttccatgaaggataaaaaatgaagatggaagattcactgtctt cttaacaaaagtgccagcactctctctgcacattgtgccctccagcctggagactctgcagtggt acttctgtgcagcaagcgagcagtaggtcaggaatatggaaacaagctggtctttggcgaggaaccatt ctgagagtcgaagtcct
	565	MAMLLGASVLI L W L Q P D W N S Q Q K N D D Q Q V K Q N S P S L S V Q E G R I S I L N C D Y T N S M F D Y F L W Y K K Y P A E G P T F L I S I S S I K D K N E D G R F T V F L N K S A K H L S L H I V P S Q P G D S A V Y F C A A S A V G Q E Y G N K L V F G A G T I L R V K S
RAS TCR-28 beta chain variable domain	566	atggggcaccagcctcctctgctggatggccctgtgtctcctgggggagatcacgcagatactggagt ctcccagaacccagacacagaatcacaagagggggacagaatgtaactttcaggtgtgatccaattt ctgaacacaaccgcctttattggtaccgacagaccctggggcagggcccagagtttctgacttacttc cagaatgaagctcaactagaaaaatcaaggctgctcagtgatcggttctctgcagagagggcctaaggg atctttctccaccttgagatccagcgacagagcagggggactcgccatgtatctctgtgccagca gtgaatatactatggggaccagctacttcggggcagggcagcggtcctggtgctcg
	567	MGTSLLCWMALCLLGADHADTGVSQNPRHKITKRGQNVTFRCDPIS E H N R L Y W Y R Q T L G Q G P E F L T Y F Q N E A Q L E K S R L L S D R F S A E R P K G S F S T L E I Q R T E Q G D S A M Y L C A S E Y T M G T Q Y F G P G T R L L V L
RAS TCR-28 alpha chain	568	MAMLLGASVLI L W L Q P D W N S Q Q K N D D Q Q V K Q N S P S L S V Q E G R I S I L N C D Y T N S M F D Y F L W Y K K Y P A E G P T F L I S I S S I K D K N E D G R F T V F L N K S A K H L S L H I V P S Q P G D S A V Y F C A A S A V G Q E Y G N K L V F G A G T I L R V K S D I Q N P E P A V Y Q L K D P R S Q D S T L C L F T D F D S Q I N V P K T M E S G T F I T D K T V L D M K A M D S K S N G A I A W S N Q T S F T C Q D I F K E T N A T Y P S S D V P C D A T L T E K S F E T D M N L N F Q N L S V M G L R I L L L K V A G F N L L M T L R L W S S
RAS TCR-28 beta chain	569	MGTSLLCWMALCLLGADHADTGVSQNPRHKITKRGQNVTFRCDPIS E H N R L Y W Y R Q T L G Q G P E F L T Y F Q N E A Q L E K S R L L S D R F S A E R P K G S F S T L E I Q R T E Q G D S A M Y L C A S E Y T M G T Q Y F G P G T R L L V L K D L R N V T P P K V S L F E P S K A E I A N K Q K A T L V C L A R G F F P D H V E L S W W V N G K E V H S G V S T D P Q A Y K E S N Y S Y C L S S R L R V S A T F W H N P R N H F R C Q V Q F H G L S E E D K W P E G S P K P V T Q N I S A E A W G R A D C G I T S A S Y H Q G V L S A T I L Y E I L L G K A T L Y A V L V S G L V L M A M V K K K N S
RAS TCR-28 peptide	600	VVGAVGVGK

Name	SEQ ID NO	Sequence
GATA3 TCR-1 alpha chain CDR1	127	NYSPAY
GATA3 TCR-1 alpha chain CDR2	128	IRENEKE
GATA3 TCR-1 alpha chain CDR3	129	ALDIYGNRLA
GATA3 TCR-1 beta chain CDR1	130	MDHEN
GATA3 TCR-1 beta chain CDR2	131	SYDVKM
GATA3 TCR-1 beta chain CDR3	132	ASSLDFVLGYSYNEQF
GATA3 TCR-1 alpha chain variable domain	133	ATGGCTTTTGGCTGAGAAGGCTGGGTCTACATTTCAAGCCACATTTGGGGAGACGAATGGAGTCATTCCTGGGAGGTGTTTTGCTGATTTTGTGGCTTCAAGTGGACTGGGTGAAGAGCCAAAAGATAGAACAGAAATCCGAGGCCCCTGAACATTGAGGAGGGTAAAACGGCCACCCTGACCTGCAACTATACAACTATTCTCCAGCATACTTACAGTGGTACCGACAAGATCCAGGAAGAGGCCCTGTTTCTTGCTACTCATACGTGAAAATGAGAAAGAAAAAGGAAAGAAAGACTGAAGGTACCTTTGATACCACCCCTTAAACAGAGTTTGTTCATATCACAGCCTCCAGCCTGCAGACTCAGCTACCTACCTCTGTGCTCTAGACATTTATGGGAACACAGACTCGCTTTTGGGAAGGGGAACCAAGTGGTGGTCATACCA
	134	ATGGCCTTCTGGCTGAGGAGACTGGGTTTACACTTCAGACCCCATTTAGGCAGAGAATGGAGAGCTTTT TAGGCGGCGTGCTGCTGATTTTATGGCTGCAAGTTGACTGGGTGAAGAGCCAGAAGATCGAGCAGAACAGCGAGGCTTTAAACATTCAAGAAGGCAAGACAGCCACTTAACTTGTAATATACCAACTACTCCCCGCTTATTTACAGTGGTACAGACAAGATCCCGGCAGAGGCCCGTGTTTTACTGCTGATTCGTGAGAACGAGAAGGAGAAGAGGAAGGAGAGACTGAAGGTGACCTTCGACACCACTTAAAGCAGTCTTTATCCACATCACCGCCAGCCAGCCCGCTGATAGCGCCACCTATTTATGCGCTTTAGACATCTACGGCAACAATCGTCTGGCCTTCGGCAAGGGCAACCAAGTTGTGGTGATCCCC
	135	MAFWLRRLLGLHFRPHLGRRMESFLGGVLLILWLQVDWVKSQKIEQNSEALNIQEGKTATLTCTNYTNYSPAYLQWYRQDPGRGPVFLLLIRENEKEKRERLKVTFDTTLKQSLFHITASQPADSATYLCALDIYGNRLAFGKGNQVVVIP
GATA3 TCR-1 beta chain variable domain	136	ATGGGAATCAGGCTCCTCTGCTGCTGTCGCTTTTGTCTTCTGGCTGTAGGCCTCGTAGATGTGAAAGTACCCAGAGCTCGAGATATCTAGTCAAAAGACGGGAGAGAAAAGTTTTCTGGAATGTGTCCAGGATATG GACCATGAAATATGTTCTGGTATCGACAAGACCAGGTCTGGGCTACGGCTGATCTATTTCTCATATGATGTAAAAATGAAAGAAAAGGAGATATTCCTGAGGGGTACAGTGCTCTAGAGAGAAGAAGGAGCGCTTCTCCCTGATTCTGGAGTCCGCCAGCACCAACCAGACATCTATGTACCTCTGTGCCAGCAGTTTAGATTTTGTGCTAGCGGGGTCTACTCTCTACAATGAGCAGTTCTTCGGGCCAGGGACAGGCTCACCGTGCTA
	137	ATGGGCATTCTGCTGTGCTGTCGTGTGGCCTTCTGCTTTTATAGCCGTGGGTTTAGTGGACGTGAAGGTGACCCAGTCTCTCGTTATTTAGTGAAGAGGACCGGCGAGAAGGTGTTTTAGAAATGCGTGCAAGATATG GACCACGAGAACATGTTCTGGTACAGACAAGATCCCGGACTGGGTTTAAAGCTGATCTACTTTCAGCTACGACGTGAAGATGAAGGAGAAGGGCAGACATCCCCGAGGGCTACTCCGTGTCTCGTGAGAAGAAGGAGAGGTTCTCTTTAATTTTAGAGTCCGCCAGCACCAACCAGACCAGCATGTATTTATGCCCGAGCTCTTTAGAC TTTGTGCTGGCCGGCAGCTACAGCTACAACGAGCAGTTCTTCGGCCCCGGCACCAGACTGACCGTGCTG
	138	MGIRLLCRVAFCF LAVGLVDVKVTQSSRYLVKRTGEKVFLQVQMDMDHENMFWRQDPGLGLRLIYFSY DVKMKEKGDIPEGYSVSREKKERFSLILESASTNQTSMYLCASSLDFVLGYSYNEQFFGPGTRLTVL
GATA3 TCR-1 alpha chain	139	MAFWLRRLLGLHFRPHLGRRMESFLGGVLLILWLQVDWVKSQKIEQNSEALNIQEGKTATLTCTNYTNYSPAYLQWYRQDPGRGPVFLLLIRENEKEKRERLKVTFDTTLKQSLFHITASQPADSATYLCALDIYGNRLAFGKGNQVVVIPDIQNPDAVYQLRDSKSSDKSVCLFTDFDSQTNVSQKSDSVYITDKTVLDMRSMDFKNSAVAWSNKSDFACANAFNNSIIPEDTFFPSPSSCDVKLVKESFETDTNLFQNLVIGFRILLK VAGFNLLMTLRLWSS
GATA3 TCR-1 beta chain	140	MGIRLLCRVAFCF LAVGLVDVKVTQSSRYLVKRTGEKVFLQVQMDMDHENMFWRQDPGLGLRLIYFSY DVKMKEKGDIPEGYSVSREKKERFSLILESASTNQTSMYLCASSLDFVLGYSYNEQFFGPGTRLTVL EDLNKVFPPPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWWVNGKEVHSGVSTDPQPLKEQPAL NDSRYCLSSRLRVSATFWQNPFRNHFRQCQVQFYGLSENDEWTQDRAKPVQIVSAEAWGRADCGFTSVSY QQGVLSATILYEILGKATLYAVLVSAVLMLAMVKKRDF
GATA3 TCR-1 peptide	141	MLTGPPARV

Name	SEQ ID NO	Sequence
GATA3 neoORF mutant protein	157	MRRLSAARRAGTSCANCQTTTTLWRRNANGDPVCNACGLYYKLHNINRPLTMKKEGIQTRNRKMSSKS KKCKKVHDSLEDFFKNSSFPGRLQTHVLPPEPHLALQPLQPHADHAHADAPAIQPVLTTPPLQHGHRH GLEPCSMLTGPPARVPAVPFDLHFCRSSIMKPKRDGYMFLKAESKIMFATLQRSSLWCLCSNH
GATA3 neoORF sequence	158	PGRPLQTHVLPPEPHLALQPLQPHADHAHADAPAIQPVLTTPPLQHGHRHGLEPCSMLTGPPARVPAVP FDLHFCRSSIMKPKRDGYMFLKAESKIMFATLQRSSLWCLCSNH
GATA3 TCR-2 alpha chain CDR1	189	NSMFDY
GATA3 TCR-2 alpha chain CDR2	190	ISSIKDK
GATA3 TCR-2 alpha chain CDR3	191	AASASNNDMR
GATA3 TCR-2 beta chain CDR1	192	SEHNR
GATA3 TCR-2 beta chain CDR2	193	FQNEAQ
GATA3 TCR-2 beta chain CDR3	194	ASSQSGQGPYEQY
GATA3 TCR-2 alpha chain variable domain	195	ATGGCCATGCTCCTGGGGGCATCAGTGCTGATTCTGTGGCTTCAGCCAGACTGGGTAACAGTCAACAG AAGAATGATGACCAGCAAGTTAAGCAAAATTCACCATCCCTGAGCGTCCAGGAAGGAAGATTTCTATT CTGAAGTGTGACTATACTAACAGCATGTTTGATTATTTCTATGGTACAAAAATACCCCTGCTGAAGGT CCTACATTCTGATATCTATAAGTTCCATTAAGGATAAAAATGAAGATGGAAGATTCACTGTCTTCTTA AACAAAAGTGCCAAGCACCTCTCTCTGCACATTGTGCCCTCCAGCCTGGAGACTCTGCAGTGTACTTC TGTGCAGCAAGCGCGTCAAACAATGACATGCGCTTTGGAGCAGGGACCAGACTGACAGTAAACCA
	196	ATGGCAATGCTGCTGGGAGCCTCTGTGCTGATCCTGTGGCTGCAGCCAGATTGGGTGAAGTCCCAGCAG AAGAATGACGATCAGCAGGTGAAGCAGAATAGCCCCCTCCCTGTCTGTGCAGGAGGGCAGAATCAGCATC CTGAAGTGCAGTACACCAATTCCATGTTGATTATTTCTGTGGTACAAGAAGTATCCAGCCGAGGGC CCCACCTTTCTGATCAGCATCTCCTCTATCAAGGACAAGAACGAGGATGGCAGGTTCACAGTGTCTCTG AATAAGTCTGCCAAGCACCTGAGCCTGCACATCGTGCCATCCCAGCCTGGCGACTCTGCCGTGTACTTC TGTGCCGCCAGCGCCTCCAACAATGATATGAGATTGGCGCCGGCACCAGGCTGACAGTGAAGCCC
	197	MAMLLGASVLILWLQPDWVNSQQKNDDQVKQNSPSLSVQEGRISILNCDYTNMFDYFLWYKKYPAEG PTFLISSISSIKDKNEDGRFTVFLNKS AKHLSLHIVPSQPGDSAVYFCAASASNNDMRFGAGTRLTVPK
GATA3 TCR-2 beta chain variable domain	198	ATGGGCACCAGCCTCCTCTGCTGGATGGCCCTGTGTCTCCTGGGGGCAGATCACGCAGATACTGGAGTC TCCCAGGACCCAGACACAAGATCACAAAGAGGGGACAGAATGTAACCTTCAGGTGTGATCCAATTTCT GAACACAACCGCCTTTATTGGTACCGACAGACCTGGGGCAGGGCCAGAGTTTCTGACTTACTTCCAG AATGAAGCTCAACTAGAAAAATCAAGGCTGCTCAGTGATCGGTTCTCTGCAGAGAGGCCAAGGGATCT TTCTCCACCTTGGAGATCCAGCGCACAGAGCAGGGGGACTCGGCCATGTATCTCTGTGCCAGCAGCCAA TCGGGACAGGGGCCCTACGAGCAGTACTTCGGGCCGGGCACCAGGCTCACGGTCACAGAG
	199	ATGGGCACCTCTCTGCTGTGCTGGATGGCACTGTGCCTGCTGGGAGCAGACCACGCAGATACAGGCGTG AGCCAGGACCCCGCCACAAGATCACCAAGCGGGGCCAGAAGTACATTGATGCGATCCTATCTCC GAGCACAATAGGCTGTACTGGTATAGGCAGACCTGGGACAGGGACCAGAGTTCTGACATACTTTTCAG AACGAGGCCCCAGCTGGAGAAGAGCCGGCTGCTGTCCGACAGATTCTCTGCCAGAGGGCCTAAGGGCAGC TTTTCCACCTGGAGATCCAGAGGACAGAGCAGGGCGATTCTGCCATGTATCTGTGCCCGCAGCTCCCAG AGCGGACAGGGACCTTACGAGCAGTATTTCCGACCAGGAACCAGGCTGACCGTGACAGAG
	200	MGTSLLCWMALCLLGADHDTGVSQDPRHKITKRQNVTFRCDPISEHNRLYWRQTLGQGPFLTYFQ NEAQLEKSRLLSDRFS AERP KGSFSTLEIQRT EQGDSAMYLCASSQSGQGPYEQYFPGPTRLTVTE
GATA3 TCR-2 alpha chain	201	MAMLLGASVLILWLQPDWVNSQQKNDDQVKQNSPSLSVQEGRISILNCDYTNMFDYFLWYKKYPAEG PTFLISSISSIKDKNEDGRFTVFLNKS AKHLSLHIVPSQPGDSAVYFCAASASNNDMRFGAGTRLTVPK IQNPDPFVYQLRDSKSSDKSVCLFTDFDSQTNVSQSKSDVYITDKTVLDMRSMDFKSN SAVAWSNKSD FACANAFNNSIIPEDTFFPSP ESSCDVLVEKSFETDTNLFQNL SVIGFRILLK VAGFNLLMTLRLW SS

Name	SEQ ID NO	Sequence
GATA3 TCR-2 beta chain	202	MGTSLLCWMALCLLGADHADTGVSQDPRHRITKRQNVTFRCDPISEHNRLYWYRQTLGQGPEFLTYFQ NEAQLEKSRLLSDRFSARPKGSFSTLEIQRTTEQGDSAMYLCASSQSGQGPYEQYFGPGTRLTVTEEDL NKVFPEEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWVWNGKEVHSGVSTDPQLKEQPALNDS RYCLSSRLRVSATFWQNP RNHFRCQVQFYGLSENDEWTQDRAKPVTQIVSAEAWGRADCGFTSVSYQQG VLSATILYEILLGKATLYAVLVLSALVLMAMVKKRDF
GATA3 TCR-2 peptide	203	KPKRDGYMF
GATA3 TCR-3 alpha chain CDR1	204	YGGTVN
GATA3 TCR-3 alpha chain CDR2	205	YFSGDPLV
GATA3 TCR-3 alpha chain CDR3	206	AVISVTGNRRKLI
GATA3 TCR-3 beta chain CDR1	207	LNHDA
GATA3 TCR-3 beta chain CDR2	208	SQIVND
GATA3 TCR-3 beta chain CDR3	209	ASSRTAMNTEAF
GATA3 TCR-3 alpha chain variable domain	210	ATGCTCCTGTTGCTCATACCAGTGCTGGGGATGATTTTTGCCCTGAGAGATGCCAGAGCCCAGTCTGTG AGCCAGCATAAACCACCACGTAATTCTCTCTGAAGCAGCCTCACTGGAGTTGGGATGCAACTATTCTCTAT GGTGGAACTGTTAATCTCTCTGTTATGTCCAGTACCCTGGTCAACACCTTCAGCTTCTCTCAAGTAC TTTTCAGGGGATCCACTGGTTAAAGGCATCAAGGGCTTTGAGGCTGAATTATAAAGAGTAAATTTCTCC TTTAATCTGAGGAAACCTCTGTGCAGTGGAGTGACACAGCTGAGTACTTCTGTGCCGTGATCTCCGTG ACTGGCAACAACCGTAAGCTGATTTGGGGATTGGGAACAAGCCTGGCAGTAAATCCG
	211	ATGTGCTGCTGCTGATCCCTGTGCTGGGCATGATCTTTGCACTGAGGGACGCAAGAGCACAGTCCGTG TCTCAGCACAAACCACCGTGATCCTGAGCGAGGCAGCCTCCCTGGAGCTGGGCTGCAACTACTCTTAT GGCGGCACAGTGAATCTGTTCTGGTACGTGCAGTATCCAGGCCAGCACCTGCAGCTGCTGCTGAAGTAC TTTAGCGGGCAGCCCTGGTGAAGGGCATCAAGGGCTTCGAGGCCGAGTTTATCAAGTCCAAGTTCTCT TTTAACCTGCGGAAGCCATCTGTGCAGTGGAGCGATACCGCCGAGTATTTCTGTGCCGTGATCAGCGTG ACAGGCAACAATAGAAAGCTGATCTGGGGACTGGGCACCTCCCTGGCCGTGAATCCC
	212	MLLLLLPVLGMI FALRDARAQSVSQHNHHVILSEAASLELGCNYSYGGTVNLFVYVQYPGQHLQLLLKY FSGDPLVKIGKGFEEFIKSKFSFNLKPSVQWSDTAIEYFCAVISVTGNRRKLIWGLTSLAVNP
GATA3 TCR-3 beta chain variable domain	213	ATGAGCAACACAGGTGCTCTGCTGTGTGGTCTTTGTCTCCTGGGAGCAAACACCGTGGATGGTGGAAATC ACTCAGTCCCCGAAGTACCTGTTTCAGAAAGGAAGGACAGAATGTGACCTGAGTTGTGAACAGAATTTG AACCACGATGCCATGTACTGGTACCGACAGGACCCAGGGCAAGGGCTGAGATTGATCTACTACTCACAG ATAGTAAATGACTTTCAGAAAGGAGATATAGCTGAAGGGTACAGCGTCTCTCGGGAGAAGAAGGAATCC TTTCCTCTCACTGTGACATCGGCCCAAAGAACCCGACAGCTTTCTATCTCTGTGCCAGTAGTCGGACT GCAATGAACACTGAAGCTTTCTTTGGACAAGGCACCAGACTCACAGTTGTA
	214	ATGTCCAACACAGGTGCTGTGCTGGTGGTCTGTGCCTGTGCTGGGAGCAAATACCGTGGACGGAGGCATC ACACAGTCCCCAAGTACCTGTTTCAGGAAGGAGGGCCAGAACGTGACCTGTCTGTGAGCAGAACCTG AATCAGCAGCCATGTACTGGTATAGGCAGGACCCGGACAGGGACTGAGACTGATCTACTATAGCCAG ATCGTGAATGACTTTCAGAAAGGGCAGATCGCCGAGGGCTACTCCGTGTCTAGGGAGAAGAAGGAGAGC TTCCCTGTACCGTGACATCGGCCAGAAGAACCCTACAGCCTTTTATCTGTGCCAGCTCCCGCACC GCCATGAATACAGAGGCCTTCTTTGGCCAGGGCACCAGGCTGACAGTGGTG
	215	MSNQVLCVVLLCGANTVDGGITQSPKYLFRKEGQNVTLSCQNLNHDAMYWYRQDPGQGLRLIYYSQ IVNDFQKGDIAEGYSVSREKKEFPLTVTSAQKNPTAFYLCASSRTAMNTEAFFGQGTRLTVV
GATA3 TCR-3 alpha chain	216	MLLLLLPVLGMI FALRDARAQSVSQHNHHVILSEAASLELGCNYSYGGTVNLFVYVQYPGQHLQLLLKY FSGDPLVKIGKGFEEFIKSKFSFNLKPSVQWSDTAIEYFCAVISVTGNRRKLIWGLTSLAVNPDIQN PDPVYQLRDSKSSDKSVCLTFDFDSQTNVSQSKSDVYITDKTVLDMRSMDFKNSAVAWSNKSDFAC ANAFNNSIIPEDTFFPSPESCDVKLVEKSFETDNLNLFQNLVIGFRILLKLVAGFNLLMTLRLWSS
GATA3 TCR-3 beta chain	217	MSNQVLCVVLLCGANTVDGGITQSPKYLFRKEGQNVTLSCQNLNHDAMYWYRQDPGQGLRLIYYSQ IVNDFQKGDIAEGYSVSREKKEFPLTVTSAQKNPTAFYLCASSRTAMNTEAFFGQGTRLTVVIEDLNKV FPPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWVWNGKEVHSGVSTDPQLKEQPALNDSRYC LSSRLRVSATFWQNP RNHFRCQVQFYGLSENDEWTQDRAKPVTQIVSAEAWGRADCGFTSVSYQQGVLS ATILYEILLGKATLYAVLVLSALVLMAMVKKRDF

Name	SEQ ID NO	Sequence
GATA3 TCR-3 peptide	218	ESKIMFATL
TMPRSS2:ERG TCR-1 alpha chain CDR1	142	TRDTTY
TMPRSS2:ERG TCR-1 alpha chain CDR2	143	RNSFDEQN
TMPRSS2:ERG TCR-1 alpha chain CDR3	144	ALSEARVFNAGNSKLT
TMPRSS2:ERG TCR-1 beta chain CDR1	145	SGHDN
TMPRSS2:ERG TCR-1 beta chain CDR2	146	FVKESK
TMPRSS2:ERG TCR-1 beta chain CDR3	147	ASSQADSPLH
TMPRSS2:ERG TCR-1 alpha chain variable domain	148	ATGCTGACTGCCAGCCTGTTGAGGGCAGTCATAGCCTCCATCTGTGTTGTATCCAGCATGGCTCAGAAG GTAACCTCAAGCGCAGACTGAAATTTCTGTGGTGGAGAAGGAGGATGTGACCTTGGACTGTGTGTATGAA ACCCGTGATACTACTTATTACTTATTCTGGTACAAGCAACCACCAAGTGGAGAATTGGTTTTCTTATT CGTCGGAACCTCTTTTGATGAGCAAAATGAATAAGTGGTCGGTATTCTTGGAACCTCCAGAAATCCACC AGTTCTTCAACTTCACCATCACAGCCTCACAAGTCGTGGACTCAGCAGTATACTTCTGTGCTCTGAGT GAGGCCCGCGTTTTCAATGGAGCCAATAGTAAGCTGACATTTGGAAAAGGAATAACTCTGAGTGTAGA CCA
	149	ATGCTGACCGCCAGCCTGCTGAGGGCTGTGATCGCCAGCATCTGCGTCGTGTCCAGCATGGCTCAAAAG GTCACACAGGCCCAGACAGAGATCTCCGTCTGCGAGAAAGAGGACGTGACCTCGACTGCGTGTATGAG ACCAGGGACACCATACCTGTTTGGTACAAGCAGCCCCCAGCGGAGAGCTCGTGTCTGATC AGAAGGAACAGCTTTGATGAACAGAAATGAGATCTCCGGCAGGTACTCTGGAACCTCCAGAAGAGCAC CTTCCAGCTTCAACTTCACAATTACAGCTTCCCAGGTGGTGGATAGCGCGGTGATTTCTGCGCTCTCAGC GAGGCCAGGGTGTTCACGCGGCCAATTCAAAACGACCTTCGGCAAAGGCATCACACTGTCCGTGAGA CCC
	150	MLTASLLRAVIASICVVSMAQKVTAQTEISVVEKEDVTLDCVYETRDTTYLFWYKQPPSGELVFLI RRNSFDEQNEISGRYSWNFQKSTSSFNFTITASQVVDASAVYFCALSEARVFNAGNSKLTFGKGITLSVR P
TMPRSS2:ERG TCR-1 beta chain variable domain	151	ATGGTTTCCAGGCTTCTCAGTTTAGTGTCCTTTGTCTCCTGGGAGCAAAGCACATAGAAGCTGGAGTT ACTCAGTTCCCCAGCCACAGCGTAATAGAGAAGGGCCAGACTGTGACTCTGAGATGTGACCCAATTTCT GGACATGATAATCTTTATTGGTATCGACGTGTATGGGAAAAGAAATAAAATTTCTGTTACATTTTGTG AAAGAGTCTAAACAGGATGAATCCGGTATGCCAACAAATCGATTCTTAGCTGAAAGGACTGGAGGGACG TATTCTACTCTGAAGGTGCAGCCTGCAGAACTGGAGGATCTGGAGTTTATTTCTGTGCCAGCAGCCAA GCGGATTCAACCTCCACTTTGGGAATGGGACCAGGCTCACTGTGACA
	152	ATGGTCTCCAGGCTGCTCTCCTCGTGAGCCTGTGTCTCCTGGGAGCCAAGCACATTGAGGCCGGCGTG ACCCAATTTCCCAGCCACAGCGTGATTGAGAAGGGACAGACCGTCACCTGAGGTGTGATCCTATCAGC GGCCACGACAACCTCTACTGGTATAGGAGAGTCATGGGCAAGGAAATTAATTTCTGCTGCATTTCTGTG AAAGAGTCCAAACAGGACGAAAGCGGCATGCCAATAATAGGTTCTCGCCGAGAGGACCGGCGGCACA TATTCCACCTGAAGGTCCAGCCCGCTGAGCTCGAAGACTCCGGCGTCTATTTCTGTGCCTCCAGCCAG GCTGACTCCCCTCTCATTTTCGGAACCGGCACAGGCTCACCCTGACC
	153	MVSRLLSLVSLCLLGAKHIEAGVTQFPSSHVIEKGQTVTLRCDPISGHDNLYWYRRVMGKEIKFLLHFV KESQDESMPNNRFLAERTGGTYSTLKVQPAELED SGVYFCASSQADSPLHFGNGTRLTVT
TMPRSS2:ERG TCR-1 alpha chain	154	MLTASLLRAVIASICVVSMAQKVTAQTEISVVEKEDVTLDCVYETRDTTYLFWYKQPPSGELVFLI RRNSFDEQNEISGRYSWNFQKSTSSFNFTITASQVVDASAVYFCALSEARVFNAGNSKLTFGKGITLSVR PDIQNPDPVYQLRDSKSSDKSVCLTFDFDSQTNVSQSKSDVYITDKTVLDMRSMDFKNSAVAWSNK SDFACANAFNNSIIPEDTFFPSPSSCDVKLVEKSFETDTNLFQNLVIGFRILLKVAGFNLLMTLR LWSS
TMPRSS2:ERG TCR-1 beta chain	155	MVSRLLSLVSLCLLGAKHIEAGVTQFPSSHVIEKGQTVTLRCDPISGHDNLYWYRRVMGKEIKFLLHFV KESQDESMPNNRFLAERTGGTYSTLKVQPAELED SGVYFCASSQADSPLHFGNGTRLTVTEDLNKVF PPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWVNGKEVHSGVSTDPQLKEQPALNDSRYCL SSRLRVSATFWQNP RNHFRCQVQFYGLSENDEWTQDRAKPVTTQIVSAEAWGRADCGFTSVSYQQGVLSA TILYEILLGKATLYAVLVLSALVLMAMVKRKDF

Name	SEQ ID NO	Sequence
TMFRSS2:ERG TCR-1 peptide	156	ALNSEALSV
BTK TCR-1 alpha chain CDR1	159	DRGSQS
BTK TCR-1 alpha chain CDR2	160	IYSNGD
BTK TCR-1 alpha chain CDR3	161	AVNDYGGSQGNLIF
BTK TCR-1 beta chain CDR1	162	SEHNR
BTK TCR-1 beta chain CDR2	163	FQNEAQ
BTK TCR-1 beta chain CDR3	164	ASSFGPDEKLFF
BTK TCR-1 alpha chain variable domain	165	ATGATGAAATCCTTGAGAGTTTACTAGTGATCCTGTGGCTTCAGTTGAGCTGGGTTTGGAGCCAAACG AAGGAGGTGGAGCAGAATTCTGGACCCCTCAGTGTTCCAGAGGGAGCCATTGCCTCTCTCAACTGCACT TACAGTGACCGAGGTTCCCACTCCTTCTTCTGGTACAGACAATATTCTGGGAAAAGCCCTGAGTTGATA ATGTTTCATATACTCCAATGGTGACAAAGAAGATGGAAGGTTTACAGCACAGCTCAATAAAGCCAGCCAG TATGTTTCTCTGCTCATCAGAGACTCCCAGCCAGTGATTCAGCCACCTACCTCTGTGCCGTGAACGAT TATGGAGGAAGCCAAGGAAATCTCATCTTTGAAAAGGCACTAAACTCTCTGTTAAACCA
	166	ATGATGAAGAGCCTGCGGGTGCTGCTGGTCATCCTGTGGCTGCAGCTGTCTTGGGTGTGGAGCCAGCAG AAGGAGGTGGAGCAGAAGCTCCGACCACTGTCTGTGCCTGAGGGAGCCATCGCCAGCCTGAATTGCACC TACTCCGACAGAGGCTCCCACTCTTTCTTTTGGTACAGGCAGTATAGCGGCAAGTCCCCGAGCTGATC ATGTTTCATCTACTCCAACGGCGACAAGGAGGATGGCCGCTTTACAGCCAGCTGAATAAGGCCAGCCAG TACGTGAGCCTGCTGATCCGGGACTCTCAGCCAAGCGATTCCGCCACCTACCTGTGCGCCGTGAACGAT TATGGCGGCAGCCAGGCAATCTGATCTTTGGCAAGGGCACAAAGCTGTCCGTGAAGCCC
	167	MMKSLRVLLVILWLQLSWVWSQQKEVEQNSGPLSVPEGAIASLNCTYSDRGSQSFFWYRQYSGKSP ELI MFIYSNGDKEDGRFTAQLNKASQYVSLIRDSQPSDSATYLCVNDYGGSQGNLIFGKGTKLSVKP
BTK TCR-1 beta chain variable domain	168	ATGGGCACCAAGCCTCTCTGCTGGATGGCCCTGTGTCTCCTGGGGGAGATCACGCAGATACTGGAGTC TCCAGAACCCAGACACAAGATCACAAGAGGGGACAGAATGTAACCTTCAGGTGTGATCCAATTTCT GAACACAACCGCCTTTATTTGGTACCGACAGACCTGGGGCAGGGCCAGAGTTTCTGACTTACTTCCAG AATGAAGCTCAACTAGAAAAATCAAGGCTGCTCAGTGATCGGTTCTCTGCAGAGAGCCCTAAGGGATCT TTCTCCACCTTGGAGATCCAGCGCACAGAGCAGGGGACTCGGCCATGTATCTCTGTGCCAGCAGCTTC GGACCTGATGAAAACTGTTTTTTGGCAGTGAACCCAGCTCTCTGTCTTG
	169	ATGGGCACCTCTCTGCTGTGCTGGATGGCACTGTGCCTGCTGGGAGCAGACCACGCAGATACAGGCGTG AGCCAGAACCACGCCACAGATCACAAGCGGGGCCAGAATGTGACATTAGATGCCACCCCATCAGC GAGCACAAACAGGCTGTACTGGTATAGGCAGACCTGGGACAGGGACCAAGTTTCTGACATACTTTTCA G AATGAGGCCAGCTGGAGAAGTCTCGGCTGCTGAGCGATAGATTCTCCGCCAGAGGCCCTAAGGGCTCC TTTTCTACCTTGGAGATCCAGAGGACAGAGCAGGGCGACTCCGCCATGTATCTGTGCGCCAGCTCCTTC GGCCCTGATGAGAAGCTGTTCTTTGGCTCTGGCACCCAGCTGAGCGTGCTG
	170	MGTSLLCWMALCCLLGADHDTGVSQNPRIKTKRQNVTFRCDFISEHNRLYWYRQTLGQGPFLTYFQ NEAQLEKSRLLSDRFSERP KGSFSTLEIQRT EQGDSAMYLCASSFGPDEKLFFGSGTQLSVL
BTK TCR-1 alpha chain	171	MMKSLRVLLVILWLQLSWVWSQQKEVEQNSGPLSVPEGAIASLNCTYSDRGSQSFFWYRQYSGKSP ELI MFIYSNGDKEDGRFTAQLNKASQYVSLIRDSQPSDSATYLCVNDYGGSQGNLIFGKGTKLSVKPDIQ NPDPVYQLRDSKSDKSVCLFTDFDSQTNVSQSKSDVYITDKTVLDMRSMDFKSN SAVAWSNKSDFA CANAFNNSIIPEDTFFPSPSSCDVKLVEKSFETDTNLFQNL SVIGFRILLKLVAGFNLLMTLRLWSS
BTK TCR-1 beta chain	172	MGTSLLCWMALCCLLGADHDTGVSQNPRIKTKRQNVTFRCDFISEHNRLYWYRQTLGQGPFLTYFQ NEAQLEKSRLLSDRFSERP KGSFSTLEIQRT EQGDSAMYLCASSFGPDEKLFFGSGTQLSVLEDLNKV FPPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWVNGKEVHSGVSTDPQPLKEQPALNDSRYC LSSRLRVSATFWQNPRIHFRQVQFYGLSENDEWTQDRAKPVTVQIVSAEAWGRADCGFTSVSYQQGVLS ATILYEILLGKATLYAVLVLSALVLMAMVKRKDF
BTK TCR-1 peptide	173	SLNLNREM
BTK TCR-2 alpha chain CDR1	174	DRGSQS
BTK TCR-2 alpha chain CDR2	175	IYSNGD

Name	SEQ ID NO	Sequence
BTK TCR-2 alpha chain CDR3	176	AVNEGDSSYKLI
BTK TCR-2 beta chain CDR1	177	SGDLS
BTK TCR-2 beta chain CDR2	178	YYNGEE
BTK TCR-2 beta chain CDR3	179	ASSPGANEKLF
BTK TCR-2 alpha chain variable domain	180	ATGATGAAATCCTTGAGAGTTTTACTAGTGATCCTGTGGCTTCAGTTGAGCTGGGTTTGGAGCCAACAG AAGGAGGTGGAGCAGAATTCTGGACCCCTCAGTGTTCAGAGGGAGCCATTCGCTCTCTCAACTGCACT TACAGTGACCGAGGTTCCCACTCCTTCTTCTGGTACAGACAATATTCTGGGAAAAGCCCTGAGTTGATA ATGTTTCATATACTCCAATGGTGACAAAGAAGATGGAAGGTTTACAGCACAGCTCAATAAAGCCAGCCAG TATGTTTCTCTGCTCATCAGAGACTCCCAGCCAGTGATTGAGCCACCTACCTCTGTGCCGTGAACGAG GGGGATAGCAGCTATAAATTGATCTTCGGGAGTGGGACCAGACTGCTGGTCAGGCCT
	181	ATGATGAAGAGCCTGCGGGTGTCTGTGGTTCATCCTGTGGCTGCAGCTGAGCTGGGTGTGGTCCCAGCAG AAGGAGGTGGAGCAGAATCTGGACCACTGAGCGTGCCTGAGGGAGCCATCGCCTCCCTGAATTGCACC TACTCTGACAGAGGAGCCAGTCTCTTTTGGTACAGGAGTATTCGGCAAGTCTCCCGAGCTGATC ATGTTTCATCTACAGCAACGCGACAAAGGAGGATGGCCGCTTTACAGCCAGCTGAATAAGGCCTCCAG TACGTGAGCCTGCTGATCCGGGACTCTCAGCCATCTGATAGCGCCACCTACCTGTGCGCCGTGAACGAG GCGGATAGCTCCTATAAGCTGATCTTTGGCAGCGGCACAGACTGCTGGTGAGGCC
	182	MMKSLRVLLVILWLQLSWVWSQQKEVEQNSGFLSVPEGAIASLNCTYSDRGSQSFYRQYSGKSPELI MFIYNGDKEDGRFTAQLNKASQYVSLIRDSQPSDSATYLCVNEGDSSYKLI FGSGLRLLVRP
BTK TCR-2 beta chain variable domain	183	ATGGGCTTCAGGCTCCTCTGTGTGGCCTTTTGTCTCCTGGGAGCAGGCCAGTGGATTCTGGAGTC ACACAAACCCCAAAGCACCTGATCACAGCAACTGGACAGCGAGTGACGCTGAGATGCTCCCTAGGTCT GGAGACCTCTCTGTGTACTGGTACCAACAGAGCCTGGACCAGGGCCTCCAGTTCTCTCATTAGTATTAT AATGGAGAAGAGAGAGCAAAAGGAAACATTCTTGAACGATTCTCCGCACAACAGTTCCCTGACTTGCAC TCTGAACATAACCTGAGCTCTCTGGAGCTGGGGACTCAGCTTTGTATTTCTGTGCCAGCAGCCCGGG GCTAATGAAAACTGTTTTTTGGCAGTGGAACCCAGCTCTCTGTCTTG
	184	ATGGGCTTCGCGCTGCTGTGTGCTGCGTGGCATTTCCTGCTGGGAGCAGGACCAGTGGACTCCGGCGTG ACCCAGACACCCAAGCACCTGATCACCGCAACAGGACAGAGGGTGACCTGAGATGTTCCCTAGGTCT GCGGACCTGAGCGTGTACTGGTATCAGCAGTCCCTGGATCAGGGCCTGCAGTTCTCTGATCCAGTACTAT AACGGCGAGGAGCGCGCCAAAGGCAATATCCTGGAGCGGTTCTCCGCCAGCAGTTTCCCGACCTGCAC TCTGAGCTGAACCTGAGCTCCCTGGAGCTGGGCGATAGCGCCCTGTACTTCTGCGCCTCTAGCCCTGGC GCCAATGAGAAGCTGTTCTTTGGCAGCGGCACCCAGCTGTCCGTGCTG
	185	MGFRLLCCVAFCLLGAGPVDGSGVTQTPKHLITATGQRVTLRCSPRSGDLSVYWYQQSLDQGLQFLIQYY NGEERAKGNILERFSAQQFPDLHSELNLSSLELGDLSALYFCASSPGANEKLF FGSGLTQLSVL
BTK TCR-2 alpha chain	186	MMKSLRVLLVILWLQLSWVWSQQKEVEQNSGFLSVPEGAIASLNCTYSDRGSQSFYRQYSGKSPELI MFIYNGDKEDGRFTAQLNKASQYVSLIRDSQPSDSATYLCVNEGDSSYKLI FGSGLRLLVRPDIQN PDPVYQLRDSKSSDKSVCLFTDFDSQTNVSQSKDSVYITDKTVLDMRSMDFKSN SAVAWSNKSDFAC ANAFNNSII PEDTFFPSPESCDVKLVEKSFETDTNLFQNL SVIGFRILLK VAGFNLM TLRWSS
BTK TCR-2 beta chain	187	MGFRLLCCVAFCLLGAGPVDGSGVTQTPKHLITATGQRVTLRCSPRSGDLSVYWYQQSLDQGLQFLIQYY NGEERAKGNILERFSAQQFPDLHSELNLSSLELGDLSALYFCASSPGANEKLF FGSGLTQLSVLEDLNKVF PPEVAVFEPSEAEISHTQKATLVCLATGFFPDHVELSWWVNGKEVHSGVSTDPQPLKEQPALNDSRYCL SSRLRVSATFWQNPRNHFRQVQFYGLSENDEWTQDRAKPVTOIVSAEAWGRADCGFTSVSYQQGVLSA TILYEILLKATLYAVLVLSALVLMAMVKRKDF
BTK TCR-2 peptide	188	SLNLYLREM
EGFR TCR-1 alpha chain CDR1	447	TRDTTTY
EGFR TCR-1 alpha chain CDR2	448	RNSFDEQN
EGFR TCR-1 alpha chain CDR3	449	ALKGANTGFQKL
EGFR TCR-1 beta chain CDR1	450	SGHDY

Name	SEQ ID NO	Sequence
EGFR TCR-1 beta chain CDR2	451	FNNNVF
EGFR TCR-1 beta chain CDR3	452	ASGGGLGLFETQY
EGFR TCR-1 alpha chain variable domains	453	ATGCTGACTGCCAGCCTGTTGAGGGCAGTCATAGCCTCCATCTGTGTTGTATCCAGCATGGCTCAGAAG GTAACCAAGCGCAGACTGAAATTTCTGTGGTGGAGAAGGAGGATGTGACCTTGGACTGTGTGTATGAA ACCCGTGATACTACTTATTACTTATCTGTGTACAAGCAACCACCAAGTGGAGAATTGGTTTTCTTATT CGTCGGAACCTCTTTTGATGAGCAAAATGAAATAAGTGGTCGGTATTCTTGGAACTTCCAGAAATCCACC AGTTCTTCAACTTCACCATCACAGCCTCACAAGTCGTGGACTCAGCAGTATACTTCTGTGCTCTGAAA GGGGCGAACACAGGCTTTCAGAAACTTGATTTGGAACTGGCACCCGACTTCTGGTCAGTCCA
	454	ATGCTGACAGCCTCCCTGCTGAGGGCCGTGATCGCCTCTATCTGCGTGGTGTCTAGCATGGCCAGAAAG GTGACCCAGGCCAGACAGAGATCAGCGTGGTGGAGAAGGAGGAGCTGACCCCTGGATTGCGTGTACGAG ACACGGGACACACATACTATCTGTTTTGGTATAAGCAGCCACCCAGCGGCGAGCTGGTGTTCCTGATC AGGGCAATTCCTTTGATGAGCAGAACGAGATCTCCGGCAGATACTCTTGGAAATTTCCAGAAAGTCCACC TCCTCTTTCAACTTTACCATCACAGCCTCCAGGTGGTGGACTCTGCCGTGTATTTTGTGCCCTGAAG GGGCCCAACACAGGCTTCCAGAAAGTGGTGTGGCACCCGACCAAGACTGCTGGTGAGCCCT
	455	MLTASLLRAVIASICVVSMAQKVTQAQTEISVVEKEDVTLDCVYETRDTTYLFWYKQPPSGELVFLI RRNSFDEQNEISGRYSWNFKSTSSFNFTITASQVVDASAVYFCALKGANTGFQKLVFQGTGTRLLVSP
EGFR TCR-1 beta chain variable domains	456	ATGGACTCCTGGACCCTCTGCTGTGTGTCCCTTTGCATCCTGGTAGCAAAGCACACAGATGCTGGAGTT ATCCAGTCACCCCGGCAGGAGGTGACAGAGATGGGACAAGAAGTGAATCTGAGATGTAAACCAATTTCA GGACACGACTACCTTTTCTGGTACAGACAGACCATGATGCGGGGACTGGAGTTGCTCATTACTTTAACA AACAAACGTTCCGATAGATGATTACGGGATGCCCCGAGGATCGATTCTCAGCTAAGATGCCTAATGCATCA TTCTCCACTCTGAAGATCCAGCCCTCAGAACCCAGGGACTCAGCTGTGTACTTCTGTGCCAGCGGAGGG GGACTAGGTCTATTTGAGACCCAGTACTTCGGGCCAGGCACGCGCTCCTGGTGCTC
	457	ATGGACAGCTGGACCCTGTGCTGCTGAGCCTGTGCATCCTGGTGGCCAAGCACACAGATGCAGGCGTG ATCCAGTCCCCAAGGCACGAGGTGACCGAGATGGGACAGGAGGTGACACTGAGGTGTAAGCCTATCTCT GGGCAGGACTACCTGTTCTGGTATCGGCAGACCATGATGAGAGGCTGGAGCTGCTGATCTACTTTAAC AATAACGTGCCTATCGACGATTCTGGCATGCCAGAGGACAGGTTTCCAGCGCAAGATGCCTAATGCCAGC TTTTCCACCCTGAAGATCCAGCCAAGCGAGCCAAGGGATTCCGCCGTGTACTTCTGCCCTCCGGAGGA GGACTGGGACTGTTTCGAGACCCAGTATTTTGGGCCAGGCACAAGCTGCTGGTGCTG
	458	MDSWTLCCVSLCILVAKHTDAGVIQSPRHEVTEMGQEVTLRCKPISGHDLFWYRQTMMRGLELLIYFN NNVPIDDSGMPEDRFSAPKMPNASFSTLKIQFSEPRDSAVYFCASGGGLGLFETQYFPGPTRLLVL
EGFR TCR-1 alpha chain	459	MLTASLLRAVIASICVVSMAQKVTQAQTEISVVEKEDVTLDCVYETRDTTYLFWYKQPPS GELVFLI RRNSFDEQNEISGRYSWNFKSTSSFNFTITASQVVDASAVYFCALKGANTGFQKL VFGTGTGTRLLVSPDIQNPFAVYQLKDPKRSQDSTLCLFTDFDSQINVPKTMESGTFITDKTVL DMKAMD SKSNGAIAWSNQTSFTCQDIFKETNATYPSSDVPCDATLTEKSFETDMNLNFQNL S VMGLRI LLLKVAGFNLMLTLRLWSS
EGFR TCR-1 beta chain	460	MDSWTLCCVSLCILVAKHTDAGVIQSPRHEVTEMGQEVTLRCKPISGHDLFWYRQTMMRGL ELLIYFN NNVPIDDSGMPEDRFSAPKMPNASFSTLKIQFSEPRDSAVYFCASGGGLGLFETQY FPGPTRLLVLKDLRNVTTPKVSLEFEPKAEIANKQKATLVCLARGFFPDHVELSWVNGKEV HSGVSTDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRQVQFHLSEEDKWPEGSPKPV T QNISAEAWGRADCGITSASYHQVLSATILYEILLGKATLYAVLVSGLVLMAMVKKKNS
Peptides	461	QLIMQLMPF
	462	LIMQLMPFGC
	463	MLMPFGCLL
EGFR TCR2 alpha chain CDR1	464	DSSSTY
EGFR TCR2 alpha chain CDR2	465	IFSNMDM
EGFR TCR2 alpha chain CDR3	466	AEWANTDKLI
EGFR TCR2 beta chain CDR1	467	DFQATT
EGFR TCR2 beta chain CDR2	468	SNEGSKA

Name	SEQ ID NO	Sequence
EGFR TCR2 beta chain CDR3	469	SARRREGEIEQY
EGFR TCR2 alpha chain variable domains	470	ATGAAGACATTTGCTGGATTTTCGTTCTGTTTTGTGGCTGCAGCTGGACTGTATGAGTAGAGGAGAGGATGTGGAGCAGAGTCTTTTCCTGAGTGTCCGAGAGGGAGACAGCTCCGTTATAAACTGCACTTACACAGACAGCTCCTCCACCTACTTATACTGGTATAAGCAAGAAGCTGGAGCAGGTCTCCAGTTGCTGACGTATATTTTTTCAAATATGGACATGAAACAAGACCAAAGACTCACTGTTCTATTGAATAAAAAGGATAAACATCTGTCTCTGCGCATTCAGACACCCAGACTGGGGACTCAGCTATCTACTTCTGTGCAGAGTGGGCTAACACCGACAAGCTCATCTTTGGGACTGGGACCAGATTACAAGTCTTTCCA
	471	ATGAAGACCTTCGCCGGCTTCTCCTTTCTGTTCCCTGTGGCTGCAGCTGGACTGCATGAGCCGGGGAGAGGATGTGGAGCAGTCCCTGTTCTGTCTGTGAGGGAGGGCGACTCCTCTGTGATCAACTGTACATATACCGATAGCTCCTCTACCTACCTGTATTGGTACAAGCAGGAGCCAGGAGCAGGACTGCAGCTGCTGACATACATCTTTAGCAACATGGACATGAAGCAGGATCAGCGCCTGACCGTGTCTGAATAAGAAGGACAAGCACCTGTCTCTGCGGATCGCCGACACAGACCGGCGATAGCGCCATCTACTTCTGTGCCGAGTGGGCCAATACCGATAAGCTGATCTTTGGCACAGGCACCCGGCTGCAGGTGTTCCCT
	472	MKTFAGFSFLFLWLQLDCMSRGEDVEQSFLSVREGDSSVINCTYTDSSSTLYWYKQEPGAGLQLLTYIFSNMDMKQDQRLTVLLNKKDKHLSLRIADTQTGDSAIYFCAEWANTDKLI FGTGTRLQVFP
EGFR TCR2 beta chain variable domains	473	ATGCTGCTGCTTCTGCTGCTTCTGGGGCCAGGCTCCGGGCTTGGTGCTGTCGTCTCTCAACATCCGAGCTGGGTTATCTGTAAGAGTGAACCTCTGTGAAGATCGAGTGCCGTTCCCTGGACTTTCAGGCCACAACCTATGTTTTGGTATCGTCAGTTCGCGAAACAGAGTCTCATGCTGATGGCAACTTCCAATGAGGGCTCCAAGGCCACATACGAGCAAGGCGTCGAGAAGGACAAGTTTCTCATCAACCATGCAAGCCTGACCTTGTCCTACTGACAGTGACCAAGTCCCCATCCTGAAGACAGCAGCTTCTACATCTGCAGTGCTAGAAGCGGGAGGGGGAGATCGAGCAGTACTTCGGGCGGGGCACCAAGGCTCACGGTCACA
	474	ATGTTATTACTGCTGCTGCTGCTGGGACCAGGCTCCGACTGGGAGCCGTGGTGTCCTCCAGCACCTTCTTGGGTCATCTGCAAGTCCGGCACATCTGTGAAGATCGAGTGTGCTCTCTGGACTTTCAGGCCACCACATGTTTTGGTATCGGCAGTTCCTCAAGCAGAGCCTGATGCTGATGGCCACAAGCAACGAGGGCTCCAAGGCCACCTACGAGCAGGGCGTGGAGAAGGACAAGTTCTGATCAATCACGCCTCTCTGACCTGAGCACCCTGACAGTGACCTCCGCCACCCTGAGGATAGCTCCTTTTATATCTGCTCTGCCCGAGAAGGGAGGGCGAGATCGAGCAGTACTTCGGGCCAGGCACAAGACTGACAGTGACC
	475	MLLLLLLLGPGSGLGAVVSWHPVSVCKSGTSVKIECRSLDFQATTMFWYRQFPKQSLMLMATSNEGSKATYEQGVKDKFLINHASLTSLTLVTSAPHPEDSSFYICSAARRREGEIEQYFPGTRLTVT
EGFR TCR2 alpha chain	476	MKTFAGFSFLFLWLQLDCMSRGEDVEQSFLSVREGDSSVINCTYTDSSSTLYWYKQEPGAGLQLLTYIFSNMDMKQDQRLTVLLNKKDKHLSLRIADTQTGDSAIYFCAEWANTDKLI FGTGTRLQVFPDIQNPEPAVYQLKDPQSQDSTLCLFTDFDSQINVPKTMESGTFITDKTVLDMKAMDKSNGAIAWSNQTSFTCQDIFKETNATYPSSDVPCDATLTEKSFETDMNLNLFQNLVSMGLRI LLLKVAGFNLLMTLRLWSS
EGFR TCR2 beta chain	477	MLLLLLLLGPGSGLGAVVSWHPVSVCKSGTSVKIECRSLDFQATTMFWYRQFPKQSLMLMATSNEGSKATYEQGVKDKFLINHASLTSLTLVTSAPHPEDSSFYICSAARRREGEIEQYFPGPTRLTVTKDLRNVTPPKVSLFEPSKAEIANKQKATLVCLARGFFPDHVELSWVWNGKEVHSGVSTDPQAYKESNYSYCLSSRLRVSATFWHNP RNHFRCQVQFHGLSEEDKWPEGSPKPVTONISAEAWGRADCGITSASYHQGVLSATILYEILLGKATLYAVLVSGVLVLMAMVKKKNS
Peptides	478	QLIMQLMPF
	479	LIMQLMPFGC
	480	MQLMPFGCLL
EGFR TCR3 alpha chain CDR1	481	TRDTTY
EGFR TCR3 alpha chain CDR2	482	RNSFDEQN
EGFR TCR3 alpha chain CDR3	483	ALTPFPNAGGTSYGKLT
EGFR TCR3 beta chain CDR1	484	SGHNS
EGFR TCR3 beta chain CDR2	485	FNNNVP
EGFR TCR3 beta chain CDR3	486	ASSLAYLTGRVEAF

Name	SEQ ID NO	Sequence
EGFR TCR3 alpha chain variable domains	487	ATGCTGACTGCCAGCCTGTTGAGGGCAGTCATAGCCTCCATCTGTGTTGTATCCAGCATGGCTCAGAAG GTAACCTCAAGCGCAGACTGAAATTTCTGTGGTGGAGAAGGAGGATGTGACCTTGGACTGTGTGTATGAA ACCCGTGATACTACTTATTACTTATTCTGGTACAAGCAACCACCAAGTGGAGAATTGGTTTTCCTTATT CGTCGGAACTCTTTTGATGAGCAAAATGAAATAAGTGGTCGGTATTCTTGAACCTCCAGAAATCCACC AGTTCTTCAACTTCACCATCACAGCCTCACAAGTCGTGGACTCAGCAGTATACTTCTGTGCTCTGACT CCCTTCCCAATGCTGGTGGTACTAGCTATGGAAAGCTGACATTTGGACAAGGGACCATCTTGAAGTGC CATCCA
	488	ATGCTGACAGCCTCTCTGCTGAGGGCCGTGATCGCCAGCATCTGCGTGGTGTCTCTATGGCCCAAGAAG GTGACCCAGGCCAGACAGAGATCAGCGTGGTGGAGAAGGAGGACGTGACCTTGGATTGCGTGTACGAG ACACGGGACACCACATACTATCTGTTCTGGTATAAGCAGCCACCCTCCGGCGAGCTGGTGTCTCTGATC AGGCGCAATTCTTTTGATGAGCAGAACGAGATCTCTGGCAGATACAGCTGGAATTTTCAGAAAGTCTACC AGCTCCTTCAACTTTACCATCACAGCCTCTCAGGTGGTGGATAGCGCCGTGTACTTCTGTGCCCTGACA CCATTTCCCAATGCCGGCGGCACACAGCTATGGCAAGCTGACATTCGGCCAGGGCACCATCTGACAGTG CACCT
	489	MLTASLLRAVIASICVSSMAQKVTQAQTEISVVEKEDVTLDCVYETRDTTYLFWYKQPPSGELVFLI RRNSFDEQNEISGRYSWNFQKSTSSFNFTITASQVVDASAVYFCALTFFPNAGGTSYGLKTFGQGTILTV HP
EGFR TCR3 beta chain variable domains	490	ATGGACTCCTGGACCTTCTGCTGTGTGTCCCTTTGCATCCTGGTAGCGAAGCATACAGATGCTGGAGTT ATCCAGTCACCCCGCCATGAGGTGACAGAGATGGGACAAGAAGTGAATCTGAGATGTAACCAATTTCA GGCCACAACCTCCCTTTTCTGGTACAGACAGACCATGATGCGGGGACTGGAGTTGCTCATTTACTTTAAC AACAACGTTCCGATAGATGATTGAGGATGCCCGAGGATCGATTCTCAGCTAAGATGCCAATGATCATCA TTCTCCACTCTGAAGATCCAGCCCTCAGAAGCCAGGGACTCAGCTGTGTACTTCTGTGCCAGCAGTTTA GCCTACCTGACAGGGAGGGTTGAAGCTTTCTTTGGACAAGGCACACAGACTCACAGTTGTA
	491	ATGGACTCCTGGACCTTCTGCTGCGTGAGCCTGTGCATCCTGGTGGCCAAGCACACAGATGCAGGCGTG ATCCAGTCCCAAGGCACGAGGTGACCGAGATGGGACAGGAGGTGACACTGAGGTGTAAGCCCATCAGC GGCCACAATCCCTGTTCTGGTACCGGCAGACCATGATGAGAGGCTGGAGCTGCTGATCTACTTCAAC AATAACGTGCCCATCGACGATAGCGGCATGCCTGAGGACCGGTTCTCCGCCAAGATGCCAACGCCTCT TTTAGCACCTGAAGATCCAGCCTTCCGAGCCAAGGATTCTGCCGTGTACTTCTGCGCCAGCTCCCTG GCCTATCTGACCGGAAGGTTGGAGGCCTTCTTTGGACAGGGCACCAGGCTGACAGTGGTG
	492	MDSWTFCCVSLCILVAKHTDAGVIQSPRHEVTEMGQEVTLRCKPISGHNSLFWYRQTMGRGLELLIYFN NNVPIDDSGMPEDRFSAKMPNASFSTLKIQSEPRDSAVYFCASSLAYLTGRVEAFFGQGTRLTVV
EGFR TCR3 alpha chain	493	MLTASLLRAVIASICVSSMAQKVTQAQTEISVVEKEDVTLDCVYETRDTTYLFWYKQPPS GELVFLIRNSFDEQNEISGRYSWNFQKSTSSFNFTITASQVVDASAVYFCALTFFPNAGGTS YGKLTFGQGTILTVHPDIQNPEPAVYQLKDPQSSTLCLFTDFDSQINVPKTMESGTFITD KTVLDMKAMDSKSNAGIAWSNQTSTFCQDIFKETNATYPSSDVPCDATLTEKSFETDMNLNF QNL SVMGLRILLLKVAGFNLLMTLRLWSS
EGFR TCR3 beta chain	494	MDSWTFCCVSLCILVAKHTDAGVIQSPRHEVTEMGQEVTLRCKPISGHNSLFWYRQTMGRGL ELLIYFN NNVPIDDSGMPEDRFSAKMPNASFSTLKIQSEPRDSAVYFCASSLAYLTGRVEA FFGQGTRLTVVKDLRNVTPPKVSLFEPKAEIANKQKATLVCLARGFFPDHVELS WVVNGKE VHSGVSTDPQAYKESNYSYCLSSRLRVSATFWHNP RNHFRCQVQFHGLSEEDKWPEGSPKPV TQNISAEAWGRADCGITSASYHQVLSATILYEILLGKATLYAVLVSGVLVLMAMVKKKNS
Peptides	495	QLIMQLMPF
	496	LIMQLMPFGC
	497	MLMPFGCLL
EGFR TCR4 alpha chain CDR1	498	TRDTTY
EGFR TCR4 alpha chain CDR2	499	RNSFDEQN
EGFR TCR4 alpha chain CDR3	500	ALIRGSYQLI
EGFR TCR4 beta chain CDR1	501	DFQATT
EGFR TCR4 beta chain CDR2	502	SNEGSKA
EGFR TCR4 beta chain CDR3	503	SAQGSSGRIEQF

Name	SEQ ID NO	Sequence
EGFR TCR4 alpha chain variable domains	504	ATGCTGACTGCCAGCCTGTTGAGGGCAGTCATAGCCTCCATCTGTGTTGTATCCAGCATGGCTCAGAAG GTAACCTCAAGCGCAGACTGAAATTTCTGTGGTGGAGAAGGAGGATGTGACCTTGGACTGTGTGTATGAA ACCCGTGATACTACTTATTACTTATTCTGGTACAAGCAACCACCAAGTGGAGAATTGGTTTTCCTTATT CGTCGGAACCTCTTTTGATGAGCAAAATGAAATAAGTGGTCGGTATTCTTGGAACTTCCAGAAATCCACC AGTTCCTTCAACTTCACCATCACAGCCTCACAAGTCGTGGACTCAGCAGTATACTTCTGTGCTCTGATT CGAGGGAGCTATCAGTTAATCTGGGGCGCTGGGACCAAGCTAATTATAAAGCCA
	505	ATGCTGACCGCTCTCTGCTGAGGGCCGTGATCGCCAGCATCTGCGTGGTGAGCTCCATGGCCCAGAAG GTGACACAGGCCCAGACCGAGATCAGCGTGGTGGAGAAGGAGGACGTGACACTGGATTGCGTGTACGAG ACCCGCGACACCACATACTATCTGTTTTGGTATAAGCAGCCACCCTCCGGCGAGCTGGTGTTCCTGATC AGGGCGAACTCTTTTGATGAGCAGAATGAGATCTCTGGCCGGTACAGCTGGAACCTCCAGAAGAGCACA TCTAGCTTCAACTTCACCATCACCGCCAGCCAGGTGGTGGACTCCGCCGTGTACTTTTGTGCCCTGATC AGAGGCTCCTATCAGCTGATCTGGGGCGCCGGCACCAAGCTGATCATCAAGCCC
	506	MLTASLLRAVIASICVVSMAQKVTQAQTEISVVEKEDVTLDVYETRDTTYLFWYKQPPSGELVFLI RRNSFDEQNEISGRYSWNFQKSTSSFNFTITASQVVD SAVYFCALIRGSYQLIWGAGTKLI IKP
EGFR TCR4 beta chain variable domains	507	ATGCTGACCGCTCTCTGCTGAGGGCCAGGCTCCGGGCTTGGTGTCTGCTGTCTCAACATCCGAGC AGGGTTATCTGTAAGAGTGGAACTCTGTGAAGATCGAGTGCCGTTCCCTGGACTTTCCAGGCCACAAC ATGTTTTGGTATCGTCAGTTCCCGAAACAGAGTCTCATGCTGATGGCAACTTCCAATGAGGGCTCCAAG GCCACATACGAGCAAGGCGTCGAGAAGGACAAGTTTCTCATCAACCATGCAAGCCTGACCTTGTCACCT CTGACAGTGACCAAGTGCCCATCCTGAAGACAGCAGCTTCTACATCTGCAGCGCCAGGGGAGTAGCGGG AGGATTGAGCAGTTCTTCGGGCCAGGGACACGGCTCACCGTGCTA
	508	ATGTTATTACTGCTGCTGCTGCTGGGACCAGGCTCCGGACTGGGAGCAGTGGTGTCTCAGCACCCAAAGC AGAGTGATCTGCAAGTCTGGCACCAGCGTGAAGATCGAGTGTAGGTCCCTGGACTTCCAGGCCACCACA ATGTTCTGGTACCGCCAGTTTCCAAAGCAGTCTCTGATGCTGATGGCCACATCCAACGAGGGCTTAAG GCCACCTATGAGCAGGGCGTGGAGAAGGACAAGTTCTGATCAATCACGCCAGCCTGACCTGTCCACC CTGACAGTGACCAAGCGCCACCCAGAGGATAGCTCCTTTTACATCTGCTCCGCCAGGGCTCTAGCGGC CGGATCGAGCAGTTCTTGGCCCTGGCACACGGCTGACCGTGCTG
	509	MLLLLLLLGPGSGLGAVVSQHPSRVICKSGTSVKIECRSLDFQATTMFYRQFPKQSLMLMATSNEGSK ATYEQGVEKDKFLINHASLTLSTLTVTSAHPEDSSFYICSAQGS SGRIEQFFGPGTRLTVL
EGFR TCR4 alpha chain	510	MLTASLLRAVIASICVVSMAQKVTQAQTEISVVEKEDVTLDVYETRDTTYLFWYKQPPS GELVFLI RRNSFDEQNEISGRYSWNFQKSTSSFNFTITASQVVD SAVYFCALIRGSYQLIWG AGTKLIIKPDIQNPEPAVYQLKDPQSQDSTLCLFTDFDSQINVPKTMESGTFITDKTVLDMK AMDSKSNGAIAWSNQSFTCQDIFKETNATYPSSDVPCDATLTLEKSFETDMNLNFQNLVSMG LRILLKLVAGFNLLMTLRLWSS
EGFR TCR4 beta chain	511	MLLLLLLLGPGSGLGAVVSQHPSRVICKSGTSVKIECRSLDFQATTMFYRQFPKQSLMLMA TSNEGSKATYEQGVEKDKFLINHASLTLSTLTVTSAHPEDSSFYICSAQGS SGRIEQFFGPG TRLTVLKDLRNVTPPKVSLFEPKAEIANKQKATLVCLARGFFPDHVELSWVNGKEVHSGV STDTPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRCQVQFHGLSEEDKWPEGSPKPVTONIS AEAWGRADCGITSASYHQGVLSATILYEILLGKATLYAVLVSGVLVLMAMVKKKNS
Peptides	512	QLIMQLMPF
	513	LIMQLMPFGC
	514	MQLMPFGCLL
EGFR TCR5 alpha chain CDR1	515	DSVNN
EGFR TCR5 alpha chain CDR2	516	IPSGT
EGFR TCR5 alpha chain CDR3	517	AVMDSSYKLI
EGFR TCR5 beta chain CDR1	518	DFQATT
EGFR TCR5 beta chain CDR2	519	SNEGSKA
EGFR TCR5 beta chain CDR3	520	SALPGFSYEQY

Name	SEQ ID NO	Sequence
EGFR TCR5 alpha chain variable domains	521	ATGAAGAGGATATTGGGAGCTCTGCTGGGGCTCTTGAGTGCCAGGTTTGTGTGTGAGAGGAATACAA GTGGAGCAGAGTCCCTCCAGACCTGATTCTCCAGGAGGGAGCCAATCCACGCTGCGGTGCAATTTTCT GACTCTGTGAACAATTTGCAGTGGTTTCATCAAAACCTTGGGGACAGCTCATCAACCTGTTTACATT CCCTCAGGGACAAAACAGAATGGAAGATTAAGCGCCACGACTGTGCTACGGAACGCTACAGCTTATTG TACATTTCTCTTCCAGACCACAGACTCAGGCGTTTATTTCTGTGCTGTGATGGATAGCAGCTATAAA TTGATCTTCGGGAGTGGGACCAGACTGCTGGTCAGGCCT
	522	ATGAAGAGAATCCTGGGCGCCTGCTGGGACTGCTGTCCGCCAGGTGTGCTGCGTGCGGGCATCCAG GTGGAGCAGAGCCCACCAGACCTGATCCTGCAGGAGGGAGCCAATCCACCCTGAGATGCAATTTCTCC GATTCTGTGAACAATCTGCAGTGGTTTCACCAGAACCCTTGGGGCCAGCTGATCAATCTGTTTACATC CCATCCGGCACAAAGCAGAACGGCAGGCTGTCTGCCACCACAGTGGCCACCGAGCGGTACTCTCTGCTG TATATCTCTCTAGCCAGACCACAGACAGCGGCGGTGTAATCTGTGCCGTGATGGATTCTCTTATAAG CTGATCTTTGGCAGCGGCACCAGGCTGCTGGTGCGCCCT
	523	MKRILGALLGLLSAQVCCVRGIQVEQSPDLILQEGANSTLRNFSDSVNNLQWFHQNFWGQLINLFYI PSGTKQNGRLSATTVATERYSLLYISSSQTTDSGVYFCAVMDSSYKLI FGSGTRLLVRP
EGFR TCR5 beta chain variable domains	524	ATGCTGCTGCTTCTGCTGCTTCTGGGGCCAGGCTCCGGGCTTGGTGCTGCTGCTCAACATCCGAGC TGGGTTATCTGTAAGAGTGAACCTCTGTGAAGATCGAGTGCCGTTCCCTGGACTTTACAGGCCACAAC TATGTTTGGTATCGTCAGTTCCCGAAACAGAGTCTCATGCTGATGGCAACTTCCAATGAGGGCTCCAAG GCCACATACGAGCAAGGCGTCGAGAAGGACAAGTTTCTCATCAACCATGCAAGCCTGACCTTGTCACCT CTGACAGTGACCAAGTGCCTATCTGAAGACAGCAGCTTCTACATCTGCAGTGTCTGCCCGGATTCTCC TACGAGCAGTACTTCGGGCCGGGCACCAGGCTCACGGTCACA
	525	ATGTTATTACTGCTGCTGCTGCTGGGACCAGGCAGCGGACTGGGAGCAGTGGTGAGCCAGCACCCCTTC TGGGTCATCTGCAAGAGCGGCACATCCGTGAAGATCGAGTGTGCGTCTCTGGACTTCCAGGCCACCACA ATGTTCTGGTACAGACAGTTTCTAAGCAGTCCCTGATGCTGATGGCCACATTAACGAGGGCAGCAAG GCCACCTATGAGCAGGCGCTGGAGAAGGACAAGTTCTGATCAATCACGCCTCCCTGACCTGTCTACC CTGACAGTGACCTCCGCCCCACAGAGGATAGCTCCTTTTACATCTGCTGTGCCCTGCCAGGCTTCAGC TACGAGCAGTATTTTGGCCCCGGCACACGGCTGACAGTGACC
	526	MLLLLLLLGPGSGLGAVVSQHPSWVICKSGTSVKIECRSLDFQATTMFWYRQFPKQSLMLMATSNEGSK ATYEQGVEKDKFLINHASLTLSTLTVTSAHPEDSSFYICSAALPGFSYEQYFGPGTRLTVT
EGFR TCR5 alpha chain	527	MKRILGALLGLLSAQVCCVRGIQVEQSPDLILQEGANSTLRNFSDSVNNLQWFHQNFWGQ LINLFYIPSGTKQNGRLSATTVATERYSLLYISSSQTTDSGVYFCAVMDSSYKLI FGSGTRL LVRPDIQNPEPAVYQLKDPQRSQDSTLCLFTDFDSQINVPKTMESGTFITDKTVLDMKAMDSK SNGAIAWSNQTSFTCQDIFKETNATYPSSDVPCDATLTEKSFETDMNLNFQNL SVMGLRILL LKVAGFNLLMTLRLWSS
EGFR TCR5 beta chain	528	MLLLLLLLGPGSGLGAVVSQHPSWVICKSGTSVKIECRSLDFQATTMFWYRQFPKQSLMLMA TSNEGSKATYEQGVEKDKFLINHASLTLSTLTVTSAHPEDSSFYICSAALPGFSYEQYFGPGT RLTVTKDLRNVTPPKVSLFEPKAEIANKQKATLVCLARGFFPDHVELSWVWNGKEVHSGVS TDPQAYKESNYSYCLSSRLRVSATFWHNPRNHFRQCQVQFHGLSEEDKWPEGSPKPVTONISA EAWGRADCGITSASYHQVLSATILYEILLGKATLYAVLVSGVLVLMAMVKKNS
Peptides	529	QLIMQLMPF
	530	LIMQLMPFGC
	531	MQLMPFGCLL

EMBODIMENTS

[00417] The following embodiments are contemplated within the disclosure:

1. A nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from RAS in complex with a human MHC, wherein the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 84% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 3, 18, 33, 49, 65, 81, 97, 113, 241, 257, 273, 289, 305, 321, 337, 353, 369, 385, 401, 417, 534, 547 and 560 and/or wherein the TCR beta chain

construct comprises a complementarity determining region 3 (CDR3) having at least 84% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 6, 21, 36, 52, 68, 84, 100, 116, 244, 260, 276, 292, 308, 324, 340, 356, 372, 388, 404, 420, 537, 550, and 563.

2. A nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from RAS in complex with a human MHC, wherein the epitope from RAS comprises a region having at least 70% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 15, 30, 45, 46, 61, 62, 77, 78, 93, 94, 109, 110, 125, 126, 219-222, 253, 254, 269, 270, 285, 286, 301, 302, 317, 318, 333, 334, 349, 350, 365, 366, 381, 382, 397, 398, 413, 414, 429, 430, 544, 557 and 600.
3. A nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes at least one T cell receptor (TCR) comprising
 - a. a TCR alpha chain construct and/or
 - b. a TCR beta chain constructwherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A03:01 allele.
4. A nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes at least one T cell receptor (TCR) comprising
 - a. a TCR alpha chain construct and/or
 - b. a TCR beta chain constructwherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A02:01 allele.
5. A nucleic acid or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes at least one T cell receptor (TCR) comprising
 - a. a TCR alpha chain construct and/or
 - b. a TCR beta chain constructwherein the TCR specifically binds to an epitope from RAS in complex with a human MHC encoded by an HLA-A11:01 allele.
6. The nucleic acid of the embodiment in paragraph 3, wherein the TCR alpha chain construct comprises a variable region having at least 80%, or at least 90%, or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 71, 87, 103, 295, 311, 327, 343, 359 and 391.
7. The nucleic acid of embodiment in paragraph 4, wherein the TCR alpha chain construct comprises a variable region having at least 80%, or at least 90%, or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 9 and 24.

8. The nucleic acid of embodiment in paragraph 5, wherein the TCR alpha chain construct comprises a variable region having at least 80%, or at least 90%, or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 39, 55, 119, 247, 263, 279, 375, 407, 423, 539, 552, and 565.
9. The nucleic acid of embodiment in paragraph 3, wherein the TCR beta chain construct comprises a variable region having at least 80%, or at least 90%, or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 74, 90, 106, 298, 314, 330, 346, 362 and 394.
10. The nucleic acid of embodiment 4, wherein the TCR beta chain construct comprises a variable region having at least 80%, or at least 90%, or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 12 and 27.
11. The nucleic acid of embodiment 5, wherein the TCR beta chain construct comprises a variable region having at least 80%, or at least 90%, or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 42, 58, 122, 250, 266, 282, 378, 410, 426, 541, 554, and 567 .
12. The nucleic acid of the embodiments any one of the embodiments in paragraphs 1-3, and 6, wherein the TCR alpha chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 63, 79, 95, 287, 303, 319, 335, 351 and 383.
13. The nucleic acid of the embodiments any one of the embodiments in paragraphs 1-3, and 6, wherein the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 66, 82, 98, 290, 306, 322, 338, 354 and 386.
14. The nucleic acid of any one of the embodiments in paragraphs 1-2, 4 and 7, wherein the TCR alpha chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 1 and 16.
15. The nucleic acid of any one of the embodiments in paragraphs 1-2, 4 and 10, wherein the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 4 and 19.
16. The nucleic acid of any one of the embodiments in paragraphs 1-2, 5 and 8, wherein the TCR alpha chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 31, 47, 111, 239, 255, 271, 367, 399, 415, 532, 545 and 558.
17. The nucleic acid of any one of the embodiments in paragraphs 1-2, 5 and 11, wherein the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 34, 50, 114, 242, 258, 274, 370, 402, 418, 53, 548 and 561.

18. The nucleic acid of the embodiments any one of the embodiments in paragraphs 1-3, 6, and 12, wherein the TCR alpha chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 64, 80, 96, 288, 304, 320, 336, 352 and 384.
19. The nucleic acid of any one of the embodiments in paragraphs 1-3, 6, and 13 wherein the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 67, 83, 99, 291, 307, 323, 339, 355 and 387.
20. The nucleic acid of the embodiments any one of the embodiments in paragraphs 1-2, 4, 7 and 14, wherein the TCR alpha chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 2 and 17.
21. The nucleic acid of any one of the embodiments in paragraphs 1-2, 4, 10 and 15, wherein the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 5 and 20.
22. The nucleic acid of any one of the embodiments in paragraphs 1-2, 5, 8, and 16 wherein the TCR alpha chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 32, 48, 112, 240, 256, 272, 368, 400, 416, 533, 546, and 559.
23. The nucleic acid of any one of the embodiments in paragraphs 1-2, 5, 11 and 17 wherein the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 35, 51, 115, 243, 259, 275, 371, 403, 419, 536, 549, and 562.
24. The nucleic acid of the embodiments any one of the in paragraphs 1-3, 6, 12 and 18 wherein the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 65, 81, 97, 289, 305, 321, 337, 353 and 385.
25. The nucleic acid of any one of the embodiments in paragraphs 1-3, 6, 13 and 19 wherein the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 68, 84, 100, 292, 308, 324, 340, 356 and 388.
26. The nucleic acid of the embodiments any one of the embodiments 1-2, 4, 7 14 and 20 wherein the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 3 and 18.

27. The nucleic acid of any one of the embodiments in paragraphs 1-2, 4, 10, 15 and 21 wherein the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 6 and 21.
28. The nucleic acid of any one of the embodiments in paragraphs 1-2, 5, 8, 16 and 22 wherein the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 33, 49, 113, 241, 257, 273, 369, 401, 417, 534, 547, and 560.
29. The nucleic acid of any one of the embodiments in paragraphs 1-2, 5, 11, 17 and 23 wherein the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 36, 52, 116, 244, 260, 276, 372, 404, 420, 537, 550, and 563.
30. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
 - a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 9; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 12.
31. The nucleic acid of any one of the embodiments in paragraphs 1-5 or 30, wherein
 - a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 1,
 - ii. a CDR2 of SEQ ID NO: 2, and
 - iii. a CDR3 of SEQ ID NO: 3; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 4,
 - ii. a CDR2 of SEQ ID NO: 5, and
 - iii. a CDR3 of SEQ ID NO: 6.
32. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
 - a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 24; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 27.
33. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 32, wherein
 - a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 16,
 - ii. a CDR2 of SEQ ID NO: 17, and
 - iii. a CDR3 of SEQ ID NO: 18; and

- b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 19,
 - ii. a CDR2 of SEQ ID NO: 20, and
 - iii. a CDR3 of SEQ ID NO: 21.
- 34. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
 - a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 39; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 42.
- 35. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 34, wherein
 - a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 31,
 - ii. a CDR2 of SEQ ID NO: 32, and
 - iii. a CDR3 of SEQ ID NO: 33; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 34,
 - ii. a CDR2 of SEQ ID NO: 35, and
 - iii. a CDR3 of SEQ ID NO: 36.
- 36. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
 - a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 55; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 58.
- 37. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 36, wherein
 - a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 47,
 - ii. a CDR2 of SEQ ID NO: 48, and
 - iii. a CDR3 of SEQ ID NO: 49; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 50,
 - ii. a CDR2 of SEQ ID NO: 51, and
 - iii. a CDR3 of SEQ ID NO: 52.
- 38. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
 - a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 71; and

- b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 74.
39. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 38, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 63,
 - ii. a CDR2 of SEQ ID NO: 64, and
 - iii. a CDR3 of SEQ ID NO: 65; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 66,
 - ii. a CDR2 of SEQ ID NO: 67, and
 - iii. a CDR3 of SEQ ID NO: 68.
40. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
- a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 87; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 90.
41. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 40, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 79,
 - ii. a CDR2 of SEQ ID NO: 80, and
 - iii. a CDR3 of SEQ ID NO: 81; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 82,
 - ii. a CDR2 of SEQ ID NO: 83, and
 - iii. a CDR3 of SEQ ID NO: 84.
42. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
- a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 103; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 106.
43. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 42, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 95,
 - ii. a CDR2 of SEQ ID NO: 96, and
 - iii. a CDR3 of SEQ ID NO: 97; and
 - b. the TCR beta chain construct comprises

- i. a CDR1 of SEQ ID NO: 98,
 - ii. a CDR2 of SEQ ID NO: 99, and
 - iii. a CDR3 of SEQ ID NO: 100.
- 44. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
 - a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 119; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 122.
- 45. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 44, wherein
 - a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 111,
 - ii. a CDR2 of SEQ ID NO: 112, and
 - iii. a CDR3 of SEQ ID NO: 113; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 114,
 - ii. a CDR2 of SEQ ID NO: 115, and
 - iii. a CDR3 of SEQ ID NO: 116.
- 46. The nucleic acid of any one of the embodiments 1-5, wherein
 - a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 247; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 250.
- 47. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 46, wherein
 - a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 239,
 - ii. a CDR2 of SEQ ID NO: 240, and
 - iii. a CDR3 of SEQ ID NO: 241; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 242,
 - ii. a CDR2 of SEQ ID NO: 243, and
 - iii. a CDR3 of SEQ ID NO: 244.
- 48. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
 - a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 263; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 266.

49. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 48, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 255,
 - ii. a CDR2 of SEQ ID NO: 256, and
 - iii. a CDR3 of SEQ ID NO: 257; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 258,
 - ii. a CDR2 of SEQ ID NO: 259, and
 - iii. a CDR3 of SEQ ID NO: 260.
50. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
- a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 279; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 282.
51. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 50, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 271,
 - ii. a CDR2 of SEQ ID NO: 272, and
 - iii. a CDR3 of SEQ ID NO: 273; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 274,
 - ii. a CDR2 of SEQ ID NO: 275, and
 - iii. a CDR3 of SEQ ID NO: 276.
52. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
- a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 295; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to S or 100% sequence identity to EQ ID NO: 298.
53. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 52, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 287,
 - ii. a CDR2 of SEQ ID NO: 288, and
 - iii. a CDR3 of SEQ ID NO: 289; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 290,
 - ii. a CDR2 of SEQ ID NO: 291, and

- iii. a CDR3 of SEQ ID NO: 292.
54. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
- a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 311; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 314.
55. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 54, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 303,
 - ii. a CDR2 of SEQ ID NO: 304, and
 - iii. a CDR3 of SEQ ID NO: 305; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 306,
 - ii. a CDR2 of SEQ ID NO: 307, and
 - iii. a CDR3 of SEQ ID NO: 308.
56. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
- a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 327; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 330.
57. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 56, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 319,
 - ii. a CDR2 of SEQ ID NO: 320, and
 - iii. a CDR3 of SEQ ID NO: 321; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 322,
 - ii. a CDR2 of SEQ ID NO: 323, and
 - iii. a CDR3 of SEQ ID NO: 324.
58. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
- a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 343; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 346.
59. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 58, wherein
- a. the TCR alpha chain construct comprises

- i. a CDR1 of SEQ ID NO: 335,
 - ii. a CDR2 of SEQ ID NO: 336, and
 - iii. a CDR3 of SEQ ID NO: 337; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 338,
 - ii. a CDR2 of SEQ ID NO: 339, and
 - iii. a CDR3 of SEQ ID NO: 340.
- 60. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
 - a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 359; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 361.
- 61. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 60, wherein
 - a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 351,
 - ii. a CDR2 of SEQ ID NO: 352, and
 - iii. a CDR3 of SEQ ID NO: 353; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 354,
 - ii. a CDR2 of SEQ ID NO: 355, and
 - iii. a CDR3 of SEQ ID NO: 356.
- 62. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
 - a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 375; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 378.
- 63. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 62, wherein
 - a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 367,
 - ii. a CDR2 of SEQ ID NO: 368, and
 - iii. a CDR3 of SEQ ID NO: 369; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 370,
 - ii. a CDR2 of SEQ ID NO: 371, and
 - iii. a CDR3 of SEQ ID NO: 372.
- 64. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein

- a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 391; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 394.
65. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 64, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 383,
 - ii. a CDR2 of SEQ ID NO: 384, and
 - iii. a CDR3 of SEQ ID NO: 385; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 386,
 - ii. a CDR2 of SEQ ID NO: 387, and
 - iii. a CDR3 of SEQ ID NO: 388.
66. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
- a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 407; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 410.
67. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 66, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 399,
 - ii. a CDR2 of SEQ ID NO: 400, and
 - iii. a CDR3 of SEQ ID NO: 401; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 402,
 - ii. a CDR2 of SEQ ID NO: 403, and
 - iii. a CDR3 of SEQ ID NO: 404.
68. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
- a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 423; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 426.
69. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 68, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 415,
 - ii. a CDR2 of SEQ ID NO: 416, and

- iii. a CDR3 of SEQ ID NO: 417; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 418,
 - ii. a CDR2 of SEQ ID NO: 419, and
 - iii. a CDR3 of SEQ ID NO: 420.
70. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
- a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 542; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 543.
71. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 70, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 532,
 - ii. a CDR2 of SEQ ID NO: 533, and
 - iii. a CDR3 of SEQ ID NO: 534; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 535,
 - ii. a CDR2 of SEQ ID NO: 536, and
 - iii. a CDR3 of SEQ ID NO: 537.
72. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
- a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 555; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 556.
73. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 72, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 545,
 - ii. a CDR2 of SEQ ID NO: 546, and
 - iii. a CDR3 of SEQ ID NO: 547; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 548,
 - ii. a CDR2 of SEQ ID NO: 549, and
 - iii. a CDR3 of SEQ ID NO: 550.
74. The nucleic acid of any one of the embodiments in paragraphs 1-5, wherein
- a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 568; and

- b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 569.
75. The nucleic acid of any one of the embodiments in paragraphs 1-5 and 74, wherein
- a. the TCR alpha chain construct comprises
- i. a CDR1 of SEQ ID NO: 558,
- ii. a CDR2 of SEQ ID NO: 559, and
- iii. a CDR3 of SEQ ID NO: 560; and
- b. the TCR beta chain construct comprises
- i. a CDR1 of SEQ ID NO: 561,
- ii. a CDR2 of SEQ ID NO: 562, and
- iii. a CDR3 of SEQ ID NO: 563.
76. A nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from TMRSS2:ERG in complex with a human MHC, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to an amino acid sequence selected from SEQ ID NO: 144 and SEQ ID NO: 147.
77. A nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from TMRSS2:ERG in complex with a human MHC, wherein the epitope from TMRSS2:ERG comprises a region having at least 90% sequence identity to amino acid sequence SEQ ID NO: 156.
78. The nucleic acid of the embodiment in paragraph 76 or 77, wherein the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 150.
79. The nucleic acid of the embodiment in paragraph 76 or 77, wherein the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 153.
80. The nucleic acid of any one of the embodiments in paragraphs 76-80, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to or 100% sequence identity to SEQ ID NO: 142 or SEQ ID NO: 145 respectively.
81. The nucleic acid of any one of the embodiments in paragraphs 76-80, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to or 100% sequence identity to SEQ ID NO: 143 or SEQ ID NO: 146.
82. The nucleic acid of any one of the embodiments in paragraphs 76-81, wherein

- a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 150; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 153.
83. The nucleic acid of any one of the embodiments in paragraphs 76-82, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 142,
 - ii. a CDR2 of SEQ ID NO: 143, and
 - iii. a CDR3 of SEQ ID NO: 144; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 145,
 - ii. a CDR2 of SEQ ID NO: 146, and
 - iii. a CDR3 of SEQ ID NO: 147.
84. A nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from GATA3 in complex with a human MHC, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 129, 132, 191, 194, 206 and 209.
85. A nucleic acid encoding at least one T cell receptor (TCR) capable of specifically binding to a mutant GATA3 peptide in complex with a protein encoded by an HLA allele of a subject with cancer, wherein the TCR comprises
- a. a TCR alpha chain construct and/or
 - b. a TCR beta chain construct.
86. A recombinant nucleic acid, or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes a T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct, wherein the TCR
- a. specifically binds to a mutant GATA3 peptide in complex with an HLA-A02:01, HLA-B07:02 or HLA-B08:01 protein;
 - b. comprises an alpha chain complementarity determining region 3 (CDR3) having at least 90% sequence identity to or 100% sequence identity to SEQ ID NOs: 129, 132, 191, 194, 206 or 209; and/or
 - c. specifically binds to a mutant GATA3 peptide comprising a region with at least 70% sequence identity to or 100% sequence identity to SEQ ID NO: 141, 203 or 218.
87. A nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from GATA3 in

complex with a human MHC, wherein the epitope from GATA3 comprises a region having at least 90% sequence identity to or 100% sequence identity to amino acid sequence SEQ ID NO: 141, 203 or 218.

88. The nucleic acid of any one of the embodiments in paragraphs 84-87, wherein the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 135, 197 or 212.
89. The nucleic acid of any one of the embodiments in paragraphs 84-87, wherein the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 138, 200 or 215.
90. The nucleic acid of any one of the embodiments in paragraphs 84-87, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 127, 130, 189, 192, 204 and 207.
91. The nucleic acid of any one of the embodiments in paragraphs 84-87, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 128, 131, 190, 193, 205 and 208.
92. The nucleic acid of any one of the embodiments in paragraphs 84-87, wherein
 - a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 135; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 138.
93. The nucleic acid of embodiment in paragraph 86, wherein
 - a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 127,
 - ii. a CDR2 of SEQ ID NO: 128, and
 - iii. a CDR3 of SEQ ID NO: 129; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 130,
 - ii. a CDR2 of SEQ ID NO: 131, and
 - iii. a CDR3 of SEQ ID NO: 132.
94. The nucleic acid of any one of the embodiments in paragraphs 84-87, wherein
 - a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 197; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 200.

95. The nucleic acid of the embodiment in paragraph 94, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 189,
 - ii. a CDR2 of SEQ ID NO: 190, and
 - iii. a CDR3 of SEQ ID NO: 191; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 192,
 - ii. a CDR2 of SEQ ID NO: 193, and
 - iii. a CDR3 of SEQ ID NO: 194.
96. The nucleic acid of any one of the embodiments in paragraphs 78-85, wherein
- a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 212; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 215.
97. The nucleic acid of the embodiment in paragraph 90, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 204,
 - ii. a CDR2 of SEQ ID NO: 205, and
 - iii. a CDR3 of SEQ ID NO: 206; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 207,
 - ii. a CDR2 of SEQ ID NO: 208, and
 - iii. a CDR3 of SEQ ID NO: 209.
98. A nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from BTK in complex with a human MHC, wherein the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NO: 161 and SEQ ID NO: 176, or wherein the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NO: 164 and SEQ ID NO: 179.
99. A nucleic acid encoding at least one T cell receptor (TCR) capable of specifically binding to a mutant BTK peptide in complex with a protein encoded by an HLA allele of a subject with cancer, wherein the TCR comprises
- (a) a TCR alpha chain construct and/or
 - (b) a TCR beta chain construct.

100. A recombinant nucleic acid, or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes a T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct, wherein the TCR
- specifically binds to a mutant BTK peptide in complex with an HLA-A02:01 protein;
 - comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to or 100% sequence identity to SEQ ID NO: 161, 164, 176, or 179; and/or
 - specifically binds to a mutant BTK peptide comprising a region with at least 70% sequence identity to or 100% sequence identity to SEQ ID NO: 173 or 188.
101. A nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from BTK in complex with a human MHC, wherein the epitope from BTK comprises a region having at least 90% sequence identity to or 100% sequence identity to amino acid sequence SEQ ID NO: 173 or 188.
102. The nucleic acid of any one of the embodiments in paragraphs 98-101, wherein the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 167 or 182.
103. The nucleic acid of any one of the embodiments in paragraphs 98-102, wherein the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 170 or 185.
104. The nucleic acid of any one of the embodiments in paragraphs 98-103, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 159, 162, 174, and 177.
105. The nucleic acid of any one of the embodiments in paragraphs 98-104, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 160, 163, 175 and 178.
106. The nucleic acid of any one of the embodiments in paragraphs 98-105, wherein
- the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 167 or 182; and
 - the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 170 or 185.
107. The nucleic acid of any one of the embodiments in paragraphs 98-106, wherein
- the TCR alpha chain construct comprises
 - a CDR1 of SEQ ID NO: 159 or 174,
 - a CDR2 of SEQ ID NO: 160 or 175, and
 - a CDR3 of SEQ ID NO: 161 or 176; and

- b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 162 or 177,
 - ii. a CDR2 of SEQ ID NO: 163 or 178, and
 - iii. a CDR3 of SEQ ID NO: 164 or 179.
- 108. A nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from EGFR in complex with a human MHC, wherein the TCR alpha chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NO: 449, SEQ ID NO: 466, SEQ ID NO: 483, SEQ ID NO: 500, and SEQ ID NO: 517, or wherein the TCR beta chain construct comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NO: 452, SEQ ID NO: 469, SEQ ID NO: 486, SEQ ID NO: 503, and SEQ ID NO: 520.
- 109. A nucleic acid encoding at least one T cell receptor (TCR) capable of specifically binding to a mutant EGFR peptide in complex with a protein encoded by an HLA allele of a subject with cancer, wherein the TCR comprises
 - a. a TCR alpha chain construct and/or
 - b. a TCR beta chain construct.
- 110. A recombinant nucleic acid, or a cell comprising a recombinant nucleic acid, wherein the nucleic acid encodes a T cell receptor (TCR) comprising a TCR alpha chain construct and/or a TCR beta chain construct, wherein the TCR
 - a. specifically binds to a mutant EGFR peptide in complex with an HLA-A02:01 protein;
 - b. comprises a complementarity determining region 3 (CDR3) having at least 90% sequence identity to or 100% sequence identity to SEQ ID NO: 449, 466, 483, 500, 517, 452, 469, 486, 503, or 520; and/or
 - c. specifically binds to a mutant EGFR peptide comprising a region with at least 70% sequence identity to or 100% sequence identity to SEQ ID NO: 461, 462, 463, 478, 479, 480, 495, 496, 497, 512, 513, 514, 529, 530 or 531.
- 111. A nucleic acid encoding at least one T cell receptor (TCR) comprising a TCR alpha chain construct and/or TCR beta chain construct capable of specifically binding to an epitope from EGFR in complex with a human MHC, wherein the epitope from EGFR comprises a region having at least 90% sequence identity to or 100% sequence identity to amino acid sequence SEQ ID NO: 461, 462, 463, 478, 479, 480, 495, 496, 497, 512, 513, 514, 529, 530 or 531.
- 112. The nucleic acid of any one of the embodiments in paragraphs 108-111, wherein the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 455, 472, 489, 506 or 526.

113. The nucleic acid of any one of the embodiments in paragraphs 108-112, wherein the TCR beta chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 458, 475, 492, 509, or 526.
114. The nucleic acid of any one of the embodiments in paragraphs 108-113, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 1 (CDR1) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 447, 464, 481, 498, 515, 450, 467, 484, 501, and 518.
115. The nucleic acid of any one of the embodiments in paragraphs 108-114, wherein the TCR alpha chain construct and/or the TCR beta chain construct comprises a complementarity determining region 2 (CDR2) having at least 90% sequence identity to or 100% sequence identity to an amino acid sequence selected from SEQ ID NOs: 448, 465, 482, 499, 516, 451, 468, 485, 502, and 519.
116. The nucleic acid of any one of the embodiments in paragraphs 108-115, wherein
- a. the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to or 100% sequence identity to SEQ ID NO: 455, 472, 489, 506, or 523; and
 - b. the TCR beta chain construct comprises a variable region having at least 80% sequence identity to SEQ ID NO: 458, 475, 492, 509 or 526.
117. The nucleic acid of any one of the embodiments in paragraphs 108-116, wherein
- a. the TCR alpha chain construct comprises
 - i. a CDR1 of SEQ ID NO: 447, 464, 481, 498 or 515,
 - ii. a CDR2 of SEQ ID NO: 448, 465, 482, 499 or 516, and
 - iii. a CDR3 of SEQ ID NO: 449, 466, 483, 500 or 517; and
 - b. the TCR beta chain construct comprises
 - i. a CDR1 of SEQ ID NO: 450, 467, 484, 501 or 518,
 - ii. a CDR2 of SEQ ID NO: 451, 468, 485, 502, or 519, and
 - iii. a CDR3 of SEQ ID NO: 452, 469, 486, 503, or 520.
118. The nucleic acid of any one of the embodiments in paragraphs 1-117, wherein the epitope comprises a mutation selected from the group consisting of a point mutation, a splice-site mutation, a frameshift mutation, a read-through mutation, a resistance mutation, a gene fusion mutation and any combination thereof
119. The nucleic acid of any one of the embodiments 1-69, wherein the human MHC is encoded by either HLA-A02:01 allele, or HLA-A03:01 allele or HLA-A11:01 allele.
120. The nucleic acid of any one of the embodiments in paragraphs 1-69, wherein the epitope comprises a point mutation.
121. The nucleic acid of the embodiment in paragraph 120, wherein the point mutation is a G12V mutation.

122. The nucleic acid of the embodiment in paragraph 120, wherein the point mutation is a G12C mutation.
123. The nucleic acid of the embodiment in paragraph 120, wherein the point mutation is a G12D mutation.
124. The nucleic acid of any one of the embodiments in paragraphs 76-83, wherein the human MHC is encoded by HLA-A02:01 allele.
125. The nucleic acid of any one of the embodiments in paragraphs 76-83 and 124, wherein the epitope comprises a gene fusion mutation.
126. The nucleic acid of any one of the embodiments in paragraphs 84-97, wherein the human MHC is encoded by HLA-A02:01, HLA-B07:02 or HLA-B08:01 allele.
127. The nucleic acid of any one of the embodiments in paragraphs 84-97 and 126, wherein the epitope comprises a frameshift mutation.
128. The nucleic acid of any one of the embodiments in paragraphs 98-107, wherein the human MHC is encoded by HLA-A02:01 allele.
129. The nucleic acid of any one of the embodiments in paragraphs 98-107 and 128, wherein the epitope comprises a point mutation.
130. The nucleic acid of the embodiment in paragraph 129, wherein the point mutation is C481S mutation.
131. The nucleic acid of any one of the embodiments in paragraphs 108-117, wherein the human MHC is encoded by HLA-A02:01 allele.
132. The nucleic acid of any one of the embodiments in paragraphs 108-117, wherein the epitope comprises a point mutation.
133. The nucleic acid of embodiment in paragraph 132, wherein the point mutation is T790M.
134. The nucleic acid of any one of the embodiments in paragraphs 1-130, wherein the epitope has a length of at least 8 amino acids.
135. The nucleic acid of any one of the embodiments in paragraphs 1-134, wherein the epitope has a length of at least 16 amino acids.
136. The nucleic acid of any one of the embodiments 1-135, wherein the epitope has a length of from 8-25 amino acids.
137. The nucleic acid of any one of the embodiments 1-136, wherein the epitope has a length of from 8-12 amino acids.
138. The nucleic acid of any one of the embodiments in paragraphs 1-136, wherein the epitope has a length of from 16-25 amino acids.
139. The nucleic acid of any one of the embodiments in paragraphs 1-136, wherein the epitope has a length of 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, or 25 amino acids.
140. The nucleic acid of any one of the embodiments in paragraphs 1-139, wherein the epitope binds to the human MHC with a greater affinity than a corresponding wild-type epitope.

141. The nucleic acid of any one of the embodiments in paragraphs 1-140, wherein the epitope binds to the human MHC with a KD or an IC50 less than 500 nM, 250 nM, 150 nM, 100 nM, 50 nM, 25 nM or 10 nM.
142. The nucleic acid of any one of the embodiments 108-141, wherein the mutation is not present in non-cancer cells of a subject.
143. The nucleic acid of any one of the embodiments in paragraphs 1-142, wherein the epitope is encoded by a gene or an expressed gene of a subject's cancer cells.
144. The nucleic acid of any one of the embodiments in paragraphs 1-143, wherein the TCR binds to a MHC-peptide complex with a KD or an IC50 of less than 500 nM, 250 nM, 150 nM, 100 nM, 50 nM, 25 nM or 10 nM.
145. The nucleic acid of any one of the embodiments in paragraphs 1-144, wherein the nucleic acid is operably linked to a promoter.
146. A vector comprising the nucleic acid of any one of the embodiments in paragraphs 1-145.
147. The vector of the embodiment in paragraph 146, wherein the vector is a self-amplifying RNA replicon, plasmid, phage, transposon, cosmid, virus, or virion.
148. The vector of the embodiment in paragraphs 146 or 147, wherein the vector is a viral vector.
149. The vector of the embodiment in paragraph 148, wherein the vector is derived from a retrovirus, lentivirus, adenovirus, adeno-associated virus, herpes virus, pox virus, alpha virus, vaccinia virus, hepatitis B virus, human papillomavirus or a pseudotype thereof.
150. The vector of the embodiment in paragraphs 146 or 147, wherein the vector is a non-viral vector.
151. The vector of the embodiment in paragraph 150, wherein the non-viral vector is a nanoparticle, a cationic lipid, a cationic polymer, a metallic nanopolymer, a nanorod, a liposome, a micelle, a microbubble, a cell-penetrating peptide, or a liposphere.
152. A protein encoded by the nucleic acid of any one of the embodiments in paragraphs 1-145.
153. A cell comprising the nucleic acid of any one embodiment in paragraphs 1-149, the vector of any one of the embodiments 144-149, or the protein of embodiment 146.
154. The cell of the embodiment 153, wherein the cell is a CD4+ T cell.
155. The cell of the embodiment 153, wherein the cell is a CD8+ T cell.
156. The cell of the embodiment 153, wherein the cell is an autologous cell.
157. The cell of the embodiment 153, wherein the cell is an allogeneic cell.
158. The cell of the embodiment 153, wherein the cell is a natural killer cell, a B cell, or an immortalized cell line.
159. The cell of any one of the embodiments in paragraphs 153-156, wherein the cell is a human cell.
160. A pharmaceutical composition comprising the nucleic acid of any one of the embodiments in paragraphs 1-143, the vector of any one of the embodiments in paragraphs 146-151, the protein of

- embodiment in paragraph 152, or the cell of any one of the embodiments in paragraphs 153-159; and a pharmaceutically acceptable excipient or diluent.
161. The pharmaceutical composition of the embodiment in paragraphs 160, further comprising an immunomodulatory agent or an adjuvant.
162. The pharmaceutical composition of the embodiment in paragraph 161, wherein the immunomodulatory agent is a cytokine.
163. The pharmaceutical composition of any one of the embodiments in paragraphs 160-162 wherein the adjuvant is poly I:C.
164. The pharmaceutical composition of any one of the embodiments in paragraphs 160-163, for use in treating an immune disease or cancer.
165. Use of the pharmaceutical composition of any one of the embodiments in paragraphs 160-164, for treating an immune disease or cancer.
166. Use of the nucleic acid of any one of the embodiments in paragraphs 1-145, the vector of any one of the embodiments in paragraphs 146-151, the protein of embodiment in paragraph 152, or the cell of any one of the embodiments 153-159, for manufacture of a medicament for treating an immune disease or cancer.
167. The use of the embodiment in paragraph 166, wherein the medicament is an adoptive T cell therapy or a TCR gene therapy.
168. A method of treating a subject with a disease or condition, comprising administering to the subject the pharmaceutical composition of any one of the embodiments in paragraphs 160-164.
169. A method of treating a subject with cancer comprising administering to the subject the pharmaceutical composition of any one of the embodiments in paragraphs 160-164.
170. A method of treating a subject with cancer comprising administering to the subject the pharmaceutical composition of any one of the embodiments in paragraphs 160-164; wherein the subject is identified as expressing or expresses a protein encoded by an HLA-A02:01 allele, an HLA-B07:02, an HLA-B08:01, an HLA-A03:01 allele, an HLA-A11:01 allele, an HLA-A03:02 allele, an HLA-A30:01 allele, an HLA-A31:01 allele, an HLA-A33:01 allele, an HLA-A33:03 allele, an HLA-A68:01 allele, or an HLA-A74:01 allele of the subject's genome.
171. A method of treating a subject with cancer comprising administering a TCR or T cell expressing the TCR to the subject, wherein the TCR specifically binds to a mutant RAS peptide in complex with a protein encoded by an HLA-A02:01, an HLA-A03:01 allele, an HLA-A11:01 allele, an HLA-A03:02 allele, an HLA-A30:01 allele, an HLA-A31:01 allele, an HLA-A33:01 allele, an HLA-A33:03 allele, an HLA-A68:01 allele, or an HLA-A74:01; wherein the subject is identified as expressing or expresses a protein encoded by an HLA-A03:01 allele, an HLA-A11:01 allele, an HLA-A03:02 allele, an HLA-A30:01 allele, an HLA-A31:01 allele, an HLA-A33:01 allele, an HLA-A33:03 allele, an HLA-A68:01 allele, or an HLA-A74:01 allele, wherein the subject expresses the HLA allele.

172. A method of treating a subject with cancer comprising administering to the subject the pharmaceutical composition of any one of the embodiments in paragraphs 154-158; wherein the TCR binds to a mutant RAS peptide comprising a mutation at G12 in complex with an HLA-A02:01, an HLA-A03:01 allele, an HLA-A11:01 allele, an HLA-A03:02 allele, an HLA-A30:01 allele, an HLA-A31:01 allele, an HLA-A33:01 allele, an HLA-A33:03 allele, an HLA-A68:01 allele, or an HLA-A74:01; wherein the subject is identified as expressing a protein encoded by an HLA-A03:01 allele, an HLA-A11:01 allele, an HLA-A03:02 allele, an HLA-A30:01 allele, an HLA-A31:01 allele, an HLA-A33:01 allele, an HLA-A33:03 allele, an HLA-A68:01 allele, or an HLA-A74:01 allele.
173. A method of treating a subject with cancer comprising administering to the subject a composition comprising a T cell receptor (TCR) specific for a mutant GATA3 peptide in complex with an HLA protein; wherein the mutant GATA3 peptide comprises at least one mutant amino acid and is fragment of at least 8 contiguous amino acids of a mutant GATA3 protein arising from a mutation in a GATA3 gene of a cancer cell; wherein the mutant GATA3 peptide binds to a protein encoded by an HLA-A02:01, HLA-B07:02 or HLA-B08:01 allele.
174. A method of treating a subject with cancer comprising administering to the subject a composition comprising a T cell receptor (TCR) specific for a mutant GATA3 peptide in complex with an HLA protein; wherein the mutant GATA3 peptide comprises one or more mutant GATA3 amino acids encoded by a GATA3 neoORF sequence, wherein the mutant GATA3 peptide binds to a protein encoded by an HLA-A02:01, HLA-B07:02 or HLA-B08:01 allele.
175. A method of treating a subject with cancer comprising administering a TCR or T cell expressing the TCR to the subject; wherein the TCR specifically binds to a mutant GATA3 peptide in complex with a protein encoded by an HLA-A02:01, HLA-B07:02 or HLA-B08:01 allele; wherein the subject is identified as expressing or expresses a protein encoded by an HLA-A02:01, HLA-B07:02 or HLA-B08:01 allele.
176. A method of treating a subject with cancer comprising administering to the subject a composition comprising a T cell receptor (TCR) specific for a mutant TMPRSS2:ERG peptide in complex with an HLA protein; wherein the mutant TMPRSS2:ERG peptide comprises at least one mutant amino acid and is a fragment of a TMPRSS2:ERG gene fusion mutation; wherein the mutant TMPRSS2:ERG peptide binds to a protein encoded by an HLA-A02:01 allele.
177. A method of treating a subject with cancer comprising administering to the subject a composition comprising a T cell receptor (TCR) specific for a mutant BTK peptide in complex with an HLA protein; wherein the mutant BTK peptide comprises at least one mutant amino acid; wherein the mutant BTK peptide binds to a protein encoded by an HLA-A02:01 allele.
178. A method of treating a subject with cancer comprising administering to the subject a composition comprising a T cell receptor (TCR) specific for a mutant BTK peptide in complex with an HLA

- protein; wherein the mutant BTK peptide comprises a resistance mutation or a point mutation; wherein the mutant BTK peptide binds to a protein encoded by an HLA-A02:01 allele.
179. A method of treating a subject with cancer comprising administering to the subject a composition comprising a T cell receptor (TCR) specific for a mutant BTK peptide in complex with an HLA protein; wherein the mutant BTK peptide comprises a C481S mutation; wherein the mutant BTK peptide binds to a protein encoded by an HLA-A02:01 allele.
180. A method of treating a subject with cancer comprising administering to the subject a composition comprising a T cell receptor (TCR) or a T cell expressing the TCR to the subject, wherein the TCR specifically binds to a mutant EGFR peptide in complex with a protein encoded by an HLA-A02:01; wherein the mutant EGFR peptide comprises a resistance mutation or a point mutation, wherein the subject is identified as expressing or expresses a protein encoded by an HLA-A02:01 allele.
181. The method of embodiment in paragraph 178, wherein the mutant EGFR peptide comprises a T790M mutation.
182. A method of preventing resistance to a cancer therapy, the method comprising administering to a subject in need thereof the pharmaceutical composition of any one of the embodiments in paragraph 160-164.
183. A method of inducing an immune response, the method comprising administering to a subject in need thereof the pharmaceutical composition of any one of the embodiments in paragraphs 160-164.
184. A method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising identifying the subject as a subject that expresses a protein encoded by an HLA-A02:01 allele, an HLA-A03:01 allele, an HLA-A11:01 allele, an HLA-A03:02 allele, an HLA-A30:01 allele, an HLA-A31:01 allele, an HLA-A33:01 allele, an HLA-A33:03 allele, an HLA-A68:01 allele, or an HLA-A74:01 allele, wherein the therapeutic is the pharmaceutical composition of any one of the embodiments in paragraphs 160-164.
185. A method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising identifying the subject as one that expresses a protein encoded by an HLA-A02:01, HLA-B07:02 or HLA-B08:01 allele, wherein the therapeutic comprises a T cell receptor (TCR) specific for a mutant GATA3 peptide in complex with an HLA protein; wherein the mutant GATA3 peptide comprises at least one mutant amino acid and is fragment of at least 8 contiguous amino acids of a mutant GATA3 protein arising from a mutation in a GATA3 gene of a cancer cell; wherein the mutant GATA3 peptide binds to a protein encoded by an HLA-A02:01, HLA-B07:02 or HLA-B08:01 allele.
186. A method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising identifying the subject as one that expresses a protein encoded by an HLA-A03:01 allele, an HLA-A11:01 allele, an HLA-A03:02 allele, an HLA-A30:01 allele, an HLA-A31:01 allele, an HLA-A33:01 allele, an HLA-A33:03 allele, an HLA-A68:01 allele, or an HLA-A74:01 allele, wherein the therapeutic comprises a T cell receptor (TCR) specific for a mutant RAS peptide comprising a

mutation at G12 in complex with an HLA protein; wherein the mutant RAS peptide binds to a protein encoded by an HLA-A03:01 allele, an HLA-A11:01 allele, an HLA-A03:02 allele, an HLA-A30:01 allele, an HLA-A31:01 allele, an HLA-A33:01 allele, an HLA-A33:03 allele, an HLA-A68:01 allele, or an HLA-A74:01 allele.

187. A method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising identifying the subject as one that expresses a protein encoded by an HLA-A02:01 allele, wherein the therapeutic comprises a T cell receptor (TCR) specific for a mutant TMPRSS2:ERG peptide in complex with an HLA protein; wherein the mutant TMPRSS2:ERG peptide comprises at least one mutant amino acid and is a fragment of a TMPRSS2:ERG gene fusion mutation; wherein the mutant TMPRSS2:ERG peptide binds to a protein encoded by an HLA-A02:01 allele.
188. A method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising identifying the subject as one that expresses a protein encoded by an HLA-A02:01 allele, wherein the therapeutic comprises a T cell receptor (TCR) specific for a mutant BTK peptide in complex with an HLA protein; wherein the mutant BTK peptide comprises at least one mutant amino acid; wherein the mutant BTK peptide binds to a protein encoded by an HLA-A02:01 allele.
189. A method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising identifying the subject as one that expresses a protein encoded by an HLA-A02:01 allele, wherein the therapeutic a T cell receptor (TCR) specific for a mutant BTK peptide in complex with an HLA protein; wherein the mutant BTK peptide comprises a resistance mutation or a point mutation; wherein the mutant BTK peptide binds to a protein encoded by an HLA-A02:01 allele.
190. A method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising identifying the subject as one that expresses a protein encoded by an HLA-A02:01 allele, wherein the therapeutic a T cell receptor (TCR) specific for a mutant BTK peptide in complex with an HLA protein; wherein the mutant BTK peptide comprises a C481S mutation; wherein the mutant BTK peptide binds to a protein encoded by an HLA-A02:01 allele.
191. A method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising identifying the subject as one that expresses a protein encoded by an HLA-A02:01 allele, wherein the therapeutic comprises a T cell receptor (TCR) specific for a mutant EGFR peptide in complex with an HLA protein; wherein the mutant EGFR peptide comprises at least one mutant amino acid T790M; wherein the mutant EGFR peptide binds to a protein encoded by an HLA-A02:01 allele.
192. The method of any one of the embodiments in paragraphs 162-185, wherein the cancer is selected from the group consisting of breast cancer, lung cancer, non-small cell lung cancer, pancreatic cancer, colorectal cancer, uterine cancer, melanoma, ovarian cancer, prostate cancer, endometrial cancer, chronic lymphocytic leukemia (CLL) and liver cancer.
193. The method of any one of the embodiments in paragraphs 162-185, wherein the subject has a breast cancer that is resistant to anti-estrogen therapy, is an MSI breast cancer, is a metastatic breast cancer,

is a Her2 negative breast cancer, is a Her2 positive breast cancer, is an ER negative breast cancer, is an ER positive breast cancer is a recurrent breast cancer, is a metastatic breast cancer, or any combination thereof.

194. The method of the embodiment 193, wherein the breast cancer expresses an estrogen receptor with a mutation.
195. The method of any one of the embodiments in paragraphs 169-191, wherein the subject has a breast cancer that is resistant to anti-estrogen therapy.
196. The method of the embodiment in paragraph 195, wherein the breast cancer expresses an estrogen receptor with a mutation.
197. The method of any one of the embodiments in paragraphs 169-196, wherein the subject has a CLL that is resistant to ibrutinib therapy.
198. The method of the embodiment in paragraph 197, wherein the CLL expresses a Bruton tyrosine kinase (BTK) with a mutation, such as a C481S mutation.
199. The method of any one of the embodiments in paragraph 169-197, wherein the subject has a lung cancer that is resistant to a tyrosine kinase inhibitor.
200. The method of the embodiment in paragraphs 199, wherein the lung cancer expresses an epidermal growth factor receptor (EGFR) with a mutation, such as a T790M, L792F, or C797S mutation.
201. The method of any one of the embodiments in paragraphs 169-200, further comprising administering at least one additional therapeutic agent or modality.
202. The method of any one of the embodiments in paragraphs 168-200, wherein an immune response is elicited in the subject.
203. The method of the embodiment in paragraph 200, wherein the immune response is a humoral response.
204. The method of the embodiment in paragraph 200, wherein the immune response is a cytotoxic T cell response.
205. The method of any one of the embodiments in paragraphs 168-204, further comprising administering at least one additional therapeutic agent or modality.
206. The method of the embodiment in paragraphs 205, wherein the at least one additional therapeutic agent or modality is surgery, a checkpoint inhibitor, an antibody or fragment thereof, a chemotherapeutic agent, radiation, a vaccine, a small molecule, a T cell, a vector, and APC, a polynucleotide, an oncolytic virus or any combination thereof.
207. The method of the embodiment in paragraph 206, wherein the at least one additional therapeutic agent is an anti-PD-1 agent and anti-PD-L1 agent, an anti-CTLA-4 agent, or an anti-CD40 agent.
208. The method of the embodiment in paragraph 206 or 207, wherein the additional therapeutic agent is administered before, simultaneously, or after administering the pharmaceutical composition of any one of the embodiments 160-164.

209. The method of any one of the embodiments in paragraphs 169-183, or any one of the embodiments in paragraphs 201-208 wherein administering comprises administering subcutaneously or intravenously.
210. The method of any one of the embodiments in paragraphs 169-209, wherein the subject is a subject that has had disease progression following endocrine therapy in combination with a CDK 4/6 inhibitor.
211. A method comprising:
- a. identifying neoantigen-specific T cells from a sample comprising a population of T cells;
 - b. identifying one or more peptides of a peptide-MHC complex that are presented by an antigen presenting cell (APC);
 - c. identifying a variable sequence of a T cell receptor (TCR) from the neoantigen-specific T cells;
 - d. expressing a recombinant TCR comprising the variable sequence of the TCR identified in a TCR cell; and
 - e. performing a functional assay, wherein the functional assay comprises contacting the TCR cell to a peptide-MHC complex comprising a peptide of the one or more peptides identified.
212. The method of the embodiment in paragraph 211, wherein the method comprises obtaining the sample comprising the population of cells comprising the neoantigen-specific T cells.
213. The method of the embodiment in paragraph 212, wherein obtaining the sample comprises obtaining a T cell sample from a healthy subject or from a subject with cancer.
214. The method of the embodiment in paragraph 213, wherein the T cell sample is from a healthy donor.
215. The method of the embodiment in paragraph 213 or 214, wherein the T cell sample is a peripheral blood mononuclear cell (PBMC) sample.
216. The method of any one of the embodiments in paragraphs 211-215, wherein identifying neoantigen-specific T cells comprises contacting the population of T cells to at least one peptide-MHC multimer complex comprising a neoantigen peptide.
217. The method of any one of the embodiments in paragraphs 205-209, wherein identifying neoantigen-specific T cells comprises contacting the population of T cells to a peptide-MHC complex comprising a neoantigen peptide.
218. The method of the embodiment in paragraph 211, wherein identifying neoantigen-specific T cells comprises contacting the population of T cells to an APC comprising the peptide-MHC complex.
219. The method of any one of the embodiments in paragraphs 216-218, wherein identifying neoantigen-specific T cells further comprises isolating T cells of the T cell population specific to the peptide-MHC complex.
220. The method of any one of the embodiments 216-218, wherein identifying neoantigen-specific T cells further comprises identifying or predicting T cells of the of the T cell population specific to the peptide-MHC complex based on TCR clonality.

- 221. The method of the embodiment in paragraphs 220, wherein identifying a variable sequence of a TCR from the neoantigen-specific T cells is performed before identifying neoantigen-specific T cells.
- 222. The method of any one of the embodiments in paragraphs 211-221, wherein identifying a variable sequence of a TCR from the neoantigen-specific T cells comprises sequencing DNA, RNA, or amplified products thereof from one or more neoantigen-specific T cells that encode the variable sequence.
- 223. The method of any one of the embodiments in paragraphs 211-222, wherein identifying a variable sequence of a TCR from the neoantigen-specific T cells comprises sequencing DNA, RNA, or amplified products thereof from a single neoantigen-specific T cell that encodes the variable sequence.
- 224. The method of any one of the embodiments in paragraphs 215-223, wherein identifying a variable sequence of a TCR from the neoantigen-specific T cells comprises sequencing barcoded DNA or barcoded RNA, or amplified products thereof, from one or more neoantigen-specific T cells that encode the variable sequence.
- 225. The method of any one of the embodiments in paragraphs 221-224, wherein identifying a variable sequence of a TCR from the neoantigen-specific T cells comprises pairing a TCR-alpha chain with a TCR-beta chain.
- 226. The method of any one of the embodiments in paragraphs 211-225, wherein expressing a recombinant TCR comprises expressing the variable sequence identified from a polynucleotide comprising a sequence encoding the variable sequence identified.
- 227. The method of the embodiment in paragraph 226, wherein the polynucleotide is a vector.
- 228. The method of the embodiment in paragraph 227, wherein the vector is a viral vector.
- 229. The method of the embodiment in paragraph 228, wherein the viral vector is a lentiviral vector.
- 230. The method of any one of the embodiments in paragraphs 226-229, wherein expressing a recombinant TCR comprises transducing or transfecting the polynucleotide into cells.
- 231. The method of embodiment in paragraph 230, wherein the cells are a T cell line or healthy donor PMBCs.
- 232. The method of any one of the embodiments in paragraphs 211-231, wherein identifying one or more peptides of a peptide-MHC complex that are presented by an APC comprises expressing the one or more peptides in cells.
- 233. The method of any one of the embodiments in paragraphs 211-231, wherein identifying one or more peptides of a peptide-MHC complex that are presented by an APC comprises loading the one or more peptides onto MHCs of cells.
- 234. The method of any one of the embodiments in paragraphs 211-233, wherein identifying one or more peptides of a peptide-MHC complex that are presented by an APC comprises eluting or isolating a peptide of the one or more peptides from a peptide MHC complex.

235. The method of any one of the embodiments in paragraphs 211-234, wherein identifying one or more peptides of a peptide-MHC complex that are presented by an APC comprises performing mass spectrometry on a peptide of the one or more peptides that was isolated or eluted from a peptide-MHC complex.
236. The method of any one of the embodiments in paragraphs 211-235, wherein performing a functional assay comprises determining expression of one or more cell markers.
237. The method of embodiment in paragraph 236, the one or more cell markers comprise TNF- α , IFN- γ , LAMP-1, 4-1BB, IL-2, IL-17A, Granzyme B, PD-1, CD25, CD69, TIM3, LAG3, CTLA-4, CD62L, CD45RA, CD45RO, FoxP3, or any combination thereof.

CLAIMS

What is claimed is:

1. A recombinant nucleic acid encoding a T cell receptor (TCR) comprising a TCR beta chain construct comprising a complementarity determining region 3 (CDR3) having an amino acid sequence set forth in SEQ ID NO: 52.
2. The recombinant nucleic acid encoding a T cell receptor (TCR) of claim 1, wherein the TCR beta chain construct further comprises a complementarity determining region 1 (CDR1) and a complementarity determining region 2 (CDR2), wherein the CDR1 has an amino acid sequence set forth in SEQ ID NO: 50; and the CDR2 has an amino acid sequence set forth in SEQ ID NO: 51.
3. The recombinant nucleic acid encoding a T cell receptor (TCR) of claim 1 or claim 2, wherein the TCR beta chain construct comprises a variable region having at least 80% sequence identity to an amino acid sequence set forth in SEQ ID NO: 58.
4. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the preceding claims, wherein, the TCR beta chain construct comprises a variable region having at least 90% sequence identity to an amino acid sequence set forth in SEQ ID NO: 58.
5. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the preceding claims, wherein, the TCR beta chain construct comprises a variable region having at least 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 58.
6. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the preceding claims, wherein, the TCR beta chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 58.
7. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the preceding claims, further comprising a TCR alpha chain construct having a CDR1, a CDR2, and a CDR3, wherein, the CDR1 has an amino acid sequence set forth in SEQ ID NO: 47;
the CDR2 has an amino acid sequence set forth in SEQ ID NO: 48; and,
the CDR has an amino acid sequence set forth in SEQ ID NO: 49.
8. The recombinant nucleic acid of any one of the preceding claims, comprising:
(a) a sequence having at least 80% sequence identity with SEQ ID NOs: 56 or 57, wherein the sequence comprises a sequence encoding at least SEQ ID NO: 52; and
(b) a sequence having at least 80% sequence identity with SEQ ID NOs: 53 or 54, wherein the sequence comprises a sequence encoding at least SEQ ID NO: 49.
9. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the preceding claims, wherein the TCR alpha chain construct comprises a variable region having at least 80% sequence identity to an amino acid sequence set forth in SEQ ID NO: 55.

10. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the preceding claims, wherein, the TCR alpha chain construct comprises a variable region having at least 90% sequence identity to an amino acid sequence set forth in SEQ ID NO: 55.
11. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the preceding claims, wherein, the TCR alpha chain construct comprises a variable region having at least 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 55.
12. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the preceding claims, wherein, the TCR alpha chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 55.
13. The recombinant nucleic acid encoding a TCR of claim 1, wherein the TCR comprises:
 - (a) a beta chain having an amino acid sequence set forth in SEQ ID NO: 60, or an amino acid sequence that is at least 80% identical to SEQ ID NO: 60.
 - (b) an alpha chain having an amino acid sequence set forth in SEQ ID NO: 59, or an amino acid sequence that is at least 80% identical to SEQ ID NO: 59.
14. The recombinant nucleic acid encoding a TCR of any one of the preceding claims, wherein the TCR binds to an epitope from human RAS comprising a mutation G12V.
15. A recombinant nucleic acid encoding a TCR comprising a TCR beta chain construct and a TCR alpha chain construct, the TCR beta chain construct comprising a complementarity determining region 3 (CDR3) having an amino acid sequence selected from SEQ ID NO: 537 and 563.
16. The recombinant nucleic acid of claim 15, wherein the TCR beta chain construct comprising a CDR3 having an amino acid sequence of SEQ ID NO: 537, comprises a variable region having at least 80%, 90%, 95%, 96%, 97%, 98%, 99% or 100% sequence identity to an amino acid sequence set forth in SEQ ID NO: 541.
17. The recombinant nucleic acid of claim 16, wherein the TCR alpha chain construct comprises a variable region having at least 80%, 90%, 95%, 96%, 97%, 98%, 99% or 100% sequence identity to an amino acid sequence set forth in SEQ ID NO: 539 or SEQ ID NO: 552.
18. The recombinant nucleic acid of claim 15, wherein the TCR beta chain construct comprising a CDR3 having an amino acid sequence of SEQ ID NO: 563, comprises a variable region having at least 80%, 90%, 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 567.
19. The recombinant nucleic acid of claim 18, wherein the TCR comprising the TCR alpha chain construct comprises a variable region having at least 80%, 90%, 95%, 96%, 97%, 98%, 99% or 100% sequence identity to an amino acid sequence set forth in SEQ ID NO: 565.
20. A vector comprising the recombinant nucleic acid of any one of the claims 1-19.
21. A cell comprising the recombinant nucleic acid of any one of the claims 1-19 or the vector of claim 20.

22. A recombinant nucleic acid encoding a TCR construct comprising:
 - (a) a TCR beta chain construct, and
 - (b) a TCR alpha chain construct;wherein the TCR recognizes and binds to an epitope from human RAS comprising a point mutation G12V or G12C, the epitope being in a human MHC-protein complex, wherein the human MHC-protein is an HLA antigen encoded by the HLA A03:01 allele.
23. The recombinant nucleic acid of claim 22, wherein the TCR beta chain construct comprises a CDR3 having an amino acid sequence set forth in SEQ ID NO: 68.
24. The recombinant nucleic acid encoding a T cell receptor (TCR) of claim 22, wherein the TCR beta chain construct further comprises a complementarity determining region 1 (CDR1) and a complementarity determining region 2 (CDR2), wherein the CDR1 has an amino acid sequence set forth in SEQ ID NO: 66; and the CDR2 has an amino acid sequence set forth in SEQ ID NO: 67.
25. The recombinant nucleic acid encoding a T cell receptor (TCR) of claim 23 or claim 24, further comprising a TCR alpha chain construct having a CDR1, a CDR2, and a CDR3, wherein, the CDR1 has an amino acid sequence set forth in SEQ ID NO: 63;
the CDR2 has an amino acid sequence set forth in SEQ ID NO: 64; and,
the CDR has an amino acid sequence set forth in SEQ ID NO: 65.
26. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the claims 23-25, wherein the TCR beta chain construct comprises a variable region having at least 80%, or at least 90%, 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 74.
27. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the claims 23-26, wherein, the TCR beta chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 74.
28. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the claims 23-27, wherein the TCR alpha chain construct comprises a variable region having at least 80%, or at least 90%, 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 71.
29. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the claims 23-28, wherein the TCR alpha chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 71.
30. A vector comprising a recombinant nucleic acid of any one of the claims 23-29.
31. A cell comprising any one of the recombinant nucleic acid of any one of the claims 23-29 or the vector of claim 30.
32. The recombinant nucleic acid of claim 22, wherein the TCR beta chain construct comprises a CDR3 having an amino acid sequence set forth in SEQ ID NO: 84.

33. The recombinant nucleic acid encoding a T cell receptor (TCR) of claim 32, wherein the TCR beta chain construct further comprises a complementarity determining region 1 (CDR1) and a complementarity determining region 2 (CDR2), wherein the CDR1 has an amino acid sequence set forth in SEQ ID NO: 82; and the CDR2 has an amino acid sequence set forth in SEQ ID NO: 83.
34. The recombinant nucleic acid encoding a T cell receptor (TCR) of claim 32 or claim 33, further comprising a TCR alpha chain construct having a CDR1, a CDR2, and a CDR3, wherein, the CDR1 has an amino acid sequence set forth in SEQ ID NO: 79;
the CDR2 has an amino acid sequence set forth in SEQ ID NO: 80; and,
the CDR3 has an amino acid sequence set forth in SEQ ID NO: 81.
35. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the claims 32-34, wherein the TCR beta chain construct comprises a variable region having at least 80%, or at least 90%, 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 90.
36. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the claims 32-35, wherein, the TCR beta chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 90.
37. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the claims 32-36, wherein the TCR alpha chain construct comprises a variable region having at least 80%, or at least 90%, 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 87.
38. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the claims 32-37, wherein the TCR alpha chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 87.
39. A vector comprising the recombinant nucleic acid of any one of the claims 32-38.
40. A cell comprising any one of the recombinant nucleic acid of any one of the claims 32-38 or the vector of claim 39.
41. The recombinant nucleic acid of claim 22, wherein the TCR beta chain construct comprises a CDR3 having an amino acid sequence set forth in SEQ ID NO: 388.
42. The recombinant nucleic acid encoding a T cell receptor (TCR) of claim 41, wherein the TCR beta chain construct further comprises a complementarity determining region 1 (CDR1) and a complementarity determining region 2 (CDR2), wherein the CDR1 has an amino acid sequence set forth in SEQ ID NO: 386; and the CDR2 has an amino acid sequence set forth in SEQ ID NO: 387.
43. The recombinant nucleic acid encoding a T cell receptor (TCR) of claim 41 or claim 42, further comprising a TCR alpha chain construct having a CDR1, a CDR2, and a CDR3, wherein, the CDR1 has an amino acid sequence set forth in SEQ ID NO: 383;
the CDR2 has an amino acid sequence set forth in SEQ ID NO: 384; and,

the CDR has an amino acid sequence set forth in SEQ ID NO: 385.

44. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the claims 41-43, wherein the TCR beta chain construct comprises a variable region having at least 80%, or at least 90%, 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 394.
45. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the claims 41-44, wherein, the TCR beta chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 394.
46. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the claims 32-36, wherein the TCR alpha chain construct comprises a variable region having at least 80%, or at least 90%, 95%, 96%, 97%, 98% or 99% sequence identity to an amino acid sequence set forth in SEQ ID NO: 391.
47. The recombinant nucleic acid encoding a T cell receptor (TCR) of any one of the claims 32-37, wherein the TCR alpha chain construct comprises a variable region having an amino acid sequence set forth in SEQ ID NO: 391.
48. A recombinant vector comprising the recombinant nucleic acid of any one of the claims 41-47.
49. A cell comprising any one of the recombinant nucleic acid of any one of the claims 41-47 or the vector of claim 48.
50. The nucleic acid of any one of claims 1-49, wherein the epitope has a length of from 8-25 amino acids.
51. The nucleic acid of any one of claims 1-50, wherein the epitope comprises a mutation that differs from the wild type epitope by at least one amino acid.
52. The nucleic acid of any one of claims 1-51, wherein the epitope binds to the human MHC with a greater affinity than a corresponding wild-type epitope.
53. The nucleic acid of any one of claims 1-52, wherein the epitope binds to the human MHC with a KD or an IC50 less than 500 nM, 250 nM, 150 nM, 100 nM, 50 nM, 25 nM or 10 nM.
54. The nucleic acid of any one of claims 1-53, wherein the mutation is not present in non-cancer cells of a subject.
55. The nucleic acid of any one of claims 1-54, wherein the TCR binds to a MHC-peptide complex with a KD or an IC50 of less than 500 nM, 250 nM, 150 nM, 100 nM, 50 nM, 25 nM or 10 nM.
56. The nucleic acid of any one of claims 1-55, wherein the nucleic acid is operably linked to a promoter.
57. The cell of any one of the claims 21, 31, 40, and 49, wherein the cell is a CD4⁺ T cell.
58. The cell of any one of the claims 21, 31, 40, and 49, wherein the cell is a CD8⁺ T cell.
59. The cell of any one of the claims 21, 31, 40, and 49, wherein the cell is isolated from a subject having a RAS mutation.
60. A pharmaceutical composition comprising:

- (a) the nucleic acid of any one of claims 1-56; or,
the vector of any one of claims 15, 25, 34, 43; or,
the cell of any one of claims 16, 26, 35, 44;
and, (b) a pharmaceutically acceptable excipient or diluent.
61. The pharmaceutical composition of claim 55, further comprising an immunomodulatory agent or an adjuvant.
62. The pharmaceutical composition of claim 56, wherein the adjuvant is poly I:C.
63. The pharmaceutical composition of any one of claims 60-62, for use in treating an immune disease or cancer.
64. Use of the pharmaceutical composition of any one of claims 60-62, for treating an immune disease or cancer.
65. A method of treating a subject having a disease or condition, comprising administering to the subject the pharmaceutical composition of any one of claims 60-63.
66. A method of treating a subject with cancer comprising administering to the subject the pharmaceutical composition of any one of claims 60-63.
67. A method of identifying a subject with cancer as a candidate for a therapeutic, the method comprising determining the subject as a subject that expresses a protein encoded by an HLA-A*03:01 allele or an HLA-A*11:01 allele, wherein the therapeutic is the pharmaceutical composition selected from any one of claims 60-63.