

CLAIMS

What is claimed is:

1. An *ex vivo* method for preparing antigen-specific T cells, the method comprising contacting T cells with antigen presenting cells (APCs) comprising one or more peptides containing an epitope with a sequence GACGVGKSA, wherein the APCs express a protein encoded by an HLA-C03:04 allele.
2. The method of claim 1, further comprising contacting T cells with APCs comprising one or more peptides containing an epitope with a sequence GAVGVGKSA, wherein the APCs express a protein encoded by an HLA-C03:03 allele.
3. The method of claim 1 or 2, wherein the T cells or APCs are from a subject with cancer.
4. The method of any one of claims 1-3, wherein the T cells or APCs are allogeneic.
5. The method of any one of claims 2-4, wherein the epitope with the sequence GACGVGKSA is capable of binding to the protein encoded by the HLA-C03:04 allele, and wherein the epitope with the sequence GAVGVGKSA is capable of binding to the protein encoded by the HLA-C03:03 allele.
6. The method of any one of claims 1-5, wherein the method comprises obtaining a biological sample comprising T cells and APCs from a subject, and wherein the biological sample is peripheral blood mononuclear cell (PBMC) sample.
7. The method of claim 6, wherein the method comprises depleting CD14⁺ cells from the biological sample.
8. The method claim 6 or 7, wherein the method comprises depleting CD25⁺ cells from the biological sample.
9. The method of any one of claims 1-8, wherein the method comprises incubating the T cells and APCs in the presence of FMS-like tyrosine kinase 3 receptor ligand (FLT3L).
10. The method of any one of claims 1-9, wherein the method comprises stimulating or expanding the T cells in the presence of the APCs for at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 or more days.
11. The method of any one of claims 1-10, wherein the method comprises expanding the T cells at least 5-fold, 10-fold, 20-fold, 50-fold, 100-fold, 500-fold or 1,000-fold or more in the presence of the APCs.
12. The method of any one of claims 1-11, wherein the antigen-specific T cells are prepared in less than 28 days.
13. The method of any one of claims 1-12, wherein the epitope:
 - (i) binds to a protein encoded by an HLA allele of the subject,

- (ii) is immunogenic according to an immunogenicity assay,
 - (iii) is presented by APCs according to a mass spectrometry assay, and/or
 - (iv) stimulates T cells to be cytotoxic according to a cytotoxicity assay.
14. Use of a composition in the manufacture of a medicament for treatment in a subject, the composition comprising:
- (a) a peptide,
 - (b) a polynucleotide encoding the peptide,
 - (c) antigen presenting cells (APCs) comprising (a) or (b), or
 - (d) T cells stimulated with APCs comprising (a) or (b);
- wherein:
- (i) the peptide comprises an epitope with a sequence GACGVGKSA and the subject expresses a protein encoded by an HLA-C03:04 allele.
15. wherein the epitope with the sequence GAVGVGKSA is capable of binding to the protein encoded by the HLA-C03:03 allele. The use of claim 14, wherein the cancer is selected from the group consisting of pancreatic ductal adenocarcinoma, non-small cell lung cancer, colorectal cancer and cholangiocarcinoma.
16. The use of claim 14 or 15, wherein the peptide comprises one or more additional epitopes, and wherein the one or more additional epitopes comprise (i) an epitope with a sequence GAVGVGKSA and the subject expresses a protein encoded by an HLA-C03:03 allele or (ii) one or more epitopes of any one of Tables 2-12.
17. The use of any one of claims 14-16, wherein the composition further comprises an additional peptide, a polynucleotide encoding the additional peptide, APCs comprising the additional peptide or the polynucleotide, or T cells stimulated with the APCs, wherein the additional peptide comprises one or more epitopes of any one of Tables 2-12.
18. The method of any one of claims 1-13, wherein the method comprises assaying the T cells for expression of a T cell activation marker or for cytokine production.
19. A pharmaceutical composition comprising:
- (a) T cells comprising a population of T cells expressing a T cell receptor (TCR) that binds to a complex of (i) an MHC protein encoded by an HLA-C03:04 allele and (ii) an epitope with a sequence GACGVGKSA; or

- (b) antigen presenting cells (APCs) expressing an MHC protein encoded by an HLA-C03:04 allele, wherein the APCs comprise (i) a peptide having an epitope with a sequence GACGVGKSA or (ii) a polynucleotide encoding the peptide.
- 20. A T cell receptor (TCR) comprising a TCR alpha chain and a TCR beta chain that binds to complex comprising a mutated RAS epitope with the sequence GACGVGKSA and an MHC encoded by C03:04 allele.
- 21. A composition comprising:
 - (a) a peptide,
 - (b) a polynucleotide encoding the peptide,
 - (c) antigen presenting cells (APCs) comprising (a) or (b), or
 - (d) T cells stimulated with APCs comprising (a) or (b);wherein:
 - (i) the peptide comprises an epitope with a sequence GACGVGKSA and the subject expresses a protein encoded by an HLA-C03:04 allelewherein the epitope with the sequence GAVGVGKSA is capable of binding to the protein encoded by the HLA-C03:03 allele for use in therapy.