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Topic 3: Allergen databases/Class of proteins/Allergen function

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1: J Allergy Clin Immunol 2000 Aug;106(2):228-38Related Articles, Books, LinkOut

Structural biology of allergens.

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One of the major challenges of molecular allergy is to predict the allergenic potential of a protein, particularly in novel foods. Two aspects have to be distinguished: immunogenicity and cross-reactivity. Immunogenicity reflects the potential of a protein to induce IgE antibodies, whereas cross-reactivity is the reactivity of (usually preexisting) IgE antibodies with the target protein. In addition to these two issues, the relation between IgE-binding potential and clinical symptoms is of interest. This is influenced by physical properties (eg, stability and size) and immunologic properties (affinity and epitope valence). Discussions on immunogenicity and cross-reactivity of allergens rely on the establishment of structural similarities and differences among allergens and between allergens and nonallergens. For comparisons between the 3-dimensional protein folds, the representation as 2-dimensional proximity plots provides a convenient visual aid.

Analysis of approximately 40 allergenic proteins (or parts of these proteins), of which the protein folds are either known or can be predicted on the basis of homology, indicates that most of these can be classified into 4 structural families:

(1) antiparallel beta-strands: the immunoglobulin-fold family (grass group 2, mite group 2), serine proteases (mite group 3, 6, and 9), and soybean-type trypsin inhibitor (Ole e 1, grass group 11);

(2) antiparallel beta-sheets intimately associated with one or more alpha-helices: tree group 1, lipocalin, profilin, aspartate protease (cockroach group 2);

(3) (alpha+beta) structures, in which the alpha- and beta-structural elements are not intimately associated: mite group 1, lysozyme/lactalbumin, vespid group ; and

(4) alpha-helical: nonspecific lipid transfer protein, seed 2S protein, insect hemoglobin, fish parvalbumin, pollen calmodulin, mellitin from bee venom, Fel d 1 chain 1, serum albumin.

Allergens with parallel beta-strands (in combination with an alpha-helix linking the two strands, a motif commonly found in, for example, nucleotide-binding proteins) seem to be underrepresented. The conclusion is that allergens have no characteristic structural features other than that they need to be able to reach (and stimulate) immune cells and mast cells. Within this constraint, any antigen may be allergenic, particularly if it avoids activation of T(H)2-suppressive mechanisms (CD8 cells and T(H)1 cells).