

B. a T cell epitope capable, in at least 10 percent of the subjects of a model population selected or defined in step (i) that is defined by HLA class II genotype, of binding to at least three HLA class II molecules of the individual subjects; or

5 C. a T cell epitope capable, in at least 10 percent of the subjects of a model population selected or defined in step (i) that is defined by HLA class I genotype, of binding to at least three HLA class I molecules of the individual subjects and a T cell epitope capable, in at least 10 percent of the subjects of a model population selected or defined in step (i) that is defined by HLA class II  
10 genotype, of binding to at least three HLA class II molecules of the individual subjects;

and

(iii) designing or preparing a polypeptide, or a polynucleic acid that encodes a polypeptide that comprises or consists of one or more polypeptide fragments  
15 identified in step (ii), optionally wherein the polypeptide fragment is flanked at the N and/or C terminus by additional amino acids that are not part of the sequence of the target polypeptide antigen.

The disclosure provides a method of inducing an immune response in a subject of a specific  
20 or target human population, the method comprising designing or preparing a polypeptide, a panel of polypeptides, a polynucleic acid encoding a polypeptide, or a pharmaceutical composition or kit for use in said specific or target human population as described above and administering the polypeptide(s), polynucleic acid, pharmaceutical composition or the active ingredient polypeptides of the kit to the subject.

25 The disclosure provides a polypeptide, panel of polypeptides, polynucleic acid, pharmaceutical composition or kit for use in a method of inducing an immune response in a subject of a specific or target human population, wherein the polypeptide, panel of polypeptides, polynucleic acid, pharmaceutical composition or kit is designed or prepared as described above

for use in said specific or target human population, and wherein the composition or kit optionally comprises at least one pharmaceutically acceptable diluent, carrier, or preservative.

This disclosure provides a pharmaceutical composition, panel of polypeptides or kit for use in a method of inducing an immune response in a human subject, wherein the pharmaceutical composition, panel of polypeptides or kit comprises as active ingredients a first and a second and optionally one or more additional peptides, wherein each peptide comprises an amino acid sequence that is a T cell epitope capable of binding to at least three HLA class I molecules of at least 10% of human subjects, wherein the T cell epitope of the first, second and optionally any additional regions are different from each other, and wherein the pharmaceutical composition or kit optionally comprises at least one pharmaceutically acceptable diluent, carrier, or preservative.

The disclosure provides a pharmaceutical composition, panel of polypeptides or kit for use in a method of inducing an immune response in a human subject, wherein the pharmaceutical composition, panel of polypeptides or kit comprises an active ingredient polypeptide comprising a first region and a second region and optionally one or more additional regions, wherein each region comprises an amino acid sequence that is a T cell epitope capable of binding to at least three HLA class I molecules of at least 10% of human subjects, wherein the T cell epitope of the first, second and optionally any additional regions are different from each other, and wherein the pharmaceutical composition or kit optionally comprises at least one pharmaceutically acceptable diluent, carrier, or preservative.

The disclosure provides a pharmaceutical composition, panel of polypeptides or kit for use in a method treating a cancer in a subject in need thereof, wherein the pharmaceutical composition, panel of polypeptides or kit comprises as active ingredients a first and a second peptide and optionally one or more additional peptides, wherein each peptide comprises an amino acid sequence that is an HLA class I-binding T cell epitope, and wherein for each said T cell epitope at least 10% of human subjects having cancer both

- i. express a tumor associated antigen selected from the antigens listed in Table 2 or Table 5 below that comprises said T cell epitope; and
- ii. have at least three HLA class I molecules capable of binding to said T cell epitope;

wherein said T cell epitope of the first, second and optionally any additional peptides are different from each other, and wherein the pharmaceutical composition or kit optionally comprises at least one pharmaceutically acceptable diluent, carrier, or preservative.

The disclosure provides a pharmaceutical composition, panel of polypeptides or kit for use in a method treating a cancer in a subject in need thereof, wherein the pharmaceutical composition, panel of polypeptides or kit comprises an active ingredient polypeptide comprising a first and a second region and optionally one or more additional regions, wherein each region comprises an amino acid sequence that is an HLA class I-binding T cell epitope, and wherein for each said T cell epitope at least 10% of human subjects having cancer both

(a) express a tumor associated antigen selected from the antigens listed in Table 2 or Table 5 below that comprises said T cell epitope; and

(b) have at least three HLA class I molecules capable of binding to said T cell epitope; wherein said T cell epitope of the first, second and optionally any additional regions are different from each other, and wherein the pharmaceutical composition or kit optionally comprises at least one pharmaceutically acceptable diluent, carrier, or preservative.

The disclosure provides a pharmaceutical composition, panel of polypeptides or kit for use in a method treating a cancer selected from colorectal, breast, ovarian, melanoma, non-melanoma

skin, lung, prostate, kidney, bladder, stomach, liver, cervix uteri, oesophagus, non-Hodgkin lymphoma, leukemia, pancreas, corpus uteri, lip, oral cavity, thyroid, brain, nervous system, gallbladder, larynx, pharynx, myeloma, nasopharynx, Hodgkin lymphoma, testis and Kaposi sarcoma in a subject in need thereof, wherein the pharmaceutical composition, panel of

5 polypeptides or kit comprises as active ingredients a first and a second peptide and optionally one or more additional polypeptides, wherein each peptide comprises an amino acid sequence that is an HLA class I-binding T cell epitope, and wherein for each said T cell epitope at least 10% of human subjects having said cancer both

(a) express a tumor associated antigen selected from the antigens listed in Table 2 or  
10 Table 5 below that comprises said T cell epitope; and

(b) have at least three HLA class I molecules capable of binding to said T cell epitope; wherein said T cell epitope of the first, second and optionally any additional peptides are different from each other, and wherein the pharmaceutical composition or kit optionally comprises at least one pharmaceutically acceptable diluent, carrier, or preservative.

15 The disclosure provides a pharmaceutical composition, panel of polypeptides or kit for use in a method treating a cancer selected from colorectal, breast, ovarian, melanoma, non-melanoma skin, lung, prostate, kidney, bladder, stomach, liver, cervix uteri, oesophagus, non-Hodgkin lymphoma, leukemia, pancreas, corpus uteri, lip, oral cavity, thyroid, brain, nervous system, gallbladder, larynx, pharynx, myeloma, nasopharynx, Hodgkin lymphoma, testis and Kaposi  
20 sarcoma in a subject in need thereof, wherein the pharmaceutical composition, panel of polypeptides or kit comprises an active ingredient polypeptide comprising a first and a second region and optionally one or more additional regions, wherein each region comprises an amino acid sequence that is an HLA class I-binding T cell epitope, and wherein for each said T cell epitope at least 10% of human subjects having said cancer both

25 (a) express a tumor associated antigen selected from the antigens listed in Table 2 or Table 5 below that comprises said T cell epitope; and

(b) have at least three HLA class I molecules capable of binding to said T cell epitope; wherein said T cell epitope of the first, second and optionally any additional polypeptides are different from each other, and wherein the pharmaceutical composition or kit

optionally comprises at least one pharmaceutically acceptable diluent, carrier, or preservative.

The disclosure provides a method of treatment of a human subject in need thereof, the method comprising administering to the subject a polypeptide, a panel of polypeptides, a pharmaceutical composition or the active ingredient polypeptides of a kit described above, wherein the subject has been determined to express at least three HLA class I molecules and/or at least three HLA class II molecules capable of binding to the polypeptide or to one or more of the active ingredient polypeptides of the pharmaceutical composition or kit.

In a further example, the disclosure provides a system comprising

(a) a storage module configured to store data comprising the class I and/or class II HLA genotypes of each subject of a model population of human subjects; and the amino acid sequence of one or more test polypeptides; wherein the model population is representative of a test target human population; and

(b) a computation module configured to identify and/or quantify the amino acid sequences in the one or more test polypeptides that are capable of binding to multiple class I HLA molecules of each subject in the model population and/or the amino acid sequences in the one or more test polypeptides that are capable of binding to multiple class II HLA molecules of each subject in the model population.

The disclosure will now be described in more detail, by way of example and not limitation, and by reference to the accompanying drawings. Many equivalent modifications and variations will be apparent, to those skilled in the art when given this disclosure. Accordingly, the exemplary examples of the disclosure set forth are considered to be illustrative and not limiting. Various changes to the described examples may be made without departing from the scope of the disclosure. All documents cited herein, whether supra or infra, are expressly incorporated by reference in their entirety.

The present disclosure includes the combination of the examples and preferred features described except where such a combination is clearly impermissible or is stated to be expressly avoided. As used in this specification and the appended claims, the singular forms “a” “an”, and

## CLAIMS

1. A method of predicting the cytotoxic T cell response rate and/or the helper T cell response rate of a specific or target human population to administration of a polypeptide, or to administration of a pharmaceutical composition, kit or panel of polypeptides comprising one or more polypeptides as active ingredients, the method comprising
  - (i) selecting or defining a relevant model human population comprising a plurality of subjects each defined by HLA class I genotype and/or HLA class II genotype;
  - (ii) determining for each subject in the model human population whether the polypeptide or polypeptides together comprise
    - (a) at least one amino acid sequence that is a T cell epitope capable of binding to at least two HLA class I molecules of the subject; and/or
    - (b) at least one amino acid sequence that is a T cell epitope capable of binding to at least two HLA class II molecules of the subject; and
  - (iii) predicting
    - A. the cytotoxic T cell response rate of said human population, wherein a higher proportion of the model human population meeting the requirements of step (ii)(a) predicts a higher cytotoxic T cell response rate in said human population; and/or
    - B. the helper T cell response rate of said human population, wherein a higher proportion of the model human population meeting the requirements of step (ii)(b) predicts a higher helper T cell response rate in said human population.
2. A method of predicting the clinical response rate of a specific or target human population to administration of a pharmaceutical composition, kit or panel of polypeptides comprising one or more polypeptides as active ingredients, the method comprising
  - (i) selecting or defining a relevant model human population comprising a plurality of individual subjects, each defined by HLA class I genotype;
  - (ii) determining
    - (a) for each subject in the model human population whether the one or more active ingredient polypeptides together comprise at least two different amino acid sequences each of which is a T cell epitope capable of binding to at least two HLA

class I molecules of the subject, optionally wherein the at least two different amino acid sequences are comprised in the amino acid sequence of two different polypeptide antigens targeted by the active ingredient polypeptide(s);

(b) in the model population the mean number of target polypeptide antigens that comprise at least one amino acid sequence that is

- A. a T cell epitope capable of binding to at least three HLA class I molecules of the individual subjects of the model population; and
- B. comprised in the amino acid sequence of the active ingredient polypeptide(s); and/or

(c) in the model population the mean number of expressed target polypeptide antigens that comprise at least one amino acid sequence that is

- A. a T cell epitope capable of binding to at least three HLA class I molecules of the individual subjects of the model population; and
- B. comprised in the amino acid sequence of the active ingredient polypeptide(s); and

(iii) predicting the clinical response rate of said human population, wherein a higher proportion of the model human population meeting the requirements of step (ii)(a), or a higher mean number of target polypeptides in step (ii)(b), or a higher mean number of expressed target polypeptides in step (ii)(c) predicts a higher clinical response rate in said human population.

3. The method of claim 1 or claim 2 further comprising repeating the method for one or more further polypeptides, pharmaceutical compositions, kits or panels of polypeptides, and ranking the polypeptides, pharmaceutical compositions, kits or panels of polypeptides according to their predicted cytotoxic T cell, helper T cell and/or or clinical response rates in said specific or target human population.

4. The method of any one of claims 1 to 3 further comprising selecting or recommending treatment of a subject in need thereof for administration of one or more polypeptides or pharmaceutical compositions or the polypeptides of one or more kits or panels of polypeptides, based on their predicted response rate or response rate ranking.

5. A method of designing or preparing a polypeptide, or a polynucleic acid that encodes a polypeptide, for use in a method of inducing an immune response in a subject of a specific or target human population, the method comprising
- (i) selecting or defining
    - (a) a relevant model human population comprising a plurality of individual subjects each defined by HLA class I genotype and/or by HLA class II genotype;  
or
    - (b) one relevant model human population comprising a plurality of individual subjects each defined by HLA class I genotype and one relevant model human population comprising a plurality of subjects each defined by HLA class II genotype;
  - (ii) identifying a fragment of up to 50 consecutive amino acids of a target polypeptide antigen that comprises or consists of
    - A. a T cell epitope capable, in at least 10 percent of the subjects of a model population selected or defined in step (i) that is defined by HLA class I genotype, of binding to at least three HLA class I molecules of the individual subjects;
    - B. a T cell epitope capable, in at least 10 percent of the subjects of a model population selected or defined in step (i) that is defined by HLA class II genotype, of binding to at least three HLA class II molecules of the individual subjects; or
    - C. a T cell epitope capable, in at least 10 percent of the subjects of a model population selected or defined in step (i) that is defined by HLA class I genotype, of binding to at least three HLA class I molecules of the individual subjects and a T cell epitope capable, in at least 10 percentage of the subjects of a model population selected or defined in step (i) that is defined by HLA class II genotype, of binding to at least three HLA class II molecules of the individual subjects;and
  - (iii) designing or preparing a polypeptide, or a polynucleic acid that encodes a polypeptide that comprises one or more polypeptide fragments identified in step (ii), optionally wherein the polypeptide fragment is flanked at the N and/or C terminus by additional amino acids that are not part of the sequence of the target polypeptide antigen.

6. The method of claim 5, wherein the polypeptide fragment selected in step (ii) is an HLA class I-binding epitope, and the method further comprises selecting a longer fragment of the target polypeptide antigen, which longer fragment comprises or consists of an amino acid sequence that

- A. comprises the fragment selected in step (ii); and
- B. is an HLA class II molecule-binding T cell epitope capable, in at least 10 percent of the subjects of a model population selected or defined in step (i) that is defined by HLA class II genotype, of binding to at least three, or the most possible HLA class II molecules of the individual subjects;

and wherein the fragment identified in step (ii) comprises or consists of said longer fragment.

7. The method of claim 5 or claim 6, comprising identifying one or more further fragments of the same or one or more different target polypeptide antigens, wherein each polypeptide fragment is a T cell epitope capable of binding to at least three HLA class I molecules or at least three HLA class II molecules of at least one subject in the model population; and ranking the fragments by

- (i) the percentage of subjects in the model population that express at least three HLA class I molecules capable of binding to the fragment;
- (ii) the percentage of subjects in the model population that are predicted to express both the target polypeptide antigen comprising the fragment and at least three HLA class I molecules capable of binding to the fragment;
- (iii) the percentage of subjects in the model population that express at least three HLA class II molecules capable of binding to the fragment;
- (iv) the percentage of subjects in the model population that are predicted to express both the target polypeptide antigen comprising the fragment and at least three HLA class II molecules capable of binding to the fragment;
- (v) the percentage of subjects in the model population that express at least three HLA class I molecules and at least three HLA class II molecules capable of binding to the fragment; or
- (iv) the percentage of subjects in the model population that are predicted to express both the target polypeptide antigen comprising the fragment and at least three HLA class I molecules and at least three HLA class II molecules capable of binding to the

fragment.

8. The method of any one of claims 5 to 7, wherein the method comprises selecting one or more of the polypeptide fragments based on their ranking, and designing or preparing the polypeptide to comprise or the polynucleic acid to encode the one of more selected polypeptide fragments.

9. The method of any one of claims 5 to 8, further comprises designing or preparing a polypeptide, a panel of polypeptides, or a pharmaceutical composition or kit comprising one or more polypeptides as active ingredients for use in a method of inducing an immune response in a subject of the specific or target human population, wherein the polypeptide(s) or active ingredient polypeptides comprises at least two polypeptide fragments, optionally between 2 and 15 polypeptide fragments, selected according to the method of any one of claims 5 to 8.

10. The method of claim 9, wherein the two or more or each of the fragments are from different target polypeptide antigens, optionally different target polypeptide antigens selected from the antigens listed in Tables 2 to 6 and/or different cancer associated antigens, optionally wherein one or more or each of the cancer associated antigens are cancer testis antigens (CTAs).

11. The method of claim 9 or claim 10, wherein two or more or each of the fragments are arranged in the polypeptide end to end.

12. The method of claim 11, wherein the method further comprises screening all of the neoepitopes formed at the join between any two of the selected polypeptide fragments arranged end to end in a single polypeptide to eliminate peptides comprising a neoepitope amino acid sequence that

- (i) corresponds to a fragment of a human polypeptide expressed in healthy cells;
- (ii) is a T cell epitope capable of binding, in more than a threshold percentage of human subjects, to at least two HLA class I molecules expressed by individual subjects; or
- (iii) meets both requirements (i) and (ii).

13. The method of any of claims 5 to 12, wherein the one or more polypeptides have been screened to eliminate polypeptides comprising an amino acid sequence that
- (i) corresponds to a fragment of a human polypeptide expressed in healthy cells; or
  - (ii) corresponds to a fragment of a human polypeptide expressed in healthy cells and is a T cell epitope capable of binding to at least two HLA class I molecules of the subject.