

CLAIMS

WHAT IS CLAIMED IS:

1. A composition comprising T cells specific to an HLA-peptide complex comprising at least one mutant RAS peptide consisting of a sequence selected from the group consisting of GAVGVGKSA, AVGVGKSAL, GADGVGKSAL and GADGVGKSA.
2. The composition of claim 1, wherein the HLA-peptide complex comprises:
 - (a) a protein encoded by an HLA-C03:03 or HLA-C03:04 allele and the at least one mutant RAS peptide consisting of the sequence GAVGVGKSA;
 - (b) a protein encoded by an HLA-C01:02 allele and the at least one mutant RAS peptide consisting of the sequence AVGVGKSAL; or
 - (c) a protein encoded by an HLA-C08:02 allele and the at least one mutant RAS peptide consisting of the sequence GADGVGKSAL or GADGVGKSA.
3. A method of preparing the composition of claim 1 or 2 comprising priming T cells with antigen presenting cells (APCs) comprising (i) the at least one polypeptide or (ii) at least one polynucleotide encoding the at least one polypeptide.
4. A composition comprising
 - (a) at least one polypeptide of the formula

$$(Xaa_N)_N-(Xaa_{RAS})_P-(Xaa_C)_C$$

wherein

P is an integer greater than 7;

$(Xaa_{RAS})_P$ is a mutant RAS peptide sequence comprising at least 8 contiguous amino acids of a mutant RAS protein;

the at least 8 contiguous amino acids comprising at least 8 contiguous amino acids of the sequence

Lys₁ Leu₂ Val₃ Val₄ Val₅ Gly₆ Ala₇ Xaa₈ Gly₉ Val₁₀ Gly₁₁ Lys₁₂ Ser₁₃ Ala₁₄ Leu₁₅;

N is (i) 0 or (ii) an integer greater than 2;

$(Xaa_N)_N$ is any amino acid sequence heterologous to the mutant RAS protein;

C is (i) 0 or (ii) an integer greater than 2;

$(Xaa_C)_C$ is any amino acid sequence heterologous to the mutant RAS protein;

Xaa₈ is selected from the group consisting of Asp, Val, Cys, Ala, Arg and Ser;

the polypeptide is not KLVVVGAVGVGKSALTIQL; and

wherein if N is 0 C is not 0 and if C is 0 N is not 0; or

- (b) at least one polynucleotide encoding the at least one polypeptide.

5. The composition of claim 4, wherein C is 0.
6. The composition of claim 4 or 5, wherein N is a polylysine sequence.
7. The composition of any one of claims 4-6, wherein N is an integer less than 50.
8. The composition of claim 7, wherein N is 2, 3, 4, 5, or 6.
9. The composition of any one of claims 4-8, wherein Xaa₈ is selected from the group consisting of Asp, Val, Cys and Arg.
10. The composition of any one of claims 4-9, wherein the at least one polypeptide comprises an amino acid sequence of VVVGAVGVGK, VVGAVGVGK, GAVGVGKSAL, GAVGVGKSA, AVGVGKSAL, VVVGADGVGK, GADGVGKSAL, GADGVGKSA, VVVGARGVGK, GARGVGKSAL or VVVGACGVGK.
11. The composition of any one of claims 4-10, wherein the at least one polypeptide comprises an amino acid sequence of TEY.
12. The composition of any one of claims 4-11, wherein the at least one polypeptide comprises an amino acid sequence of GKSALTIQL or GKSALTI.
13. A method of preparing T cells specific to an HLA-peptide complex comprising at least one mutant RAS peptide sequence comprising priming T cells with antigen presenting cells (APCs) comprising the composition of any one of claims 4-12.
14. A pharmaceutical composition comprising (i) the composition of claim 1 or 2; and (ii) a pharmaceutically acceptable excipient.
15. A pharmaceutical composition comprising T cells primed with antigen presenting cells (APCs) comprising (i) the composition of any one of claims 4-12; and (ii) a pharmaceutically acceptable excipient.
16. A pharmaceutical composition comprising T cells specific to an HLA-peptide complex comprising at least one mutant RAS peptide sequence, wherein:
 - (a) the HLA-peptide complex comprises a protein encoded by an HLA-A03:01 or HLA-A30:01 allele and the at least one mutant RAS peptide consists of the sequence VVVGAVGVGK;
 - (b) the HLA-peptide complex comprises a protein encoded by an HLA-A30:01 or HLA-A68:01 allele and the at least one mutant RAS peptide consists of the sequence VVGAVGVGK;
 - (c) the HLA-peptide complex comprises a protein encoded by an HLA-C03:03, or HLA-C03:04 allele and the at least one mutant RAS peptide consists of the sequence GAVGVGKSAL;
 - (d) the HLA-peptide complex comprises a protein encoded by an HLA-A03:01 or HLA-A68:01 allele and the at least one mutant RAS peptide consists of the sequence VVVGADGVGK;

- (e) the HLA-peptide complex comprises a protein encoded by an HLA-A03:01, HLA-A30:01 or HLA-A68:01 allele and the at least one mutant RAS peptide consists of the sequence VVVGARGVGK; or
 - (f) the HLA-peptide complex comprises a protein encoded by an HLA-A03:01 or HLA-A68:01 allele and the at least one mutant RAS peptide consists of the sequence VVVGACGVGK.
17. A method of preparing T cells specific to an HLA-peptide complex comprising at least one mutant RAS peptide sequence, the method comprising priming T cells with antigen presenting cells (APCs) comprising (i) at least one polypeptide comprising the at least one mutant RAS peptide sequence or (ii) at least one polynucleotide encoding the at least one polypeptide; wherein:
 - (a) the APCs express a protein encoded by an HLA-A03:01 or HLA-A30:01 allele and the at least one mutant RAS peptide consists of the sequence VVVGAVGVGK;
 - (b) the APCs express a protein encoded by an HLA-A30:01 or HLA-A68:01 allele and the at least one mutant RAS peptide consists of the sequence VVGAVGVGK;
 - (c) the APCs express a protein encoded by an HLA-C03:03, or HLA-C03:04 allele and the at least one mutant RAS peptide consists of the sequence GAVGVGKSAL;
 - (d) the APCs express a protein encoded by an HLA-A03:01 or HLA-A68:01 allele and the at least one mutant RAS peptide consists of the sequence VVVGADGVGK;
 - (e) the APCs express a protein encoded by an HLA-A03:01, HLA-A30:01 or HLA-A68:01 allele and the at least one mutant RAS peptide consists of the sequence VVVGARGVGK; or
 - (f) the APCs express a protein encoded by an HLA-A03:01 or HLA-A68:01 allele and the at least one mutant RAS peptide consists of the sequence VVVGACGVGK.
 18. The method of claim 3 or 13 or 17, or the composition of any one of claims 4-12, wherein the at least one polynucleotide encoding the at least one polypeptide is RNA.
 19. The method of any one of claims 3, 17 and 18, wherein the T cells are from a human subject with a cancer that expresses the at least one mutant RAS peptide sequence, and wherein the human subject's genome comprises an HLA-allele encoding the HLA of the HLA-peptide complex.
 20. The method of claim 13, wherein the APCs express 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, an HLA-A74:01 allele, an HLA-C01:02 allele, an HLA-C03:03 allele, an HLA-C03:04 allele or an HLA-C08:02 allele.