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SUMMARY

The present disclosure is directed to individual peptide immunogen constructs targeting the extracellular membrane proximal domain of membrane-bound IgE (IgE EMPD) for the treatment and/or prevention of IgE mediated allergic diseases. The present disclosure is also directed to compositions containing the peptide immunogen constructs, methods of making and using the peptide immunogen constructs, and antibodies produced by the peptide immunogen constructs.

Thus, in one aspect, the present disclosure refers to an extracellular membrane-proximal domain of membrane-bound IgE (IgE EMPD) peptide immunogen construct represented by the formulae: $(Th)_m-(A)_n$ -(IgE EMPD fragment)-X or (IgE EMPD fragment)- $(A)_n$ -(Th)_m-X or $(Th)_m$ -($A)_n$ -(IgE EMPD fragment)- $(A)_n$ -(Th)_m-X wherein Th is a heterologous T helper epitope; A is a heterologous spacer; (IgE EMPD fragment) is a B cell epitope ~~having about 20 to about 40 amino acid residues from the central intramolecular loop of IgE EMPD~~ selected from the group consisting of SEQ ID Nos 5, 6, 8, and 9; X is an α -COOH or α -CONH₂ of an amino acid; m is from 1 to about 4; and n is from 0 to about 10.

In another aspect, the present disclosure refers to an IgE EMPD peptide immunogen construct comprising: a B cell epitope ~~comprising about 20 to about 40 amino acid residues from the IgE EMPD sequence of SEQ ID NO: 1 or SEQ ID NO: 2~~ selected from the group consisting of SEQ ID Nos: 5, 6, 8, and 9; a T helper epitope comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 59-87; and an optional heterologous spacer selected from the group consisting of an amino acid, Lys-, Gly-, Lys-Lys-Lys-, (α , ϵ -N)Lys, and ϵ -N-Lys-Lys-Lys-Lys (SEQ ID NO: 129), wherein the B cell epitope is covalently linked to the T helper epitope directly or through the optional heterologous spacer.

In yet another aspect, the present disclosure refers to a composition comprising a peptide immunogen construction as disclosed herein.

In yet another aspect, the present disclosure refers to a pharmaceutical composition comprising: a. a peptide immunogen construct as disclosed herein; and b. and a pharmaceutically acceptable delivery vehicle and/or adjuvant.

In yet another aspect, ~~the present disclosure refers to~~ example, there is disclosed an isolated antibody or epitope-binding

fragment thereof that specifically binds to the B cell epitope of the IgE EMPD peptide immunogen construct as disclosed herein.

In yet another ~~aspect, the present disclosure refers to~~example, there is disclosed an isolated antibody or epitope-binding fragment thereof that specifically binds to the B cell epitope of the IgE EMPD peptide immunogen construct as disclosed herein.

In yet another ~~aspect, the present disclosure refers to~~example, there is disclosed a composition comprising the isolated antibody or epitope-binding fragment thereof as disclosed herein.

The disclosed peptide immunogen constructs contain about 20 or more amino acids. The peptide immunogen constructs contain a B cell epitope from the 67 amino acid sequence of the full-length IgE EMPD (SEQ ID NO: 1). The B cell epitope can be linked to a heterologous T helper cell (Th) epitope derived from pathogen proteins through an optional heterologous spacer. The disclosed peptide immunogen constructs stimulate the generation of highly specific antibodies directed against IgE EMPD and can bind to recombinant IgE EMPD-containing protein, IgE EMPD on mIgE bearing B cells, and/or a recombinant, soluble IgE EMPD protein containing the Fc portion of human IgG1 and the IgE EMPD of human membrane-bound IgE (referred to as “ γ 1-em67”). The disclosed peptide immunogen constructs can be used as an allergen-independent, cost-effective, universal immunotherapy for global patients suffering from IgE mediated allergic diseases.

The B cell epitope portion of the peptide immunogen constructs have amino acid sequences from the full-length IgE EMPD sequence (SEQ ID NO: 1). In some examples, the B cell epitope has a sequence containing the internal intra-molecular loop formed by endogenous cysteines (C18-C39), according to numbering of the full-length IgE EMPD sequence (SEQ ID NO: 1). In certain specific examples, the B cell epitope has an amino acid sequence of IgE EMPD-1-39 (SEQ ID NO: 5), IgE EMPD-7-40 (SEQ ID NO: 6), IgE EMPD-19-38 (SEQ ID NO: 8), or IgE EMPD-1-40 (SEQ ID NO: 9).

The peptide immunogen constructs of the present disclosure can contain a heterologous

CLAIMS

1. An extracellular membrane-proximal domain of membrane-bound IgE (IgE EMPD) peptide immunogen construct represented by the formulae:

$(Th)_m-(A)_n-(IgE\ EMPD\ fragment)-X$

or

$(IgE\ EMPD\ fragment)-(A)_n-(Th)_m-X$

or

$(Th)_m-(A)_n-(IgE\ EMPD\ fragment)-(A)_n-(Th)_m-X$

wherein

Th is a heterologous T helper epitope;

A is a heterologous spacer;

(IgE EMPD fragment) is a B cell epitope having about 20 to about 40 amino acid residues from the central intramolecular loop of IgE EMPD selected from the group consisting of SEQ ID NOs: 5, 6, 8, and 9;

X is an α -COOH or α -CONH₂ of an amino acid;

m is from 1 to ~~about~~ 4; and

n is from 0 to ~~about~~ 10.

~~2. The IgE EMPD peptide immunogen construct according to claim 1, wherein the IgE EMPD fragment is selected from the group consisting of SEQ ID NOs: 5, 6, 8, and 9.~~

~~32.~~ The IgE EMPD peptide immunogen construct according to ~~any of claims 1 or 2~~ claim 1, wherein the Th epitope is selected from the group consisting of SEQ ID NOs: 59-87.

~~43.~~ The IgE EMPD peptide immunogen construct according to claim 1, wherein the peptide immunogen construct is selected from the group consisting of SEQ ID NOs: 88-95, 98-124, and 130.

~~54.~~ An IgE EMPD peptide immunogen construct comprising:
a B cell epitope ~~comprising about 20 to about 40 amino acid residues from the IgE EMPD sequence of SEQ ID NO: 1 or SEQ ID NO: 2~~ selected from the group consisting of SEQ ID NOs: 5, 6, 8, and 9;

a T helper epitope comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 59-87; and
an optional heterologous spacer selected from the group consisting of an amino acid, Lys-, Gly-, Lys-Lys-Lys-, (α , ϵ -N)Lys, and ϵ -N-Lys-Lys-Lys-Lys (SEQ ID NO: 129),
wherein the B cell epitope is covalently linked to the T helper epitope directly or through the optional heterologous spacer.

~~6. The IgE EMPD peptide immunogen construct of claim 5, wherein the B cell epitope is selected from the group consisting of SEQ ID NOs: 5, 6, 8, and 9.~~

~~7. The IgE EMPD peptide immunogen construct of claim 5, wherein the T helper epitope is selected from the group consisting of SEQ ID NOs: 59-87.~~

85. The IgE EMPD peptide immunogen construct of claim 54, wherein the optional heterologous spacer is (α , ϵ -N)Lys or ϵ -N-Lys-Lys-Lys-Lys (SEQ ID NO: 129).

96. The IgE EMPD peptide immunogen construct of claim 54, wherein the T helper epitope is covalently linked to the amino terminus of the B cell epitope.

107. The IgE EMPD peptide immunogen construct of claim 54, wherein the T helper epitope is covalently linked to the amino terminus of the B cell epitope through the optional heterologous spacer.

118. A composition comprising a peptide immunogen construction according to any of claims 1 to 107.

129. A pharmaceutical composition comprising:

- a. a peptide immunogen construct according to any of claims 1 to 107; and
- b. and a pharmaceutically acceptable delivery vehicle and/or adjuvant.

1310. The pharmaceutical composition of claim 129, wherein

- a. the IgE EMPD peptide immunogen construct is selected from the group consisting of SEQ ID NOs: 88-95, 98-124, and 130; and

- b. the IgE EMPD peptide immunogen construct is mixed with an CpG oligodeoxynucleotide (ODN) to form a stabilized immunostimulatory complex.

~~14.—An isolated antibody or epitope binding fragment thereof that specifically binds to the B-cell epitope of the IgE EMPD peptide immunogen construct according to any of claims 1 to 10.~~

~~15.—The isolated antibody or epitope binding fragment thereof according to claim 14 bound to the IgE EMPD peptide immunogen construct.~~

~~16.—An isolated antibody or epitope binding fragment thereof that specifically binds to the B-cell epitope of the IgE EMPD peptide immunogen construct according to any of claims 1 to 10.~~

~~17.—A composition comprising the isolated antibody or epitope binding fragment thereof according to any of claims 14 to 16.~~