SUMMARY OF THE INVENTION

[0013] The present disclosure relates to novel peptide epitopes derived from the CH3 domain of IgE. These peptide epitopes are recognized by high affinity antibodies that specifically bind IgE. These novel peptides may be used for both the active immunization of a mammal by administering these peptides to generate high affinity antibodies in the mammal. The peptide epitopes may also be used in generating high affinity anti-IgE antibodies in a non-human host that specifically bind to these regions of IgE and use the resulting antibodies for the passive immunization of a of a mammal.

[0014] One immunogen (epitope A, Fig. 11) described herein comprises the amino acid sequence:

Asn Pro Arg Gly Val Ser Xaa Tyr Xaa Xaa Arg Xaa (SEQ ID NO. 72).

One example of epitope A is:

Asn Pro Arg Gly Val Ser Ala Tyr Leu Ser Arg Pro (SEQ ID NO. 73)

Another immunogen (epitope B, Fig. 11) comprises the amino acid sequence:

Leu Pro Arg Ala Leu Xaa Arg Ser Xaa (SEQ ID NO. 74).

Examples of Epitope B include:

Leu Pro Arg Ala Leu Met Arg Ser Thr (SEQ ID NO. 75)

His Pro His Leu Pro Arg Ala Leu Met Arg Ser Thr (SEQ ID NO 76)

Leu Pro Arg Ala Leu Met Arg Ser Thr Thr Lys Thr (SEQ ID NO 77).

In either SEQ ID NO: 72 or SEQ ID NO: 74, Xaa may be any amino acid.

[0015] These peptides may be included in a composition comprising at least one of the peptides and a physiologically acceptable carrier, diluent, stabilizer or excipient, as well as an immunogenic carrier. The immunogenic carrier may be, e.g., BSA, KLH, tetanus toxoid, and diphtheria toxoid. The present disclosure also relates to polynucleotides encoding SEQ ID NOS. 72-77, vectors comprising said polynucleotides, and cells harboring said vectors.

[0016] The present disclosure also relates to antibodies that specifically bind to epitope A and/or epitope B. The present disclosure is also directed to a method of making antibodies that specifically bind to epitope A and/or epitope B.

[0017] The present disclosure relates to the administration of peptides comprising SEQ ID NO: 72 and/or SEQ ID NO 74 to a subject suffering from an IgE-mediated disease or condition.

[0018] The present disclosure relates to the administration of high affinity antibodies generated using peptides comprising SEQ ID NO: 72 and/or SEQ ID NO 74 to a mammal suffering from an IgE-mediated disease or condition. The high affinity antibody may be human, humanized, or chimeric. The antibody may be polyclonal or monoclonal. Such IgE mediated diseases or conditions include, e.g., asthma, atopic dermatitis, urticaria, allergic rhinitis and eczema. In one aspect, the present invention refers to an isolated antibody or an antigen binding fragment thereof comprising a variable light chain region comprising CDRL1, CDRL2, and CDRL3 and a variable heavy chain region comprising CDRH1, CDRH2, and CDRH3, wherein CDRL1 consists of SEQ ID NO:5, CDRL2 consists of SEQ ID NO:8, CDRL3 consists of the amino acid sequence consisting of QQSWSWPTT, CDRH1 consists of SEQ ID NO:16, CDRH2 consists of SEQ ID NO:20, and CDRH3 consists of SEQ ID NO:26. In another aspect, the present invention refers to an isolated antibody or an antigen binding fragment thereof comprising a variable light chain region comprising CDRL1, CDRL2, and CDRL3 and a variable heavy chain region comprising CDRH1, CDRH2, and CDRH3, wherein CDRL1 consists of SEQ ID NO:5, CDRL2 consists of SEQ ID NO:8, CDRL3 consists of QQSWSWPTT, CDRH1 consists of SEQ ID NO:15, CDRH2 consists of SEQ ID NO:25, and CDRH3 consists of SEQ ID NO:26. In still another aspect the present invention refers to an isolated antibody or an antigen binding fragment thereof comprising a variable light chain region comprising CDRL1, CDRL2, and CDRL3 and a variable heavy chain region comprising CDRH1, CDRH2, and CDRH3, wherein CDRL1 consists of SEQ ID NO:5, CDRL2 consists of SEQ ID NO:8, CDRL3 consists of QQSWSWPTT, CDRH1 consists of SEQ ID NO:16, CDRH2 consists of SEQ ID NO:24, and CDRH3 consists of SEQ ID NO:26. In another aspect the present invention refers to a composition comprising a therapeutically effective amount of the antibody of the present invention and a pharmaceutically acceptable carrier. In still another aspect, the present invention refers to a diagnostic kit comprising the antibody of the present invention. In one other aspect the present invention refers to the use of an antibody of the present invention in the manufacture of a medicament for treating of an IgE-mediated disorder, wherein the IgE-mediated disorder is selected from the group consisting of asthma, allergic rhinitis, eczema, urticaria, atopic dermatitis, and a food allergy. In one other aspect, the present invention refers to an isolated nucleic acid

encoding the antibody of the present invention. In one other aspect, the present invention refers to a vector comprising the isolated nucleic acid of the present invention. In another aspect, the present invention refers to an isolated host cell comprising the vector of the present invention. In one other aspect, the present invention refers to a method for producing the antibody of the present invention, comprising culturing the cell of the present invention under conditions appropriate for the production of said antibody, and isolating the antibody produced.

BRIEF DESCRIPTION OF THE FIGURES

[0019] Figure 1 is a schematic representation of the phage vector used in antibody cloning and screening.

[0020] Figure 2 is a schematic representation of oligonucleotides useful in generating antibody variants.

[0021] Figure 3A depicts the comparison of the light chains of the murine anti-IgE antibody TES-C21 and the combined human template of L16 and JK4.

[0022] Figure 3B depicts the comparison of the heavy chains of TES-C21 and the combined human template DP88 and JH4b.

[0023] Figure 4 presents a table of the framework residue variants having high affinity as compared to the parent TES-C21.

[0024] Figure 5A and B depict the ELISA titration curves for clones 4, 49, 72, 78, and 136, as compared to the parent Fab of TES-C21 and negative control (5D12).

[0025] Figure 6 depicts an inhibition assay of clones 2C, 5A, and 5I, as compared to the parent TES-C21 and a negative control antibody.

[0026] Figure 7A depicts the sequences of clones having a combination of beneficial mutations which resulted in even greater affinity for IgE.

[0027] Figure 8A & 8B depict the framework sequences of the entire light chain variable region for clones 136, 1, 2, 4, 8, 13, 15, 21, 30, 31, 35, 43, 44, 53, 81, 90, and 113.

[0028] Figure 9A & 9B depict the framework sequences of the entire heavy chain variable region for 35 clones.

[0029] Figures 10 A-F depict the complete heavy and light chain sequences for clones 136, 2C, 5I, 5A, 2B, and 1136-2C.

[0030] Figure11 depicts the CH3 region amino acid sequence of human IgE and highlights Epitope "A" and Epitope "B".

[0031] Figure 12 depicts the overlapping peptides used to identify Epitope B.