Accordingly, there is an immediate need for a vaccine that is effective in a high proportion of the global human population, robust to viral antigen mutation, and could proceed rapidly through the necessary steps for clinical validation and manufacture.

Summary

The inventors have focused efforts on the development of a global peptide vaccine against SARS-CoV-2 that addresses the dual challenges of heterogeneity in the immune responses of different individuals and potential heterogeneity in the infecting virus. The peptide design concept detailed here merges shared personal epitope design with the further selection of B cell epitope sequences resulting in overlapping, multi-HLA binding epitopes within an individual aiming to induce CD4+, CD8+ and antibody-producing B-cell responses. Accordingly, the inventors have identified 30mer polypeptide fragments of the conserved regions of the presently known SARS-CoV-2 viral antigens that comprise (i) maximum CD8+ personal epitopes (PEPIs) in a model population of human subjects having HLA genotypes that are representative of the global population; (ii) maximum CD4+ personal epitopes (PEPIs) in the global population; and (iii) linear B cell epitopes. Peptide vaccines comprising the polypeptides identified by the inventors are predicted to induce cytotoxic T cell, helper T cell and B cell responses in a surprisingly high proportion of subjects in the human population. Even higher response rates in the human population, and continued efficacy against an evolving heterologous infecting virus, can be achieved by combining more than one of the antigen fragments identified by the inventors, preferably by combining antigen fragments identified by the inventors from different SARS-CoV-2 structural proteins.

Accordingly, in a first aspect, the disclosure provides a panel of two or more polypeptides of up to 50 amino acids in length, wherein each polypeptide comprises a different amino acid sequence selected from SEQ ID NOs: 1 to 17.

In a second aspect, the disclosure provides a pharmaceutical composition or kit having the panel of polypeptides according to the disclosure as active ingredients.

In a third aspect, the disclosure provides a use of the panel of polypeptides of the disclosure or the pharmaceutical composition of the disclosure, in the manufacture of a medicament for providing immunotherapy or inducing immune responses in a subject.

Accordingly, in a first example the disclosure provides a polypeptide or a panel of polypeptides of up to 50 amino acids in length, or up to 60 amino acids in length, wherein the polypeptide comprises or consists of an amino acid sequence selected from SEQ ID NOs: 1 to 17.

In a further example, the disclosure provides a panel of polypeptides of up to 50 amino acids in length, or up to 60 amino acids in length, wherein each polypeptide comprises or consists of a different amino acid sequence selected from SEQ ID NOs: 1 to 17.

One or more of the polypeptides may consist of a fragment of a Coronaviridae, Beta-coronaviridae or SARS-CoV-2 protein. Each of the polypeptides may comprise an amino acid sequence selected from SEQ ID NOs: 1 to 17 that is a fragment of a different Coronaviridae, Beta-coronaviridae or SARS-CoV-2 protein. The panel of polypeptides may include at least one sequence from at least two, three or all four of the following groups: (a) SEQ ID NOs: 1 to 11 (fragments of SARS-CoV-2 surface protein); (b) SEQ ID NOs: 12 to 15 (fragments of SARS-CoV-2 nucleocapsid protein); (c) SEQ ID NO: 16 (fragment of SARS-CoV-2 membrane protein); and (d) SEQ ID NO: 17 (fragment of SARS-CoV-2 envelope protein). In some cases, the panel of peptides may comprise at least 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17 different polypeptides, each comprising a different amino acid sequence selected from SEQ ID NOs: 1 to 17. In one example, the panel comprises the amino acid sequences of SEQ ID NOs: 2, 5, 7, 9, 12, 13, 14, 15, 16, and 17. In one example, the panel comprises the amino acid sequences of SEQ ID NOs: 2, 5, 9, 12, 13, 14, 15, 16, and 17. In one example, the panel comprises the amino acid sequences of SEQ ID NOs: 6, and 9 to 17. In one example, the panel of polypeptides comprises ten polypeptides, wherein each of the ten polypeptide comprises or consists of a different amino acid sequence selected from SEQ ID NOs: 2, 5, 7, 9, 12, 13, 14, 15, 16, and 17. In another example, the panel of polypeptides comprises nine polypeptides, wherein each of the nine polypeptide comprises or consists of a different amino acid sequence selected from SEQ ID NOs: 2, 5, 9, 12, 13, 14, 15, 16, and 17. In another example, the panel of polypeptides comprises ten polypeptides wherein each of the ten polypeptide comprises or consists of a different amino acid sequence selected from SEQ ID NOs: 6, and 9 to 17.

In a further example, the present disclosure provides a pharmaceutical composition or kit having the polypeptide or panel of polypeptides described above as active ingredient(s). In some cases, the pharmaceutical composition or kit may comprise ribonucleic acid that encodes each of the polypeptide(s).

In a further example, the present disclosure provides a method of vaccination, providing immunotherapy or inducing immune responses in a subject, the method comprising administering to the subject the polypeptide, panel of polypeptides or pharmaceutical composition described above. In some cases the method is a method of treating a Coronaviridae infection, Beta-coronaviridae infection, SARS-CoV-2 infection, or a SARS-CoV infection, a disease or condition associated with a Coronaviridae or Beta-

coronaviridae infection, COVID-19 or Severe Acute Rspiratory Syndrome (SARS) in the subject. In some cases the method is a method of preventing a Coronaviridae infection, Beta-coronaviridae infection, a SARS-CoV-2 or a SARS-CoV infection, or of preventing the development of a disease or condition associated with a Coronaviridae or Beta-coronaviridae infection, or of COVID-19 or SARS in the subject. In some cases, at least one, or at least two, three, four, five, six or each of the polypeptides comprises a fragment of a Coronaviridae protein, a Beta-coronaviridae protein, a SARS-CoV-2, or a SARS-CoV protein that is a CD8+ T cell epitope predicted to be restricted to at least two, or in some cases three or at least three, HLA class I alleles of the subject. In some cases, at least one, or at least two, three, four, five, six or each of the polypeptides comprises a fragment of a Coronaviridae protein, a Beta-coronaviridae protein, a SARS-CoV-2, or a SARS-CoV protein that is a CD4+ T cell epitope predicted to be restricted to at least two, or in some cases at least three, or in some cases four or at least four, HLA class II alleles of the subject. In some cases, at least one, or at least two, three, four, five, six or each of the polypeptides comprises a linear B cell epitope.

In further examples, the disclosure provides

- a peptide, panel of polypeptides or pharmaceutical composition as described above for use in a method of vaccination, providing immunotherapy or inducing a cytotoxic T cell response in a subject, or in a method of treating or preventing or a Coronaviridae infection, a Beta-coronaviridae infection, a SARS-CoV-2 infection or a SARS-CoV infection, or treating or preventing the development of a disease or condition associated with a Coronaviridae or Beta-coronaviridae infection, or COVID-19 or SARS in a subject, optionally wherein the subject is as described above; and
- use of a polypeptide, a panel of polypeptides or one or more polynucleotides or cells encoding a polypeptide or panel of polypeptides as described above in the manufacture of a medicament for vaccination, providing immunotherapy or inducing a cytotoxic T cell response in a subject, or in a method of treating or preventing Coronaviridae infection, a Beta-coronaviridae infection, SARS-CoV-2 infection or a SARS-CoV infection, treating or preventing the development of a disease or condition associated with a Coronaviridae or Beta-

coronaviridae infection, or or COVID-19 or SARS in a subject, optionally wherein the subject is as described above.

In some cases, the methods described herein may comprise the step of determining the HLA class I and/or class II genotype of the subject.

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 "the" include plural referents unless the content clearly dictates otherwise. Thus, for example, reference to "a peptide" includes two or more such peptides.

Section headings are used herein for convenience only and are not to be construed as limiting in any way.

Description of the Figures

Fig. 1. Immune responses measured by enriched ELISPOT assay upon vaccination with PolyPEPI1018 vaccine. A) Number of vaccine antigens with immune response plotted by patients. Dark grey solid bars: decreased or no change compared to pre-vaccination, dark grey striped bars: response boosted compared to pre-vaccination (at least twofold increase), light grey striped bars: de novo induced vaccine-specific immune responses. B) PolyPEPI1018 vaccine-specific CD4 T cell responses detected pre-vaccination (black), after one vaccination (dark grey), after two doses (light grey), and after 3 doses (white), C) Time course of the immune response through baseline (pre-vaccination) and week 12 measured after a single vaccination for the eight patients who had data for all three points. Each line represents a single patient (n=8).

CLAIMS

1. A panel of two or more polypeptides of up to 50 amino acids in length, wherein each polypeptide comprises a different amino acid sequence selected from SEQ ID NOs: 1 to 17.

2. The panel of polypeptides of claim 1, wherein each polypeptide consists of a fragment of a Coronaviridae protein.

3. The panel of polypeptides of claim 2, wherein each polypeptide consists of a fragment of a SARS-CoV-2 protein.

4. The panel of polypeptides of any one of claims 1 to 3, wherein each polypeptide comprises an amino acid sequence selected from SEQ ID NOs: 1 to 17 that is a fragment of a different Coronaviridae or SARS-CoV-2 protein.

5. The panel of polypeptides of any one of claims 1 to 4, wherein the panel of polypeptides includes at least one sequence from at least two, three or all four of the following groups:

(a) SEQ ID NOs: 1 to 11;

(b) SEQ ID NOs: 12 to 15;

(c) SEQ ID NO: 16; and

(d) SEQ ID NO: 17.

6. The panel of polypeptides of claim 5, wherein the panel comprises ten polypeptides comprising or consisting of the amino acid sequences of SEQ ID NOs: 2, 5, 7, 9, 12, 13, 14, 15, 16, and 17.

7. The panel of polypeptides of claim 5, wherein the panel comprises nine polypeptides comprising or consisting of the amino acid sequences of SEQ ID NOs: 2, 5, 9, 12, 13, 14, 15, 16, and 17.

8. A pharmaceutical composition or kit having the panel of polypeptides according to claim any one of claims 1 to 7 as active ingredients.

9. The pharmaceutical composition or kit of claim 8, comprising polynucleic acid, ribonucleic acid, or one or more vectors or cells that together encode each of the polypeptides.

10. The pharmaceutical composition or kit of claim 9, comprising one or more polynucleotides or polyribonucleotides comprising at least two sequences selected from SEQ ID NOs: 234 to 251 or 252 to 268.

11. Use of the panel of polypeptides of any one of claims 1 to 7 or the pharmaceutical composition of any one of claims 8 to 10, in the manufacture of a medicament for providing immunotherapy or inducing immune responses in a subject.

12. The use of claim 11, wherein the use comprises treating a Coronaviridae infection or a disease or condition associated with a Coronaviridae infection in the subject.

13. The use of claim 12, wherein the use comprises treating a SARS-CoV-2 infection or COVID-19 disease in the subject.

14. The use of claim 11, wherein the use comprises preventing a Coronaviridae infection or the development of a disease or condition associated with Coronaviridae infection in the subject.

15. The use of claim 14, wherein the use comprises preventing a SARS-CoV-2 infection or development of COVID-19 disease in the subject.

16. The use of any one of claims 11 to 15, wherein one or more of the polypeptides comprises a fragment of a Coronaviridae protein that is a CD8+ T cell epitope predicted to be restricted to at least two HLA class I alleles of the subject.

17. The use of claim 16, wherein one or more of the polypeptides comprises a fragment of a Coronaviridae protein that is a CD4+ T cell epitope predicted to be restricted to at least two HLA class II alleles of the subject.

18. The use of any one of claims 11 to 17, wherein one or more of the polypeptides comprises a linear B cell epitope.