ANTI-MUTATED KRAS T CELL RECEPTORS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This patent application claims the benefit of U.S. Provisional Patent Application No. 62/084,654, filed November 26, 2014 and U.S. Provisional Patent Application No. 62/171,321, filed June 5, 2015, each of which is incorporated by reference in its entirety herein.

INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ELECTRONICALLY

[0002] Incorporated by reference in its entirety herein is a computer-readable nucleotide/amino acid sequence listing submitted concurrently herewith and identified as follows: One 231,164 Byte ASCII (Text) file named "722261_ST25.txt," dated November 20, 2015.

BACKGROUND OF THE INVENTION

[0003] Some cancers may have very limited treatment options, particularly when the cancer becomes metastatic and unresectable. Despite advances in treatments such as, for example, surgery, chemotherapy, and radiation therapy, the prognosis for many cancers, such as, for example, pancreatic, colorectal, lung, endometrial, ovarian, and prostate cancers, may be poor. Accordingly, there exists an unmet need for additional treatments for cancer.

SUMMARY

[0004] The present disclosure refers to subject matter as defined in the attached set of claims. An example disclosed herein describes an isolated or purified T cell receptor (TCR) having antigenic specificity for a mutated epitope, the mutated epitope (a) comprising VVVGADGVGK (SEQ ID NO: 2) or (b) consisting of VVVGAVGVGK (SEQ ID NO: 33) or VVGAVGVGK (SEQ ID NO: 35).

[0005] The disclosure further describes related polypeptides and proteins, as well as related nucleic acids, recombinant expression vectors, host cells, populations of cells, and pharmaceutical compositions relating to the TCRs of the disclosure.

[0006] Methods of detecting the presence of cancer in a mammal and methods of treating or preventing cancer in a mammal are further described by the disclosure.

CLAIM(S):

1. An isolated or purified T cell receptor (TCR) having antigenic specificity for a mutated epitope, the mutated epitope consisting of the amino acid sequence of VVVGADGVGK (SEQ ID NO: 2), VVVGAVGVGK (SEQ ID NO: 33) or VVGAVGVGK (SEQ ID NO: 35), wherein the TCR has antigenic specificity for the mutated epitope presented in the context of an HLA-A11 molecule.

2. The TCR of claim 1, comprising
an α chain constant region and a β chain constant region wherein:

(a) the α chain constant region comprises an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 13 and the β chain constant region comprises an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 14;

(b) the α chain constant region comprises an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 135 and the β chain constant region comprises an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 136;

(c) the α chain constant region comprises an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 147 and the β chain constant region comprises an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 148; or

(d) the α chain constant region comprises an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 159 and the β chain constant region comprises an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 160.

3. The TCR of claim 1 or 2, having antigenic specificity for the mutated epitope consisting of the amino acid sequence of VVVGADGVGK (SEQ ID NO: 2).

4. The TCR of claim 1 or 2, having antigenic specificity for the mutated epitope consisting of the amino acid sequence of VVVGAVGVGK (SEQ ID NO: 33) or VVGAVGVGK (SEQ ID NO: 35).

5. An isolated or purified nucleic acid comprising a nucleotide sequence encoding the TCR of any one of claims 1-4.

6. A recombinant expression vector comprising the nucleic acid of claim 5.

7. An isolated host cell comprising the recombinant expression vector of claim 6.

8. The host cell of claim 7, wherein the cell is human.

9. The host cell of claim 8, wherein the cell is a T cell.

10. A population of cells comprising at least one host cell of any one of claims 7-9.

11. A pharmaceutical composition comprising the TCR of any one of claims 1-4, the nucleic acid of claim 5, the recombinant expression vector of claim 6, the host cell of any one of claims 7-9, or the population of cells of claim 10, and a pharmaceutically acceptable carrier.

12. Use of the TCR according to any one of claims 1-4, the nucleic acid of claim 5, the recombinant expression vector of claim 6, the host cell of any one of claims 7-9, the population of cells of claim 10, or the pharmaceutical composition of claim 11, in the manufacture of a medicament for the detection, treatment or prevention of a cancer expressing a mutated epitope comprising the amino acid sequence of VVVGADGVGK (SEQ ID NO: 2), VVVGAVGVGK (SEQ ID NO: 33) or VVGAVGVGK (SEQ ID NO: 35) in a mammal.

13. A method of detecting the presence of a cancer expressing a mutated epitope comprising the amino acid sequence of VVVGADGVGK (SEQ ID NO: 2), VVVGAVGVGK (SEQ ID NO: 33) or VVGAVGVGK (SEQ ID NO: 35) in a mammal, the method comprising

contacting a sample obtained from the mammal comprising one or more cells from the mammal with the TCR of any one of claims 1-4, the nucleic acid according to claim 5, the recombinant expression vector of claim 6, the host cell of any one of claims 7-9, the population of cells of claim 10, or the pharmaceutical composition of claim 11, thereby forming a complex, and

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

14. The use of claim 12 or the method of claim 13, wherein the cancer is pancreatic, colorectal, lung, endometrial, ovarian, or prostate cancer.