

molecules present different peptides. The inventors have demonstrated that an epitope that binds to a single HLA class I allele expressed in a subject is essential, but not sufficient to induce tumor specific T cell responses. Instead tumour specific T cell responses are optimally activated when an epitope is recognised and presented by the HLA molecules encoded by at least three HLA class I genes of an individual (PCT/EP2018/055231, PCT/EP2018/055232, PCT/EP2018/055230, EP 3370065 and EP 3369431).

Based on this discovery the inventors have developed a method for designing and preparing peptides to induce T cell responses in the highest proportion of subjects in a given target human population and have used this method to design a set of peptides for use in treating cancer.

In one aspect, the present disclosure provides a panel of six or more peptides, or one or more polynucleic acids or vectors that encode a panel of six or more peptides, wherein each of the peptides, or each of the encoded peptides, is 20 to 35 amino acids in length, wherein each peptide or encoded peptide comprises a different amino acid sequence selected from any of SEQ ID NOs: 1 to 2786 and/or 5432-5931, wherein the amino acid sequence selected from SEQ ID NOs: 1 to 2786 and/or 5432-5931 of each peptide or encoded peptide is a fragment of a different cancer-associated antigen listed in Table 24, and wherein each peptide, or each encoded peptide, comprises a T cell epitope capable of binding to at least three HLA class I alleles and/or a T cell epitope capable of binding to at least three HLA class II alleles of an individual human subject.

In another example, the present disclosure provides a polynucleic acid or a vector that encodes a peptide as described herein that is up to 50 amino acids in length, and that comprises the amino acid sequence of any of SEQ ID NOs: 1 to 2786 and/or 5432-5931. In another aspect, the present disclosure provides a pharmaceutical composition or kit, comprising a panel of six or more peptides, or one or more polynucleic acids or vectors that encode a panel of six or more peptides as claimed herein, wherein the composition or kit optionally comprises at least one pharmaceutically acceptable diluent, carrier, or preservative. In yet another aspect, the present disclosure provides a method of predicting that a specific human subject will have a CD8⁺ T cell response and/or a CD4⁺ T cell response to each peptide, or encoded peptide, of a pharmaceutical composition or kit according to claim 5, the method comprising (i) a. determining that each peptide, or encoded peptide comprises at least one amino acid sequence that is a T cell epitope capable of binding to at least three HLA class I molecules of the subject; and b. predicting that the subject will have a CD8⁺ T cell response to each peptide or encoded peptide of the pharmaceutical composition or kit; and/or (ii) a. determining that each peptide, or encoded peptide comprises at least one amino acid sequence

that is a T cell epitope capable of binding to at least three HLA class II molecules of the subject; and b. predicting that the subject will have a CD4+ T cell response to each peptide or encoded peptide of the pharmaceutical composition or kit.

In yet another aspect, the present disclosure provides use of the pharmaceutical composition as described herein in the manufacture of a medicament for treating cancer, optionally bladder cancer, brain cancer, breast cancer, colorectal cancer, gastric cancer, hepatocellular cancer, leukemia, lung cancer, lymphoma, melanoma, ovarian cancer, pancreatic cancer, pediatric cancer, thyroid cancer, prostate cancer, kidney cancer, head and neck cancer, esophageal cancer and cervical cancer.

In yet another aspect, the present disclosure provides a method of preparing a pharmaceutical composition or kit for treating cancer in a specific human subject, the method comprising a. selecting six or more peptides, or one or more polynucleic acids or vectors that encode six or more peptides, wherein each peptide, or each encoded peptide, is 20 to 35 amino acids in length, wherein each peptide, or each encoded peptide, comprises a different amino acid sequence selected from SEQ ID NOs: 1 to 2786 and/or 5432-5931 that comprises a T cell epitope capable of binding to at least three HLA class I alleles and/or a T cell epitope capable of binding to at least three HLA class II alleles of the specific human subject; and wherein the amino acid sequence selected from SEQ ID NOs: 1 to 2786 and/or 5432-5931 of each peptide or encoded peptide is a fragment of a different cancer-associated antigen listed in Table 24; and b. preparing a pharmaceutical composition or kit comprising the six or more peptides, or one or more polynucleic acids or vectors selected in step a.

In yet another aspect, the present disclosure provides a pharmaceutical composition or kit as described herein for use in therapy for vaccination, providing immunotherapy or inducing a cytotoxic T cell response in said human subject, wherein the pharmaceutical composition or the
5 peptides, polynucleic acids or vectors of the kit are to be administered to the subject.

Accordingly, in a first example the disclosure provides a peptide of up to 50 amino acids in length and comprising the amino acid sequence of any of SEQ ID NOs: 1 to 2786 and/or 5432-5931.

5 In a further example, the disclosure provides a polynucleic acid or a vector that encodes a peptide of up to 50 amino acids in length and comprising the amino acid sequence of any of SEQ ID NOs: 1 to 2786 and/or 5432-5931.

 In a further example, the disclosure provides a panel of two or more of the peptides or two or more of the polynucleic acids or vectors, wherein each peptide comprises, or each
10 polynucleic acid or vector encodes a peptide that comprises, a different amino acid sequence selected from SEQ ID NOs: 1 to 2786 and/or 5432-5931.

 In a further example, the disclosure provides a pharmaceutical composition or kit, comprising one or more of the peptides, polynucleic acids, vectors or panels, wherein the composition or kit optionally comprise at least one pharmaceutically acceptable diluent, carrier,
15 or preservative.

 In a further example, the disclosure provides a method of predicting that a specific human subject will have a cytotoxic T cell response and/or a helper T cell response to administration of the pharmaceutical composition or the peptides, polynucleic acids or vectors of the kit, the method comprising

- 20 (i) a. determining that the one or more peptides, or encoded peptides, of the pharmaceutical composition or kit, comprise at least one amino acid sequence that is a T cell epitope capable of binding to at least three HLA class I molecules of the subject; and
- b. predicting that the subject will have a cytotoxic T cell response to
25 administration of the pharmaceutical composition; or
- (ii) a. determining that the one or more peptides, or encoded peptides, of the pharmaceutical composition or kit comprise at least one amino acid sequence that is a T cell epitope capable of binding to at least three HLA class II molecules of the subject; and

CLAIMS

1. A panel of six or more peptides, or one or more polynucleic acids or vectors that encode a panel of six or more peptides, wherein each of the peptides, or each of the encoded peptides, is 20 to 35 amino acids in length, wherein each peptide or encoded peptide comprises a different amino acid sequence selected from any of SEQ ID NOs: 1 to 2786 and/or 5432-5931, wherein the amino acid sequence selected from SEQ ID NOs: 1 to 2786 and/or 5432-5931 of each peptide or encoded peptide is a fragment of a different cancer-associated antigen listed in Table 24, and wherein each peptide, or each encoded peptide, comprises a T cell epitope capable of binding to at least three HLA class I alleles and/or a T cell epitope capable of binding to at least three HLA class II alleles of an individual human subject.
2. The panel of peptides, polynucleic acid(s) or vector(s) according to claim 1, wherein each of the peptides or encoded peptides comprises an amino acid sequence selected from one of the following groups:
 - (a) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a breast cancer-associated antigen listed in Table 24;
 - (b) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a lung cancer-associated antigen listed in Table 24;
 - (c) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a prostate cancer-associated antigen listed in Table 24;
 - (d) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a colorectal cancer-associated antigen listed in Table 24;
 - (e) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a bladder cancer-associated antigen listed in Table 24;

- (f) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a ovarian cancer-associated antigen listed in Table 24;
- (g) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a pancreatic cancer-associated antigen listed in Table 24;
- (h) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a brain cancer-associated antigen listed in Table 24;
- (i) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a leukemia-associated antigen listed in Table 24;
- (j) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a lymphoma-associated antigen listed in Table 24;
- (k) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a hepatocellular cancer-associated antigen listed in Table 24;
- (l) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a melanoma-associated antigen listed in Table 24;
- (m) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a thyroid cancer-associated antigen listed in Table 24;
- (n) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a pediatric cancer-associated antigen listed in Table 24;
- (o) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a gastric cancer-associated antigen listed in Table 24;
- (p) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a kidney cancer-associated antigen listed in Table 24

- (q) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a head and neck cancer-associated antigen listed in Table 24; and
 - (r) the sequences listed in Table 25A and/or Table 25B and indicated in Table 25A or 25B to be a fragment of a cervical cancer-associated antigen listed in Table 24.
- 3. A pharmaceutical composition or kit, comprising a panel of six or more peptides, or one or more polynucleic acids or vectors that encode a panel of six or more peptides, according to claim 1 or claim 2, wherein the composition or kit optionally comprises at least one pharmaceutically acceptable diluent, carrier, or preservative.
- 4. A method of predicting that a specific human subject will have a CD8⁺ T cell response and/or a CD4⁺ T cell response to each peptide, or encoded peptide, of a pharmaceutical composition or kit according to claim 3, the method comprising
 - (i)
 - a. determining that each peptide, or encoded peptide comprises at least one amino acid sequence that is a T cell epitope capable of binding to at least three HLA class I molecules of the subject; and
 - b. predicting that the subject will have a CD8⁺ T cell response to each peptide or encoded peptide of the pharmaceutical composition or kit; and/or
 - (ii)
 - a. determining that each peptide, or encoded peptide comprises at least one amino acid sequence that is a T cell epitope capable of binding to at least three HLA class II molecules of the subject; and
 - b. predicting that the subject will have a CD4⁺ T cell response to each peptide or encoded peptide of the pharmaceutical composition or kit.
- 5. The pharmaceutical composition or kit according to claim 3 for use in therapy for vaccination, providing immunotherapy or inducing a cytotoxic T cell response in said human subject, wherein the pharmaceutical composition or the peptides, polynucleic acids or vectors of the kit are to be administered to the subject.

6. The pharmaceutical composition or kit for use according to claim 5, wherein the therapy is prophylactic.
7. The pharmaceutical composition or kit for use according to claim 5 or claim 6, wherein the pharmaceutical composition or the peptides, polynucleic acids or vectors of the kit have been predicted to induce a cytotoxic T cell response and/or a helper T cell response in the subject using a method according to claim 4.
8. The pharmaceutical composition or kit for use according to any one of claims 5 to 7 wherein the therapy is for treating cancer, optionally bladder cancer, brain cancer, breast cancer, colorectal cancer, gastric cancer, hepatocellular cancer, leukemia, lung cancer, lymphoma, melanoma, ovarian cancer, pancreatic cancer, pediatric cancer, thyroid cancer, prostate cancer, kidney cancer, head and neck cancer, esophageal cancer and cervical cancer.
9. Use of the pharmaceutical composition of claim 3 in the manufacture of a medicament for treating cancer, optionally bladder cancer, brain cancer, breast cancer, colorectal cancer, gastric cancer, hepatocellular cancer, leukemia, lung cancer, lymphoma, melanoma, ovarian cancer, pancreatic cancer, pediatric cancer, thyroid cancer, prostate cancer, kidney cancer, head and neck cancer, esophageal cancer and cervical cancer.
10. A method of preparing a pharmaceutical composition or kit for treating cancer in a specific human subject, the method comprising
 - a. selecting six or more peptides, or one or more polynucleic acids or vectors that encode six or more peptides, wherein each peptide, or each encoded peptide, is 20 to 35 amino acids in length, wherein each peptide, or each encoded peptide, comprises a different amino acid sequence selected from SEQ ID NOs: 1 to 2786 and/or 5432-5931 that

comprises a T cell epitope capable of binding to at least three HLA class I alleles and/or a T cell epitope capable of binding to at least three HLA class II alleles of the specific human subject, and wherein the amino acid sequence selected from SEQ ID NOs: 1 to 2786 and/or 5432-5931 of each peptide or encoded peptide is a fragment of a different cancer-associated antigen listed in Table 24; and

- b. preparing a pharmaceutical composition or kit comprising the six or more peptides, or one or more polynucleic acids or vectors selected in step a.