

Foreword



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Allergens are, by definition, antigens that cause allergies. This definition points to an important difference between an antigen and an allergen, and we have yet to fully understand this difference. An understanding of this difference is important for several reasons. It is likely to provide a clue to the fact that allergens preferentially induce a Th2 immune response. The antigenic structure/sequence alone does not explain this bias for the Th2 response. It is likely that a pattern (eg, an allergen-associated molecular pattern) recognition mechanism is involved. Pattern recognition is the domain of the innate immune system and is mediated via toll-like receptors and non-TLR mechanisms. It is important to note that only a small fraction of the population is affected by allergies. Therefore, the host genetic background must be critically important. This issue of the *Immunology and Allergy Clinics of North America* addresses a few aspects of this important matter.

The study of allergen structure through the bioinformatic approach could not only facilitate the classification but also predict their function and immune response. Calcium-binding proteins are an example of this approach. They represent a structural pattern that is common to many allergens. The first two articles in this issue deal with these important structural aspects. For many years we have known that proteases play an important role in the allergenicity of dust mites and fungal antigens. Pollen-associated NADPH oxidase has now been identified as another component of allergens that is important for a robust allergic response. Interference with the NADPH oxidase prevents the development of allergy in the animal model.

Allergen-associated lipids could constitute a molecular pattern for a biased immune response. The recognition of pollen-derived lipids by the non-polymorphic CD1 transmembrane protein is an exciting development, the relevance of which is discussed in the fifth article in this issue.

The second half of the issue is dedicated to novel interventions employing modified allergens. One approach is to eliminate the IgE-binding component and create linear fusion proteins of T cell epitopes. This genetically modified allergen vaccine is less likely to have serious side effects when compared with immunotherapy with conventional allergens. Another approach exploits mucosal tolerance to orally fed rice or killed bacteria that express recombinant allergens or their T cell epitopes. This “Trojan horse” approach has shown promise in the model of mountain cedar allergy and peanut allergy. A third approach takes advantage of the inhibitory signaling mechanism of FcR γ II. The investigators have generated a fusion protein of the cat allergen and IgG—which, when it binds to mast cell-associated IgE, delivers an inhibitory signal through the IgG receptor. As a result, mast cell activation is blocked, and the allergic reaction is aborted. These clever approaches await clinical trials for their efficacy; nonetheless, they bring cutting edge molecular biology techniques to the bedside.

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